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**Rethinking Dementia:
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18th International Congress of the Asian Society Against Dementia

In conjunction with

**32nd Malaysian Society of Neurosciences Annual
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6th Malaysia Stroke Conference (MSC 2024),
12th Malaysian Paediatric Neurology Update Meeting
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OP-ASAD-02	The Protective Effect Of Vitamin B12 On Neuropsychiatric Symptoms In Asian Dementia-Free Older Adults	Yingqi Liao Zhang H, Zhang Y, Cheuk NK, Chen C, Xu X
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OP-ASAD-05	Automatic Brain Segmentation With AQUA: A Comparative Validation Study In The Southeast Asian BIOCIS Cohort	Ashwati Vipin Mohamed Salim RS, EY Kim R, Lee M, Kim HW, Rieu ZH, Kandiah N
OP-ASAD-06	Diagnostic Efficacy Of Visual Cognitive Assessment Test In Cerebral Small Vessel Disease And Neuroimaging Validation	Dang Chao Yu L, Guo J, Liu M, Kandiah N, Fan Y
OP-ASAD-07	Neuroprotective Effects Of <i>Ficus Deltoidea</i> On Spatial Memory And Learning In The Alzheimer's Disease-Like Rat Model Using Behavioral And Histological Methods	Michael Ayuba Abdul Hamid H, Mohd Moklas MA, Modu BA, Isa UB, Mehat MZ

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PP-ASAD-01	The Association Between Left Ventricular Geometric Patterns, Cortical Cerebral Microinfarcts, And Cognition	Jiannan Huang Robert C, Ling LH, Chen C, Hilal S
PP-ASAD-02	The Association Between Left Ventricular Dysfunction, Cerebral Small Vessel Disease, And Cognitive Impairment	Jiannan Huang Robert C, Ling LH, Chen C, Hilal S
PP-ASAD-03	Cognitive Impairment Among Elderly Patients With Chronic Illness Attending Primary Care And Its Association With Cardiovascular Risk Using The Framingham Risk Score	Nimelesh Balanthiren Ali MF, Abdul Aziz AF
PP-ASAD-04	Cognitive Card Intervention Program: A Preliminary Study On Cognitive Function, Emotional Performance, And Quality Of Life	Lin Dai Wei Cheng YH, Chuang YC, Lin YR, Huang CN, Hsiao YY , Huang HL, Fuh JL
PP-ASAD-05	Challenges And Experiences In Recruitment For A Multidomain Lifestyle Intervention Study To Prevent Cognitive Decline: Comparison Of Recruitment Strategies In A Single Recruiting Site For The SINGapore GERiatric Intervention Study To Reduce Cognitive Decline And Physical Frailty (SINGER) Study.	Kwong Hsia Yap Toh A, Chen C
PP-ASAD-06	Predictors And Reasons For Non-Thrombolysis In Acute Ischemic Stroke In Seberang Jaya Hospital	Nur Nazurah Abdul Hamid
PP-ASAD-07	Interplay Of Cerebral Blood Flow, Brain Volume, And Cognitive Function In Dementia Pathologies	Tetsuro Sekine Happo S, Kumita S
PP-ASAD-08	Exploring Dementia Awareness In Community Initiatives: A Knowledge Assessment Study	Ong Wan Feng Ho YB, Tay HW, Janardanan N, Mohamad Zahir MZ, Kok SH, Suppamutharwyam M, Embong J, Razali RM
PP-ASAD-09	Plasma P-Tau181 Is Associated With Executive Dysfunction In An A β -Negative Southeast Asian Population - Biomarkers And Cognition Study, Singapore (BIOCIS)	Timothy Aw Bang Hao Leow YJ, Sandhu GK, Vipin A, Tanoto P, Zailan FZ, Lee FPHE, Ghildiyal S, Liew SY, Kandiah N



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PP-ASAD-11	Development And Validation Of The ReCOGnAIze App For Detection Of Vascular Mild Cognitive Impairment Using Digital Gamified Assessments	Adnan Azam Mohammed Tan F, Vipin A, Tanoto P, Sandhu GK, Leow YJ, Zailan FZ, Lee FPHE, Ghildiyal S, Liew SY, Kandiah N
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PD-ASAD-09	Understanding Dementia Through An Ethnographic Exploration Of Local Perspectives And Experiences In Kuantan, Malaysia	Matthew Robert Kuiper Ibrahim R, Singh S, Ibrahim AF
PD-ASAD-10	Current Practices In The Diagnosis And Management Of Mild Cognitive Impairment Due To Alzheimer's Disease: Findings From The Asia Prime Project	Amitabh Dash Choi SH, Kim SY, Chen C, Senanarong V, Jiang G
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PD-ASAD-14	Clinical Characteristics Of Behavioral And Psychological Symptoms In Patients With Drug-Naïve Alzheimer's Disease	Young Soon Yang Kwak YT
PD-ASAD-15	Service Evaluation Of Caregivers' For Persons With Dementia Support Group At Pantai Jerudong Specialist Centre, Brunei Darussalam.	Yvonne Lee Keen Lyn Awang Mohamed Ali DNH, Sheikh Haji Said SHMAA
PD-ASAD-16	Dementia Care In Malaysia: The Informal Care Partners' Narrative	Tay Chia Yi Jones CH
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PD-ASAD-18	Interaction Between Thyroid Function, APOE E4, And Cognitive Function In Cognitively Normal Elders	Seok Woo Moon Kim B
PD-ASAD-19	Comparing Efficacy Of Plasma Phosphorylated Tau 181 And 217 On Predicting Amyloid Pet Positivity	Seong Ho Koh Choi SH, Kwon HS
PD-ASAD-20	Biological Potential Of Atractylodin For Their Effects On Inflammation-Related Neurodegenerative Diseases With Their Underlying Molecular Mechanisms	Dinesh Kumar Patel
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PD-ASAD-27	Exploring The Psychosocial Factors Associated With Good Quality Of Life Among Family Caregivers Of Dementia Patients In Malaysia	Chong Zi En Mohamed NF, Yusoff N
PD-ASAD-28	Prospective Changes In Anticholinergic Cognitive Burden Is Associated With Changes In Physical Performance In MELoR Study	Xu Xiang Jiang Myint PK, Sami S, Ramasamy K, Lim SM, Abdul Majeed AB, Lee SWH, Mat S, Ajit Singh DK, Tan MP
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PD-ASAD-31	Characteristics Of Patients Attending Memory Clinic At A Teaching Hospital In East Coast Malaysia	Mohd Zulkifli Mohamad Zahir Baharudin MA

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PD-ASAD-33	Clarity AD: Asia Region Analysis Of A Phase III Trial Of Lecanemab In Early Alzheimer's Disease	Christopher Chen Iwatsubo T, Dash A, Ogawa T, Dhadha S, Hersch S, Irizarry M, Lee JH, Lee JY
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PD-ASAD-36	Randomized Controlled Trial Of The Effect Of Integrated Care For Dementia (ICD) In Persons With Dementia (PWDS) And Their Caregivers	Suhaila Mohamad Zahir Rezali MS, Haidhir H, Nuruddin A, Harun N, Chen FJ, Muthusamy G, Chong Qianzhen J, Kassim MSA
PD-ASAD-38	Evaluation Of The Blood-Brain Barrier Function And Neuroinflammatory Response In The Conditions Of Prolonged Exposure To <i>Mitragyna Speciosa</i> (Ketum) Alkaloids And Decoction In Rats	Siti Nurhafamasmirza Maisarah Hamid Yusof SR
PD-ASAD-39	The Triglyceride-Glucose Index And Altered Mental Status Are Associated With Early Neurological Deteriorations In Acute Ischemic Stroke Patients	Khoironi Rachmad Damarjati Ar Rochmah M, Asmedi A, Malueka RG
PD-ASAD-40	Plasma P-Tau181 And Other Blood-Based Biomarkers Can Be Used To Predict Amyloid Pet Positivity	Seong Ho Koh Yu HJ, Kwon HS, Choi SH, Lee JH

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PD-ASAD-42	Preliminary Study Of Validity And Reliability Of The Frontal Assessment Battery In Vascular Cognitive Impairment: A Cross-Sectional Study In Indonesian Tertiary Care Hospital	Diba Anindhita Nandawardhani Vidyanti AN, Prodjohardjono A, Setyaningrum CTS
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PD-ASAD-48	Mitragynine (KRATOM)-Withdrawal Behaviour And Cognitive Impairments Can Be Ameliorated By An Epigenetic Mechanism	Suleiman Yunusa Müller CP, Hassan Z
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PD-ASAD-53	Hemolytic Uremic Syndrome: Atypical Yet Typical	Tilaga Elancheran Teng LY
PD-ASAD-54	Anosognosia Of Apathy In Three Major Neurodegenerative Dementia: A Cross-Sectional Study	Hideki Kanemoto Suehiro T, Taomoto D, Satake Y, Yoshiyama K, Ikeda M
PD-ASAD-55	The Impact Of Social Isolation And Loneliness On Psychiatric Symptoms In Patients With Mild Cognitive Impairment	Kayo Takeda Kanemoto H, Suehiro T, Ikeda M
PD-ASAD-56	Prevalence Of Cognitive Impairment And The Effect Of Continuous Positive Airway Pressure (CPAP) Towards Cognition Among Patients With Obstructive Sleep Apnoea (OSA)	Muhammad Farid Mohd Fauad Bhaskar S, Ismail AI, Ahmad Tarmizi NA
PD-ASAD-57	ATN Classification And Clinical Progression Of The Amyloid-Negative Group In Alzheimer's Disease Neuroimaging Initiative Participants	Byeong Chae Kim Cho SH, Kim S, Choi SM
PD-ASAD-58	Subcutaneous Injection Of D-Galactose At 500 mg/kg Induces Dementia-Like Conditions In An 8-Weeks Old Swiss Albino Mice Model	Wan Mohd Norsyam Wan Norman Mohammad Naser AN, Shaharudin S, Azmi A, Zulkurnain M, Wong YF, Patar A

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PD-ASAD-59	Predisposing And Precipitating Factors For Delirium Among Older Hospitalized Adults: A Prospective Cross-Sectional Study	Tan Shin Wuei Keng JN, Khoo SI, Albart SA
PD-ASAD-60	Unveiling Neurodegenerative Disorders Through Cognitive Deficits: A Case Series Of Huntington's Disease	Michelle Maryanne Tan Tan JK, Hung SKY, Lau YH
PD-ASAD-61	Characterizing Early Vs Late Onset Vascular Cognitive Impairment Features In Indonesian Population: A Cross-Sectional Study	Asnelia Devicaesaria Adhitama N, Wedariani MA, Puspa R, Lumempouw S, Mutiara Putri AN
PD-ASAD-62	The Lack Of Awareness Of Depressive Symptoms And The Neuroanatomical Differences Between Depression With And Without Awareness Among Early-Onset Alzheimer's Disease.	Takashi Suehiro Kanemoto H, Suzuki M, Satake Y, Taomoto D, Takeda K, Katakami S, Yoshiyama K, Ikeda M
PD-ASAD-63	The Association Between APOE Genotypes, Gut Microbiota, And Cognitive Frailty Among The Ageless Cohort	Vilassiny Gunaselvan Annuar AA, Ramasamy K, Tan MP
PD-ASAD-64	Investigating Structural Neuroimaging Variances Using Voxel-Based Morphometry (VBM) Between Behaviorally Impaired And Non-Impaired Individuals - Biomarkers And Cognition Study, Singapore	Rasyiqah Shaik Mohamed Salim Leow YJ, Vipin A, Kandiah N
PD-ASAD-65	A Case Of Probable Dementia With Lewy Bodies Preceded By Functional Neurological Disorder	Firdaus Abdul Hamid Ibrahim KA, Azizan MNK
PD-ASAD-66	Egb761 In Amnestic Type Of Mild Cognitive Impairment And Mild Dementia: Experience From Singe Center In Thailand	Pongsatorn Paholpak Aphisitphinyo S, Rangseekajee P, Paholpak P
PD-ASAD-67	Demographic, Clinical, And Neuropsychological Profiles Of Urine Amyloid Test Kit Positivity	Liew Shan Yao Leow YJ, Vipin A, Sandhu GK, Tanoto P, Mohammed AA, Zailan FZ, Lee FPHE, Ghildiyal S, Chong WFW, Tan F, Jacklyn L, Mohamed Salim RS, Qiu B, Bhalla G, Chen JXY, Gu BJ, Kandiah N

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PD-ASAD-69	Retinal Nerve Fiber Thickness And Blood Flow As Biomarkers For Early Detection Of Cognitive Impairment In A Multi-Ethnic Asian Cohort: Preliminary Insights From BIOCIS	Bocheng Qiu Gutierrez-Sinisterra L, Leow YJ, Agrawal R, Kandiah N
PD-ASAD-70	Cognitive Profiles Of At Risk Mixed Dementia, Alzheimer's Dementia And Vascular Dementia In The Biomarker And Cognition Study, Singapore (BIOCIS) Cohort.	Abilash Elango Lekshmanan Tanoto P, Leow YJ, Kaur GS, Vipin A, Lee FPHE, Ghildiyal S, Liew SY, Chong WFW, Bhalla G, Zailan FZ, Jacklyn L, Qiu BC, Mohamed Salim RS, Mohammed AA, Kandiah N
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PD-ASAD-72	A Cognitive Stress Test App For Early Detection Of Mild Cognitive Impairment In The Community	Gursimar Bhalla Mohammed AA, Leow YJ, Vipin A, Elango A, Sandhu GK, Tanoto P, Zailan FZ, Lee FPHE, Ghildiyal S, Liew SY, Chong WFW, Jacklyn L, Mohamed Salim RS, Qiu B, Chen JXY, Kandiah N, Hasyim Tan FT
PD-ASAD-73	Assessing Serum mBDNF and Pro-BDNF Levels in Mild Cognitive Impairment and Early Dementia: A Systematic Review	Saneed Khaliq Ling KH, Cheah PS
PD-ASAD-74	Utility Of Plasma P-tau181 / Aβ42 And A Brief Cognitive Test As A Screening Tool For Elevated Brain Amyloid	Mitchell Lai Chong JR, Hilal S, Tan BY, Venketasubramanian N, Chen CP

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PD-ASAD-76	Characteristics Of Cognitive Function And Sleep Quality In Post Covid Healthcare Worker At Zainoel Abidin Regional Hospital In Banda Aceh	Cut Risya Firlana Marlia I, Suherman
PD-ASAD-77	Delayed Development In Language And Isolated Seizure In Young Child Due To Schizencephaly - A Rare Case	Maulida Hastuti S
PD-ASAD-79	<i>Centella Asiatica L.</i> Extract Attenuates Chronic Stress Induced Changes In Hippocampus And Catalase Levels In Brain Of Male Wistar Rats	Saravanan Jagadeesan Vishnumukkala T, Sreenivasulu S, Gopalakrishna PK, Chiroma SM, Mohamad Moklas MA
PD-ASAD-80	Blood Biomarkers And Neuropsychiatric Symptoms, Pathways To Early Detection Of Cognitive Impairment In A Southeast Asian Population - Biomarkers And Cognition Study, Singapore (BIOCIS)	Leow Yi Jin Sandhu GK, Vipin A, Tanoto P, Mohammed AA, Zailan FZ, Lee FPHE, Ghildiyal S, Liew SY, Elango A, Bhalla G, Tan F, Qiu B, Leonardo J, Mohamed Salim RS, Kandiah N
PD-ASAD-81	Ischemic Stroke Patients Undergoing DSA: A Clinical Profile	Nurhasanah Musadir N
PD-ASAD-82	<i>Centella Asiatica</i> Attenuates Aluminium Chloride And D-Galactose Induced Alzheimer's Disease Via TNF- α Inhibition By Microglia In The Hippocampus Of Male Albino Wistar Rats	Vishnumukkala Thirupathirao Jagadeesan S, Gopalakrishna PK, Baharuldin MTH, Sreenivasulu S, Mohd Nor NH, Mohamad Moklas MA

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PD-ASAD-84	The Role Of Methiopropamine In Regulating Spatial Cognition In Mice	Mohd Khairulanwar Bunaim Azmi N
PD-ASAD-85	Case Report: Hypoactive Delirium In Refractory Chronic Hyponatremia And Late-Stage Alzheimer's Disease With BPSD Elderly Patient	Haniyyah Wahyudi ER
PD-ASAD-86	Predictors Of Cognitive Impairment Following Intracerebral Haemorrhage: An Observational Study	Juen Kiem Tan Shamsul Murfiz NQA, Tan MM, Wan Zaidi WA, Wan Yahya WNN, Chamhuri NS, Rajah R, Zolkafli N, Sahibulddin SZ, Tan HJ, Law ZK
PD-ASAD-87	Associations Between Potential Risk Factors And Blood-Brain Barrier Water Permeability In Middle-Aged And Older Adults	Mervin Tee Padrelab BE, Dupeyronb M, Huang J, Low M, Konstandin S, Eickel K, Günther M, Minta K, Schinazi VR, Colombo G, Petr J, Mutsaerts HJMM, Hilal S
PD-ASAD-88	Multi-Domain Lifestyle Behavioural Factors And Cognitive Impairment In An Asian Population	Xiangyuan Huang Samad MH, Koh GCH, van Dam RM, Hilal S
PD-ASAD-89	Association Of Combined Risk Factors With Cognitive Function Among Singaporeans	Xiangyuan Huang Tan WY, Robert C, Hilal S
PD-ASAD-90	<i>Ficus Deltoidea</i> Improves Cognitive Impairment And Prevents Neurodegeneration In Alzheimer's Disease-Liked Rats	Abdulhamid Sani Usman Abdul Hamid H, Chiroma SM, Norazit A, Mohd Moklas MA, Mustapha M, Murthy J, Zainol M, Mehat MZ

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PD-ASAD-91	Case Report: An Elderly Lady With Frequent Falls And Impaired Memory Treated For Normal Pressure Hydrocephalus	Khaveenraj Devarajah
PD-ASAD-92	Case Description Of Frontotemporal Dementia Admitted To Dr. Cipto Mangunkusumo National Central Public Hospital In 2023	Elizabeth Divina Lastr DN, Ramli Y, Ikhromi N, Permata R, Fakhri A, Prawiroharjo P
PD-ASAD-93	Subarachnoid Haemorrhage: Rare Presentation Of Cerebral Venous Sinus Thrombosis That Should Not Be Overlooked	Intan Bazilah Abu Bakar Christina SZM, Hassan R, K. Kutty S
PD-ASAD-94	Effectiveness Of The Interventions Implemented To Increase The Completion Rate Of The Cognitive Function Assessments (CFA) Via A Smartphone App.	Nor Fazlin Zabudin Tan MP, Rosli R, Kumanan SD, Ning WX, Low S, Devine SA, Khemakhem M, Au R
PD-ASAD-95	The Impact Of Glycemic Variability On Cognitive Decline And Alzheimer Disease: A Systematic Review	Paul Nichol G. Gonzales Ampil ER, Catindig-Dela Rosa JAS, Villaraza SG, Corrales-Joson MLP
PD-ASAD-96	MSSA Bacteremia Associated Acute Hemorrhagic Leukoencephalopathy	Dayang Corieza Febriany Zubair AS
PD-ASAD-97	3D Genomic Profiling Of Alzheimer's Disease (AD) Patients For The Development Of Blood-Based Episwitch® Biomarkers.	Lim Chun Ren Ebenezer EG, Danial M, Looi I, Ch'ng SH, Chee KY, The HL, Ng S, Janisha SP, Hunter E, Akoulitchiev A, Ong KY
PD-ASAD-98	Effect Of Chewing Gum On Cognitive Function	So Hee Park Jeong JH, Moon SY, Lim HG, Choi SH, Na HR

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ORAL ID	TITLE	AUTHORS
OP-A-01	Charles Bonnet Syndrome (CBS) Following Treatment Of Nivolumab And Ipilimumab, In The Setting Of Posterior Reversible Encephalopathy Syndrome (PRES): A First Case Report In Malaysia	Wai Keong Ng Ng WH, Supuramaniam C, Abdullah MM, Teoh SL
OP-A-02	Electroconvulsive Therapy In Refractory And Super-Refractory Status Epilepticus In Adults: A Scoping Review	Marjorie Jia Yi Ong Lee VLL, Teo SL, Tan HJ, Trinkia E, Khoo CS
OP-A-03	Insights Into Abnormal Electroencephalogram Patterns In Acute Ischaemic Stroke: An Observational Study	Juen Kiem Tan Khoo CS, Tan MM, Liew KL, Saeed N, Payus AO, Rajah R, Mohd Khaili NA, Rahmat NL, Hassan H, Tan HJ
OP-A-04	Rituximab Doses And Health-Related Outcomes In Multiple Sclerosis: A Systematic Review	Sutha Rajakumar Rajah R, Yin TB, Nabila F, Shanmugam G, Malini N, Peng HC, Mohamed Micdhadhu MA, Looi I
OP-A-05	Tenecteplase Versus Alteplase For Hyperacute Ischaemic Stroke: A Retrospective Analysis On Efficacy And Safety Outcomes	Ahmad Firdaus Hanapai Ab Manan N, Baharin J, Sardi A, Ishak FH, Zulkifli AS, A. Rauf MAL
OP-A-06	Exploring Therapeutic Effects Of Qur'anic Recitation And Classical Music Therapy In Cognitive Impairment: A Comparative Case Series	Muhamad Naufal Rafif Hafizhan M, Putra SE, Suyatmi, Ristinawati I, Budianto P
OP-A-07	Safety And Efficacy Of Frexalimab In Relapsing Multiple Sclerosis: 48-Week Results From The Phase 2 Open-Label Extension	Stéphane Saubadu Giovannoni G, Granziera C, Mao-Draayer Y, Cutter G, Kalbus O, Staikov I, Dufek M, Bejuit R, Djukic B, Truffinet P, Wallstroem E, Vermersch P, Wang C
OP-A-08	Frexalimab In Relapsing Multiple Sclerosis And Non-Relapsing Secondary Progressive Multiple Sclerosis: Design Of Phase 3 Frexalt And Freviva Trials	Stéphane Saubadu Krieger S, Vermersch P, Chitnis T, Mao-Draayer Y, Granziera C, Havrdova EK, Montalban X, Gargaun E, Truffinet P, Wiendl H, Giovannoni G, Wang C

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PD-A-01	Cerebral Sinus Venous Thrombosis In Middle-Aged Males: A Serial Case Report	Anthonius Kurniadi
PD-A-02	Focal Seizure? Intracerebral Hemorrhage? A Case Of Sudden Onset Movement Disorder	Chai Siew Yap
PD-A-03	Paradoxical Treatment In Subarachnoid Hemorrhage With Anticoagulant	Koh Lee Peng Raja Lope Ahmad RAR, Achok HN
PD-A-04	Intubation Prior To Thrombolysis : A Case Series	Aina Salihah Shahrniza Gan KX, Sim CY, Tay JS, Law WC
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PD-A-06	Cerebral Venous Sinus Thrombosis: Unusual Clot-Forming Phenomenon Post Head Trauma	Khoo Siew Im Mohamed Micdhadhu MA, Tan SK, Looi I
PD-A-07	Primary Central Nervous System Lymphoma In AIDS Patient; A Neuroimaging Diagnostic Challenge	Clarita Clarence Ganesan Payus AO
PD-A-08	The Early Utilization Of Electroencephalogram In First Onset Seizures	Alvin Oliver Payus Tan HJ
PD-A-09	An Epidemiology Study On Seizure Disorder In Neurology Clinic, Hospital Sultanah Bahiyah (HSB): Local Data	Chew Beng Hoong Khor LF, Choy WL
PD-A-10	Longitudinal Extensive Transverse Myelitis With Meningitis Secondary To Mycobacterium Tuberculosis	Nur Atikah Tajul Lile Saleh N
PD-A-11	Headache That Should Not Be Missed In Pregnancy	Nur Atikah Tajul Lile Saleh N
PD-A-12	Motor Neuron Disease Coexistence With Sjogren's Syndrome: An Underreported Entity	Goh Jin Yi Remli R, Tan HJ
PD-A-13	The Rare Mimicker: Miliary Tuberculosis Of The Brain	Rathika Rajah Chang SA, Wan Zaidi WA, Kamaruzaman L

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PD-A-15	An Unusual Case Of Acute Tetraparesis In Spinal Cord Injury: A Case Report	Arinal Haq Setyaningsih I, Dananjoyo K, Subagya S
PD-A-16	A Great Masquerader Not To Be Missed: A Single Centre Treatment Experience From The Northern Sarawak	Wan Chung Law Lai BJ, Lau WJ
PD-A-17	A Challenging Diagnosis Of Neurological Manifestation In Systemic Lupus Erythematosus	Ahmad Zeiree Abdullah Mariam S, Azmi K
PD-A-18	Socio-Demographic And Clinical Profile Of Patients With Parkinson's Disease In A Tertiary Care Hospital Of Terengganu, Malaysia	Ting Yoong Tee Sidek NN, Husin M, Ibrahim KA, Abdul Aziz Z
PD-A-19	Prevalence Of Psychotropics Used And Occurrence Of Falls Among Older Patients With Parkinson's Disease	Ng Tyng Sam Pok WP
PD-A-20	A Case Of Immune Mediated Necrotising Myopathy After COVID-19 Vaccination	Lim Oon Keat Ch'ng IXY, Tan YY, Wong CK, Hor JY, Eow GB
PD-A-21	Cervical Spondylotic Myelopathy With Paravertebral Tumour Mimicking Motor Neuron Disease	Gan Kai Xin Tay JS, Sim CY, Then LYY, Law WC
PD-A-22	Gluten Ataxia - A Case Report	Gan Kai Xin Sim CY, Tay JS, Then LYY, Law WC
PD-A-23	Challenges In Diagnosing And Managing Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) In Patients With Diabetes Mellitus (DM) And End Stage Renal Failure (ESRF): A Case Report	Ng Sock Hoon Najman H
PD-A-24	A Case Report: Rabies Presenting With Acute Flaccid Paraplegia Mimicking Guillain-Barre Syndrome	Tan Jef Wayne Law ZT, Tan JGL, Gan KX, Tay JS

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PD-A-25	Manifestation Of LG1 Autoimmune Encephelitis And Dengue Encephalitis	Choo Xin Hui Ong JS, Wong DYJ, Wong WK, Cheah CF, Lau WK
PD-A-26	A Rare Case Of Parvimonas Micra Orbital Cellulitis Complicated With Cerebrovascular Thrombosis And Mycotic Aneurysm	Sak Yeow Hong Pillai P, Arthimulam G, Chia YK
PD-A-27	Occipital Condyle Syndrome As The First Manifestation Of Tracheal Carcinoma	Law Zhen Theng Tan JW, Chai IJW, Gan KX, Law WC, Shaaya FN
PD-A-28	Focal Seizure As The First Presentation Of Small Cell Lung Carcinoma	Ivana Chai Jia Wei Lee TW, Law ZT, Tan JW, Ho WL, Tan HK, Gan KX, Law WC
PD-A-29	Qiasat Meningitis/Encephalitis Panel - An Important Tool For Microbiological Diagnosis Of CNS Infection	Law Zhen Theng Tan JW, Chai IJW, Gan KX, Law WC
PD-A-30	Tongue Myokymia Occurring 9 Years After Radiotherapy For Nasopharyngeal Carcinoma	Wong Chee Keong Goh JY, Choo WK, Tan YY, Hor JY, Eow GB
PD-A-31	Atypical Presentation Of Polyneuropathy – An Ominous Foreboding?	Jea Sheng Ong Choo XH, Lau WK, Lee AK, Cheah CF
PD-A-32	Idiopathic Intracranial Hypertension As The Initial Manifestation Of Systemic Lupus Erythematosus	Tan Hui Min Kweh TL, Tan YY, Wong CK, Hor JY, Eow GB
PD-A-33	Doctors Views On Epilepsy Management: A Qualitative Study On Cardiac-Based Seizure Prediction Device	Eryse Amira Seth Watterson J, Xie J, Khoo CS, Shaikh MF, Arulsamy A
PD-A-34	EQ-5D-3L Health State Utility Values In People With Epilepsy In Malaysia	Zheng Yang Lee Fong SL, Lim KS, Kherul Anuwar AH, Chong HY
PD-A-35	Neurology Training In ASEAN Countries	Khine Yee Mon Fong SL, Law WC, Thuy Le MA, Lim SH, Charnnarong N, Casanova-Gutierrez J, Octaviana F, Vorachit S, Navuth C, Yassin N, de Deus BS, Lim KS, Tan CT

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PD-A-36	A Case Of Disseminated Cryptococcosis With Multiple Rare Complications In An Immunocompetent Patient	Fatin Arsyida Abd Rashid Mohamed Micdadhu MA, Looi I
PD-A-37	A Case Of Spinocerebellar Ataxia 6 With Good Response To Acetazolamide	Ian Ch'ng Xiang Yuan Lim OK, Tan YY, Wong CK, Hor JY, Eow GB
PD-A-38	Neuromyelitis Optica Spectrum Disorder (NMOSD) And Anti-N-Methyl-D-Aspartate Receptor (Anti-NMDAR) Encephalitis Overlap	Yeoh Jie Jun Choo WK, Anderson S, Wong CK, Tan YY, Hor JY
PD-A-39	A Case Of GAD Antibody Positive Stiff Person Syndrome	Kweh Ting Ling Tan HM, Phua JPF, Wong CK, Tan YY, Hor JY
PD-A-40	AMPA Receptor Encephalitis With Memory Loss	Joyce Phua Pau Fung Kweh TL, Wong CK, Hor JY, Tan YY, Eow GB
PD-A-41	Inclusion Body Myositis Presenting Like LGMD2G	Shobashinee Tanapalla Yue HL, Chun HP, Kar SYH
PD-A-42	A Case Of Spinocerebellar Ataxia 3	Khoo Yi Jian Teoh KW, Tan YY, Wong CK, Hor JY, Eow GB
PD-A-43	Lambert Eaton Myasthenic Syndrome In Small Cell Lung Cancer	Nathaniel Arutus Arutus JR, Wong CK, Hor JY, Eow GB
PD-A-44	Anti-HMGCR Myopathy And Statins	Goy Shuh Ming Mohamed Micdadhu MA
PD-A-45	Thoracic Cord Lesion Presenting With Lower Motor Neuron Lesion	Aina Salihah Shahrniza Law ZT, Tan JW, Gan KX, Tay JS
PD-A-46	A Case Of Co-Occurrence Of Progressive Supranuclear Palsy (PSP) And Idiopathic Normal Pressure Hydrocephalus (INPH) Or Hydrocephalic Mimic?	Lee Teck Wui Tan HK, Chai IJW, Tay JS, Sim CY
PD-A-47	Novel Variants In Familial Polymicrogyria	Lim Kheng Seang Kaliapan K, Ho JH, Ng CC, Tsai MH, Fong SL, Chee YC

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PD-A-48	Ascending Infection Following Sinus Surgery: A Case Report	Nor Afifah Iberahim Wong CF, Abdul Hamid RI, Nik Hasan NS, Mohd Rosli NS
PD-A-49	Anti-Ri Paraneoplastic Syndrome – A Case Report	Gan Kai Xin Tay JS, Sim CY, Then LYY, Law WC
PD-A-50	Managing MELAS Crisis In Resource-Limited Setting	Gan Kai Xin Tay JS, Sim CY, Then LYY, Law WC
PD-A-51	An Indolent Yet Sinister Adverse Effect Of IL-5 Monoclonal Antibody-Benralizumab	Tee Ting Yoong Alias NE, Ng BH, Ban AYL, Wan Yahya WNN, Tan HJ
PD-A-52	“Lock Jaw” Masquerading As Guillain-Barre Syndrome	Daalleni Inndra Indraraja Ling CJ, Chow TH, Chong JY, Tan HJ, Cheah CF
PD-A-53	An Isolated Case Of Methanol Poisoning With Basal Ganglia Necrosis And Haemorrhage In A District Hospital In Malaysia	Xiu Xin Teng Hii DW, Looi I
PD-A-54	Anti-Myelin Oligodendrocyte Glycoprotein Antibodies And Acute Haemorrhagic Encephalomyelitis - <i>MOGAD And AHM: Friends, Lovers, Or Nothing?</i>	Say Ying Tan Pillai P, Wee JS, Krishna PJ, Chia YK, Chin JEO
PD-A-55	Prevalence Of Intracranial Atherosclerotic Disease (ICAD) In Acute Ischemic Stroke (AIS) And Transient Ischemic Attack (TIA) In Malaysia	Aminuddin Sardi Hanapai AF, Ishak FH, Zulkifli AS, A. Rauf MAL, Kamarudin F, Yusof Khan AHK
PD-A-56	An Incidental Finding Of Fibromuscular Dysplasia During Mechanical Thrombectomy In A Stroke Patient	Nithiya Malini Narayani Rajakumar S, Shanmugam G, Mohamed Micdhadhu MA, Mow WC, Balamurugan, Looi I, Wong YC, Saw CB
PD-A-57	Sociodemographic, Severity, And Quality Of Life Profiles Among Migraine Patients At A Malaysian Tertiary Hospital	Eddy Saputra Rohmatul Amin Zabid IN, Loo RY, Poravi R, Abdul Rashid AM

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PD-A-58	Association Between Retinal Microvascular Changes And Depressive Symptoms In Cerebral Small Vessel Disease	Dang Chao Guo J, Liu M
PD-A-59	A Patient's Journey: Severe Basal Exudative Tuberculous Meningitis	Noor Hazwani Ruzanna Abdul Talib Abd Halim S, Chandran N
PD-A-60	Post COVID-19 Inflammatory Demyelinating Polyradiculoneuropathy: A Review	Noelle Tan Lihui Abd Halim S
PD-A-61	Short Lasting, Unilateral, Neuralgiform Headache Attacks With Conjunctival Injection And Tearing (SUNCT): A Forgotten Entity	Phan Chun How Tanapalla S, Hung SKY, Yue HL
PD-A-62	Hemorrhagic Cerebral Toxoplasmosis In An HIV Infected Patient	Dayang Corieza Febriany Ahmad NH
PD-A-63	Incidental Foreign Bodies In The Gastrointestinal Tract Of A Vagrant Female: An Adult Neurological Perspective On Understanding Psychiatric States And Behavioral Patterns	Aman Kumar Shah Yadav AK, Shah A, Thapa N
PD-A-64	Wilson's Disease In A 15 Years Old Boy: A Rare Case	Munzirul Akbar Hastuti S
PD-A-65	Unveiling The Restorative Potential Of Imatinib Against 3-Nitropropionic Acid (3-NPA) - Induced Huntington's Disease (HD) In Mice	Vrinda Gupta Singh S, Singh TG
PD-A-66	Multiple System Atrophy-Cerebellar Type (MSA-C) Survived For 6 Years After Diagnosis	Sang Hak Yi
PD-A-67	Inflammatory Demyelinating Disease In A Young Girl With Impaired Consciousness	Siti Nashrah Azmi Abd Halim S
PD-A-68	Navigating Diagnostic Dilemma: Miller Fisher Syndrome In Pregnancy Masquerading As Stroke	Priyadarsini Appalaramoo Nadaraj K, Yusof Khan AHK

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PD-A-69	Prevalence Of Large Vessel Occlusion (LVO) Among Acute Ischemic Stroke (AIS) Patients With Low NIHSS In Malaysia	Asyrafu Syafiq Zulkifli Ibrahim A, Sardi A, Hanapai AF, Ishak FH, A. Rauf MAL
PD-A-70	Disseminated Tuberculosis Masquerading As A Psychiatric Illness – A Case Report	Mimi Nashra Mohd Noh Bhaskar S
PD-A-71	A Case Report On Anti-Yo Antibody Associated Paraneoplastic Cerebellar Degeneration	Mimi Nashra Mohd Noh Fauzi NA
PD-A-72	A Rare Presentation Of Anti-Sulfatide Positive In Tuberculosis	Mimi Nashra Mohd Noh Bhaskar S
PD-A-73	Lies Unraveling Truth: Ethico-Legal Analysis Of Saline Provocation (Nocebo) Test In Diagnosing Psychogenic Nonepileptic Seizure	Shi Hao Chun
PD-A-74	Miller Fisher Syndrome Mimicking Brainstem Stroke Syndrome	Aina Salihah Shahrniza Lee ZY, Sim CY
PD-A-75	Outcome Of Intravenous Thrombolysis In Hyperacute Stroke Treatment In Tertiary Centre: A 3 Year Experience In Hospital Sultan Abdul Aziz Shah	Ahmad Firdaus Hanapai Sardi A, Ishak FH, Zulkifli AS, A. Rauf MAL, Yusuf Khan AHK
PD-A-76	A Case Of Early Onset Parkinson's Disease With SNCA Duplication In A Bidayuh Gentleman From Sarawak	Siaw Cheng Wong Tay YW, Law WC, Ahmad-Annuar A, Tan AH, Lim SY
PD-A-77	Clinical Features, EEG Correlates, And Outcomes Of Patients Admitted With Meningitis In The Medical Wards Of Hospital Canselor Tuanku Muhriz, Malaysia	Nasheeda Saeed Rajah R, Tan JK, Payus AO, Remli R, Khoo CS, Tan HJ

CHILD NEUROLOGY & DEVELOPMENTAL PAEDIATRICS POSTER PRESENTATION ABSTRACT LIST

POSTER ID	TITLE	AUTHORS
PP-P-01	Executive Function Among Malaysian Children With Epilepsy	Naily Athirah Hamidun Majid Fong CY, Jayanath S
PP-P-02	Validation Of The Hattori Score As A Screening Tool For Dravet Syndrome In Two Malaysian Tertiary Care Centres	Pooven Raj Selva Rajah Chow SY, Husainy K, Yahya NA, Viswanathan S
PP-P-03	Use Of Telemedicine By Parents Of Autistic Children During The COVID-19 Pandemic At Hospital Sultan Ismail Johor Bahru	Wong Guo Wai Jayanath S, Ching BH, Azanan MS
PP-P-04	Juvenile Myasthenia Gravis: A Cross Sectional Study Of Clinical Characteristics And Treatment Outcomes In A Tertiary Paediatric Neurology Center In Malaysia	Teo Yan Lian Sumitha M, Dianah H, Ng CW, Cheah AL, Mohamed AR
PP-P-05	Factors Predicting Poor Mental Health Among Parents Of Preschool Children With Autism Spectrum Disorder	Chua Ker Yung Khoo CS, Chua KY, Suhaini NS, Peliyen R, Lim BC
PD-P-01	Hypotonic Male Infant With Neurodevelopmental Delay; Think Of MCT 8 Deficiency	Yashini Mohan Muhammad SR
PD-P-02	Curious Cases Of Intractable Hiccups And Vomiting	Muhamad Azamin Anuar Majid M, Kamarudzan S, Mohamad R, Yahaya NA
PD-P-03	These Children Don't Feel Pain	Muhamad Azamin Anuar Whitehouse W, Varma U, McCullagh G, Hughes I
PD-P-04	Effectiveness Of Parent Training In Children With Autism Spectrum Disorder (ASD) And Avoidant Restrictive Food Intake Disorder (ARFID) At Child Development Clinic, Hospital Pulau Pinang (CDC HPP)	Yuong Chie Tan Ramachandram S
PD-P-05	Preparing Parents Of Children With Autism Spectrum Disorder (ASD) For Adolescence: Child Development Center Hospital Pulau Pinang (CDC HPP) Experience	Wong Yen Yin Ramachandram S

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PD-P-06	Jamuar Syndrome: A Case Report On An Exceedingly Rare Developmental And Epileptic Encephalopathy Due To A Glycosylation Disorder	Song Yeow Leong Viswanathan S, Toh TH
PD-P-07	Autistic Regression As A Predictor Of Non-Verbal Ability Among Children With ASD	Tan Hang Swee Lim BC, Khoo CS
PD-P-08	Experience With Duchenne Muscular Dystrophy Patients In Hospital Tengku Ampuan Afzan Kuantan, Pahang	Mohd Fazrul Shafiq Kamarudzaman Majid M, Anuar MA
PD-P-09	Novel Case Of UNC13A Homozygous Loss Of Function Causing Early Infantile Developmental And Epileptic Encephalopathy (EIDEE) With Prominent Myoclonic Seizures And Congenital Myasthenia	Cheah Ai Ling Chan MY, Murugesu S, Khoo TB, Rithauddin A
PD-P-10	Methadone Induced Toxic Leukoencephalopathy: A CASE REPORT	Pooven Raj Selva Rajah Yahaya NA
PD-P-11	GLS-Related Neonatal (Lethal) Encephalopathy In A Pair Of Siblings	Anis Suaidah Mohd Sukri Tan KA
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PD-P-13	Early Signs And Actions: Navigating Autism Diagnosis In Early Childhood	Muhammad Amiro Rasheeq Mohd Radzi Kamaruzaman MH
PD-P-14	Navigating Delayed Presentation: Selective Mutism Complicating The Recognition Of Autism Spectrum Disorder	Nur Amanda Zainal Abidin Jayanath S, Samingan N
PD-P-15	Methotrexate Leukoencephalopathy In Childhood Acute Leukaemia: The University Of Malaya Medical Centre Experience	Wan Hanaa Mardhiah Wan Zainuddin Chiew XY, Foo JC, Ariffin H, Lim WK, Li L, Adnan A, Fong CY

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PD-P-17	Rescue Medication Practice In Patients With Dravet Syndrome In A Malaysian Tertiary Hospital	Su Ying Chow Selva Rajah PR, Viswanathan S
PD-P-18	Haemopoietic Stem Cell Transplant, A Pause For Cerebral Adrenoleukodystrophy: A Case Report	Sin Yi Tiong Ganesan VM, Viswanathan S, The CM, Raj P, Raja Abdullah RA, Yeoh SL, Ch'ng GS, Chow SY
PD-P-19	Vehicular Entrapment And Heat Related Injury (VEHRI) - A Subset Of Heat Related Injury Or An Important Domain On Its Own?	A. Wannard Tan KA
PD-P-20	Unveiling The Clinical Spectrum: Insights From The University Of Malaya Medical Centre's Case Series On MOGAD (Myelin Oligodendrocyte Glycoprotein Associated Disease)	Siti Khadijah Mazli Azri Dzulzalani MM, Fong CY, Li L, Wan Zainuddin WHM
PD-P-21	Malaysian Parents' Perception And Effects Of Gastrostomy Tube Insertion For Children With Severe Neurological Impairment	Lim Sze Yee Fong CY, Li L, Wan Zainuddin WHM, Chew KS
PD-P-22	A Case With Acute Post-Measles Encephalitis Associated With Acute Leukoencephalopathy With Restricted Diffusion	Boo Jian An Yeoh SL, Tan KA
PD-P-23	Seizing 'Far Away': An Approach Of Neonatal Seizure In Limited Resource Setting In Borneo	Adlina Awanis Abdullah
PD-P-24	Chemical Stability Of Midazolam Injection Solution For Intranasal Use As Paediatric Home Rescue Medication By High-Performance Liquid Chromatography	Tan Jing Wen Hassan A, Mohd Said M, Ain @Ibrahim N, Balan S, Azman SH, Khoo TB



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PD-P-26	Unveiling Rare Presentation Of Scurvy: Muscular Weakness In The Paediatric Population	Tse En Cheng Malini Mahalingam, Jananheendaran R

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OP-B-02	Effects Of Seizure On Cognitive Decline In An Alzheimer's Disease With Epilepsy Rodent Model	Alina Arulsamy Yee L, Retinasamy T, Shaikh MF
OP-B-03	Investigation Into The Role Of Orphan G-Protein Coupled Receptor GPR151 In Obesity Associated Habenular Cognitive Deficits	Timothy Yee Ong Yu Ogawa S
OP-B-04	Behaviour And Hippocampal Plasticity In A Ketamine-Based Model Of Schizophrenia	Muhammad Hazim Abdullah Hassan Z
OP-B-05	In Vitro Epilepsy Model Using Intracellular Calcium Fluctuation Measurement	Machlusil Husna Sujuti H, Aulanni'am A, Karimah R
OP-B-06	$\alpha 7$ NACHR Activation Prevents Neuroinflammation Associated With Cerebral Ischemia Reperfusion Injury In Zebrafish Model	Mohd Kaisan Mahadi Azmi N, Mohamed Ibrahim N, Siran R, Arulsamy A, Lee V, Hasan MY
OP-B-07	Habenular Orphan G-Protein Coupled Receptors As Novel Therapeutic Targets For Neuropsychiatric Disorders	Satoshi Ogawa
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OP-B-09	The Therapeutic Effects Of <i>Lactacaseibacillus rhamnosus</i> On Stress-Induced Anxiety: A Systematic Review	Iman Imtiyaz Ahmed Juvale Arulsamy A
OP-B-10	Exploring The Therapeutic Potential Of <i>Swietenia macrophylla</i> In Alzheimer's Disease Pathology: Insights From Preclinical Studies	Yatinesh Kumari Jazuli I
OP-B-11	Philanthotoxin-343: A Promising Neuroprotective Agent Against NMDA-Induced Retinal Injury In Glaucoma	Izuddin Fahmy Abu Fazel MF, Mohamad MHN, Agarwal R, Iezhitsa I, Mellor I, Franzyk H

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OP-B-13	Artemisinin Ameliorates The Neurotoxic Effect Of 3-Nitropropionic Acid: A Possible Involvement Of The Nrf2/HO-1 And ERK/BDNF Signaling Pathway	Richmond Arthur Shanker U, Kumar P
OP-B-14	Protective Effect Of A Reduced <i>PDLIM5</i> Expression Against Phencyclidine-Induced Cognitive Impairment	Mohd Aizat Mohd Mohd Zain Pandy V, Abdul Majeed AB, Mohamed Z, Wong WF
OP-B-15	The Neuroprotective Roles Of Xanthones In Alzheimer's Disease: A Systematic Review	Hui Yin Yow Hamzah S, Tan SLJ, Mah SH, Pang LW
OP-B-16	Unravelling The Neuroprotective Properties Of <i>Ficus deltoidea</i> Jack In Alzheimer's Disease-Like Rat Model: Insights From Histological And Molecular Perspectives	Sushmitaa Dhevii Manoharan Abdul Hamid H, Md Hashim NF, Norazit A, Mohd Moklas MA, Mustapha M, Murthy J, Zainol M, Mehat MZ
OP-B-17	Evaluating The Pathogenic Role Of Synthesized Human Neuromelanin Analogues Through Intranigral Injection In Mice And Its Implication In Parkinson's Disease	Jhanvi Soni Khairnar A, Zucca F, Zecca L
OP-B-18	Effects Of Clitorienolactones From <i>Clitoria ternatea</i> Root On Calcium Channel Mediating Hippocampal Long-Term Potentiation In Rats Induced Chronic Cerebral Hypoperfusion	Mohamad Anuar Ahad Chear NJY, Abdullah MH, Ching-Ga TAF, Liao P, Wei S, MurugaiyahV, Hassan Z



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OP-B-20	Subacute Effects Of Methiopropamine On Behaviour And Dopamine Neurotransmitter System In Mice	Norazrina Azmi Bunaim MK, Damanhuri HA, Yow HY, Yaakob NS

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PP-B-02	Tears Of Melioidosis: A Rare Presentation Of Lacrimal Gland Melioidosis With Intracranial Extension	Sharmathi Dhanapal Rajahram GS, Perianen PP
PP-B-03	Repurposing Anakinra For Neuroinflammation Mediated Alzheimer's Disease: <i>In Vitro And In Vivo</i> Effects	Thaarvena Retinasamy Lee ALY, Lee HS, Lee VLL, Shaikh MF, Yeong KY
PP-B-04	The Role Of Orexin Signalling In Fear Memory And Learning In Zebrafish	Elisha Ab Rashid Ogawa S
PP-B-05	<i>Channa striatus</i> Prevents Pentylenetetrazole-induced Seizures and Modulates Inflammatory Markers	Vanessa Lin Lin Lee Chung YS, Mat Jais AM, Zainal Abidin SA, Musa AF, Othman I, Shaikh MF
PP-B-06	Mechanistic Insights Into The Role Of GPR139, An Orphan Receptor, In Modulating The Anti-Addictive Effect And Kratom-Derived Alkaloid (Mitragynine)	Nur Sabrina Abdul Basit Ogawa S
PP-B-07	The Role Of Spexin In Female Infertility	Tan Jie Wei Jaafar F, Hamdan M, Zainal Abidin SA, Ayub Q, Ogawa S
PP-B-08	Morphological And Electrophysiological Analysis Of Down Syndrome Cerebral Organoids	Lim Chong Teik Jusoh N, Reisi P, Ismail EN, Cheah PS, Ling KH
PP-B-09	Upgrading The Effectivity Of Anti-Seizure Medications For Status Epilepticus With Nanoformulation - A Systematic Review	Nuraziemah Ahmad Shaikhab MF, Arulsamy A

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PP-B-11	Therapeutic Effect Of Stingless Bee Honey On Cognitive Impairments Of Aluminium Chloride And D-Galactose Induced Rodent Alzheimer's Model	Muhammad Danial Che Ramli Shajahan SR, Mustafa Z
PP-B-12	Alpha-Tocopherol Rescues Interferon Induced Mood Disorders In Mice	Ming Tatt Lee Lai JY, Ho JX, Siew AFK, Tham CL, Ho YC
PP-B-13	Effect Of Javanese Music On Anxiety And Depression-Like Behaviour After Chronic Stress: An Animal Study	Muhana Fawwazy Ilyas Wiyono N, Asrini NE, Handoko LE, Hastami Y, Muthmainah M, Hanifa SN, Rahma AA
PP-B-14	Differential Effect Of <i>In Vitro</i> Ruxolitinib Treatment On Neural Stem/Progenitor Cell (NSPC) And Oligodendrocyte Precursor Cell (OPC)	Cheng Wei Lim Hamanaka G, Liang AC, Chan SJ, Ling KH, Lo EH, Arai K, Cheah PS
PP-B-15	Novel Therapeutic Option Using Synthetic MRNAS Transcription Factor In Reprogramming Stem Cell Into Insulin Producing Cells	Ayesha Shahira Mohd Fauzi Tang YQ, Chia AYY
PP-B-16	Cognitive Enhancement And Antioxidant Properties Of The Cannabinoid Receptor Agonist, Win55,212-2, On Cognitive Impairments Induced By Aluminum Chloride And D-Galactose In Rats.	Nurul Huda Mohd Nor Mahdi O, Masrudin SS, Baharuldin MTH, Mohd Moklas MA
PP-B-17	Co-Culture With Glioblastoma Induces Morphological Changes And Apoptosis In Cholinergic Cells Through Regulation Of Inflammation-Related Proteins	Sylvia Sue Xian Liew Zainal Abidin SA, Bhuvanendran S, Naidu R, Alfarizal Kamarudin MN
PP-B-18	Effects Of CBD-Enriched Hemp Extract And CBD Isolate On Anxiety And Recognition Memory In Chronic Unpredictable Mild Stress Induced Rats	Wanfrutkon Waehama Roboon J, Temkitthawon P, Thanoi S, Nudmamud-Thanoi S
PP-B-19	Neurotherapeutic Effects Of Cannabidiol (CBD) On Cognition And Hippocampal Synaptic Changes In D-Galactose And AICl ₃ Induced Alzheimer's Like Animal Model In Male Wistar Rats	Sura Sreenivasulu Mohd Nor NH, Mohd Moklas MA, Masrudin SS, Jagadeesan S, Kamaruzzaman MA, Vishnumukkala T

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PP-B-22	Characterizing Somatic Line1 Insertions In Human Neurons And Glia With Deep Learning Methods	Zhinan Lin Zhu X
PP-B-23	Extracellular Signal Regulated Protein Kinase (ERK) Inhibition Ameliorates Allodynia And Hyperalgesia In Painful Diabetic Neuropathy Rat Model	Khalilah Haris Wan Ahmad WAN, Mustafa MZ, Long I
PP-B-24	Modulation Of Glial Cells By Endocannabinoid Systems Leads To Cognitive Amelioration: A Systematic Review And Meta-Analysis In Rodents	Mohd Amir Kamaruzzaman Abas R, Vidyadaran S, Baharuldin MTH, Mohd Nor NH, Sreenivasulu S, Vishnumukkala T, Mohd Moklas MA
PP-B-25	Assessing The Neuroprotective Role Of Cannabinoid Receptor Agonist, WIN55,212-2 Through Histomorphometry In Aluminium Chloride And D-Galactose Induced Cognitive Impairments In Male Wistar Rats	Siti Saleha Masrudin Mahdi O, Mohd Nor NH, Baharuldin MTH, Mohd Moklas MA
PP-B-26	Deterioration Of Cognitive Performance In Ageing Spontaneously Hypertensive Rats: An Animal Model Of Cerebral Small Vessel Disease	Siti Nurulnabila A Rahaman Mehat MZ, Mohd Moklas MA, Norazit A, Mustapha M, Murthy J, Abdul Hamid H
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PP-B-29	Effects Of Lithium On Anxiety, Locomotor Activity, And Learning And Memory In Mice: A Neurobehavioral And Electrophysiological Study	Mansour Azimzadeh Goh BC, Lim CW, Cheah PS, Ling KH
PP-B-30	<i>In Vitro</i> And <i>In Vivo</i> Screening Of <i>Coccoloba uvifera</i> , <i>Mimusops elengi</i> And <i>Syzygium aqueum</i> Extracts On Cognitive Function In Vascular Dementia Rats Model.	Kesevan Rajah Kumaran Abdul Wahab H, Hassan Z

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OP-S-01	Intracranial Hemorrhage Following Intravenous Thrombolysis In Old Acute Ischemic Stroke Patients: Single Stroke Center	Tan Shin Wuei Keng JN, Alan Ch'ng, Looi I, Chin CJ
OP-S-02	An Unexpected Turn Of Stroke Code Activation	Chow Tse Hui Inndra ID, Ling CJ, Chong JY, Tan HJ, Cheah CF
OP-S-03	Navigating The Unknown: Rehabilitation Journey Of People With Post-Stroke Aphasia In Malaysia	Zhi Zhi Diong Som VS
OP-S-04	Convulsive Basilar Artery Occlusion – An Underreported Malignant Entity: Case Series And Literature Review	Wee Jack Son Pillai P, Kang CY
OP-S-05	Stroke Awareness And Education Among Children In Malaysia: Fast Heroes Program	Ng Kim Khim Ishak FH, Maat N, Abdullah NS, Zakaria SH, Omar M, Abdul Rashid AM
OP-S-06	Persistence Of Non-Vitamin K Antagonist Oral Anticoagulant Treatment For Stroke Prevention Among Older Adults With Atrial Fibrillation	Victoria Boey Wei Fang Tan KM, Goh SSL, Lee ZY, Cheah WC, Kunaseelan NK

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PD-S-02	A Large Intracranial Vessel Occlusion Treated By Intravenous Thrombolysis Without Mechanical Thrombectomy: A Case Report	Anthonius Kurniadi
PD-S-03	Correlation Between De Ritis Ratio With Cognitive Impairment In Acute Stroke Patients : A Cross Sectional Study In Sardjito General Hospital, Yogyakarta	Shintia Eka Wulandari Gofir A, Vidyanti AN, Ar Rochmah M
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PD-S-05	Blood Pressure And Different Types Of Stroke : A Study In Seberang Jaya Hospital, Penang, Malaysia	Angelina Tang Siing Ng Chin CJ, Azlam M, Looi I
PD-S-06	Atrial Fibrillation And Ischemic Stroke : A Study In Seberang Jaya Hospital, Penang, Malaysia	Angelina Tang Siing Ng Chin CJ, Azlam M, Looi I
PD-S-07	Case Series Of New Stroke Onset Post Stopping Of Anticoagulant In Patients With Atrial Fibrillation	Neoh Kar Keong Kee KL, Toh CH, Tan MKC, Teoh SK, Lee SL, Tan SSY, Thor TG, Looi I
PD-S-08	Association Of Admission Blood Pressure And Severity Of Stroke Among Patients Who Received Treatment In Kek Lok Si Charitable Hospital	Toh Chin Heng Kee KL, Tan MKC, Teoh SK, Lee SL, Tan SSY, Neoh KK, Thor TG, Looi I
PD-S-09	Association Of Atrial Fibrillation And Severity Of Stroke Among Patients Who Received Treatment In Kek Lok Si Charitable Hospital	Toh Chin Heng Kee KL, Tan MKC, Teoh SK, Lee SL, Tan SSY, Neoh KK, Thor TG, Looi I
PD-S-10	Association Between Admission Blood Glucose Levels And Severity Of Stroke (NIHSS) Among Patients Who Received Acute Stroke Treatment In Kek Lok Si Charitable Hospital	Toh Chin Heng Kee KL, Toh CH, Tan MKC, Teoh SK, Lee SL, Tan SSY, Neoh KK, Thor TG, Looi I

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PD-S-12	Association Of Pre-Admission Use Of Antiplatelet/Anticoagulant And Severity Of Stroke: Experience In Kek Lok Si Charitable Hospital	Sylvia Tan Su Ying Toh CH, Tan MKC, Teoh SK, Lee SL, Kee KL, Neoh KK, Thor TG, Looi I
PD-S-13	Association Of Pre-Admission Antiplatelets/Anticoagulants, And Stroke Types And Duration Of Hospital Stay: A Study In Kek Lok Si Charitable Hospital	Sylvia Tan Su Ying Toh CH, Tan MKC, Teoh SK, Lee SL, Kee KL, Neoh KK, Thor TG, Looi I
PD-S-14	A Study On Gender Difference With Stroke Severity Among Patient Who Received Treatment In Kek Lok Si Charitable Hospital	Teoh Su Keat Tan SSY, Toh CH, Tan MKC, Lee SL, Kee KL, Neoh KK, Thor TG, Looi I
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PD-S-17	Determinants Of Ambulance Utilization Among Stroke Patients Who Received Stroke Treatments In Kek Lok Si Charitable Hospital	Kee Kai Ling Toh CH, Tan MKC, Teoh SK, Lee SL, Tan SSY, Neoh KK, Thor TG, Looi I
PD-S-18	A Descriptive Study Of Stroke Patients In Kek Lok Si Charitable Hospital	Lee Shin Ling Kee KL, Toh CH, Tan MKC, Teoh SK, Tan SSY, Neoh KK, Thor TG, Looi I
PD-S-19	Impact Of Age On Stroke Severity And Functional Outcomes	Lee Shin Ling Kee KL, Toh CH, Tan MKC, Teoh SK, Tan SSY, Neoh KK, Thor TG, Looi I

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PD-S-21	Acute Anterior Cerebral Artery Infarction With Acute Dystonia	Nur Atikah Tajul Lile Mohamed Micdhadhu MA, Looi I
PD-S-22	Does Smoking History Increased Risk Of Stroke-Associated Pneumonia?	Naufal Gofir A, Paryono, Satiti S
PD-S-23	A Case Report Of Claude Syndrome	Choo Wei Kei Yeoh JJ, Wong CK, Goh JY, Hor JY, Eow GB
PD-S-24	Prospective Observational Study On Acute Ischemic Stroke Recognition Accuracy By Medical Emergency Coordination Centre (MECC) - An Emergency Department Quality Measures Improvement	Muhammad Ashraf Khairul Azmi Chow CT, Zambri SNA
PD-S-25	Evaluation Of Thrombolysis Service Quality In Hyperacute Ischemic Stroke Patients: A One-Year Review In A District Hospital	Tan Zhun Foo Khit KH, Ho WL
PD-S-26	Post Haemodialysis Thrombolysis, To Give Or Not To Give?	Adilah Aminuddin Micdhadhu MA, Looi I
PD-S-27	Unraveling The Complexity: A Case Of Thromboembolic Event In Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVC/D) Leading To Top Of Basilar Artery Occlusion Treated With Intravenous Thrombolysis And Mechanical Thrombectomy	Amirul Asyraf Ab Ghapar Chu GSE, Idris I, Mei SLT, New RP, Zainal Abidin I, Abd Kadir KA, Tan KS
PD-S-28	Three-Month Outcomes Of Acute Ischemic Stroke And Predictive Factors In Penang: Insights From Hospital Seberang Jaya Stroke Registry Data	Ng Li Yun Chin JC, Lee NH, Looi I
PD-S-29	Factors Associated With Inpatient Mortality Among The Hospitalized Stroke Patients	Chin Chen Joo Lee NH, Ng LY, Looi I

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PD-S-31	A Clinical Audit On The Use Of Alteplase For Thrombolysis In A Malaysian Hospital	Loh Hong Chuan Mohamed Micdhadhu MA, Chin CJ, Looi I
PD-S-32	Am I Too Young? Anterior Spinal Artery Syndrome (ASAS)	Balqis Zulkefli
PD-S-33	Albatross Around One's Neck: Stroke Post Motor Vehicle Accident	Chong Jia Yih Inndra ID, Ling CJ, Chow TH, Tan HJ, Cheah CF
PD-S-34	Bilateral Middle Cerebellar Peduncle Infarction : A Rare Stroke Presentation	Nur Amalina Ramli Abd Halim S, Aziz ME
PD-S-35	Prevalence Of Branch Atheromatous Disease (BAD) In Acute Ischemic Stroke (AIS) In Hospital Sultan Abdul Aziz Shah	Md Adnan Lutfi A. Rauf Sardi A, Hanapai AF, Ishak FH, Zulkifli AS, Yusof Khan AHK
PD-S-36	Basilar Artery Thrombosis Secondary To Atrial Septal Defect With Successful Endovascular Thrombectomy	En Hui Tan Muthuraman V, Viswanathan S
PD-S-37	Stroke And Atrial Fibrillation: A Descriptive Study On Characteristics And Outcomes Of Patients Who Received Intravenous Thrombolysis From The HSNZ Stroke Registry	Alia Anis Yahya Khalid SN, Ibrahim KA, M Unit H, Husin M
PD-S-38	Exploring The Therapeutic Potential Of Stingless Bee Honey As A Novel Therapeutic Approach For Middle Cerebral Artery Occlusion Stroke Models	Poo Chin Long Noor Tuah MA, Azlan NA, Mustafa MZ, Wan Ahmad WAN, Muhammad H, Ping L, Bo C, Che Ramli MD, Nik Ramli NN
PD-S-39	Successful Thrombolysis Of Basilar Artery Stroke Beyond The 4.5-Hour Guideline: A Case Report	Ang Zi Heng Micdhadhu MA

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PD-S-40	A Case Report: Tuberculous Meningitis Presenting As A Stroke Mimic. A Diagnostic Dilemma.	Manraj Singh Grewal Kaur H, Gan KX, Tan JW, Chai IJW
PD-S-41	Neuroprotective Effects Of Stingless Bee Honey (Trigona spp) On The Level Of Antioxidant Enzymes In Patients With Post-Stroke Cognitive Impairment	Nor Liyana Ja'afar Mustapha M, Hashim S, Mohamed M
PD-S-42	Demographics, Clinical Manifestations And Outcomes Of Posterior Circulation Infarct (POCI) In Hospital Sultan Abdul Aziz Shah (UPM): A Two-Year Retrospective Study	Fadhilah Hani Ishak Hanapai AF, Sardi A, Zulkifli AS, A. Rauf MAL, Abdul Rashid AM
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A POINT-BASED COGNITIVE IMPAIRMENT SCORING SYSTEM FOR MULTIETHNIC ASIAN ADULTS

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BACKGROUND

Identifying individuals in their prodromal stages early is needed to inform intervention efforts to prevent or delay progression to dementia. However, existing diagnostic tools (i.e. cognitive assessments, informant reports) has limitations in detecting early and subtle deficits and many fail to consider a range of clinical characteristics when diagnosing cognitive impairment in older adults. In Asia, vascular dementia (VaD) is more prevalent than Alzheimer's Disease (AD) due to the high burden of cardiovascular and cerebrovascular diseases (CeVD). This study developed a simple, point-based scoring model using vascular risk factors and neurodegenerative markers to identify individuals with cognitive impairment in a multiethnic Asian population.

METHOD

This cross-sectional study included individuals aged ≥ 45 years, who were free from dementia, from two population-based studies. Cognitive impairment scores were calculated using sociodemographic factors, vascular risk factors, and neuroimaging markers of CeVD and brain atrophy. Cognitive diagnosis was defined as no cognitive impairment (NCI) or cognitive impairment without dementia (CIND). The cognitive impairment scoring system (CISS) was developed using a clinical risk scoring framework that combines machine learning and multivariable logistic regression to translate the estimate of CIND into a point-based scoring system. Ten machine learning (ML) algorithms were trained to predict CIND, with feature importance scores for the top three algorithms, based on the area under the curve (AUC) measure, extracted for ensemble variable ranking. Logistic regression was utilized for score derivation. A basic and an extended CISS model were developed to estimate the likelihood of CIND. Model performances were assessed using the area under the receiver operating characteristic curve (AUC) and calibration plot.

RESULTS

Among the 1,426 participants (mean age 65.5 ± 8.8 , 68.3% female), 657 (46.0%) had CIND. After feature selection, the basic model included ten sociodemographic (age, sex, race, years of education, depression) and vascular risk factors (smoking, diabetes, systolic blood pressure, BMI, stroke history); the extended model included variables in the basic model with additional seven neuroimaging markers (age-related white matter changes, atrophy in central, cortical and medial temporal atrophy (MTA) region, presence of lacunes, cortical infarcts and intracranial stenosis). The AUC for CISS basic and extended model were 0.81 (95%CI, 0.76–0.88) and

0.84 (95%CI, 0.79–0.88) respectively. Calibration was satisfactory based on plots of predicted vs observed risk. The user-friendliness of the CISS is illustrated through the two case studies in Fig 1.

FIG 1

(A)

Case 1



Risk factor	Points	Scores	Risk of CIND (%)
Age 75	19	0 – 5	5.0
Sex Male	0	6 – 10	12.1
Race Chinese	0	11 – 15	18.2
BMI 20.8	0	16 – 20	26.4
Education (in years) 6	9	21 – 25	36.6
Systolic blood pressure (mmHg) 130	0	26 – 30	48.2
Smoking Former smoker	3	31 – 35	59.9
Diabetes Absent	0	36 – 40	70.7
Stroke history Present	15	41 – 45	79.5
Depression Absent	0	46 – 50	86.2
		51 – 55	91.0
		56 – 60	94.2
		61 – 65	96.4
		66 – 70	97.7
		71 – 75	98.6
		76 – 80	99.3
		81 – 85	99.5
		≥ 86	100
Total	46		
Estimated risk of CIND 86.2%			

(B)

Case 2



Risk factor	Points	Scores	Risk of CIND (%)
Age 65	7	0 – 5	5.0
Sex Female	3	6 – 10	12.1
Race Non Chinese	8	11 – 15	18.2
BMI 26.3	1	16 – 20	26.4
Education (in years) 10	0	21 – 25	36.6
Systolic blood pressure (mmHg) 155	3	26 – 30	48.2
Smoking Non smoker	0	31 – 35	59.9
Diabetes Present	8	36 – 40	70.7
Stroke history Absent	0	41 – 45	79.5
Depression (mild/moderate) Absent	0	46 – 50	86.2
		51 – 55	91.0
		56 – 60	94.2
		61 – 65	96.4
		66 – 70	97.7
		71 – 75	98.6
		76 – 80	99.3
		81 – 85	99.5
		≥ 86	100
Total	30		
Estimated risk of CIND 48.2%			

CONCLUSION

In community-dwelling individuals, the CISS basic model, utilizing readily available predictors in the primary care setting, performed well in the identification of individuals with CIND. The extended model, which included additional neuroimaging markers, may allow for improved prognostication. The point-based scoring system offers a quick and objective assessment of one's cognitive impairment status and is user-friendly for clinicians, requiring no calculator or computer.

KEYWORDS

Cognitive impairment, point-based scoring, Asian population

THE PROTECTIVE EFFECT OF VITAMIN B12 ON NEUROPSYCHIATRIC SYMPTOMS IN ASIAN DEMENTIA-FREE OLDER ADULTS

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BACKGROUND

Vitamin B12 plays an important role in the central nervous system (CNS), which is implicated in neuropsychiatric manifestations including both cognitive impairment and neuropsychiatric symptoms (NPS) ^{1,2}. While vitamin B12 deficiency was linked to NPS in dementia, little is known about the relationship between vitamin B12 levels and NPS in the preclinical and prodromal stages of dementia. To understand the role of vitamin B12 in the pathogenesis of NPS, this study aimed to examine the associations between vitamin B12 levels and NPS in an Asian cohort of dementia-free individuals.

METHODS

Participants from the Epidemiology of Dementia in Singapore (EDIS) Study aged ≥ 60 years underwent comprehensive neuropsychological testing and clinical assessments. NPS were assessed using the 12-item Neuropsychiatric Inventory (NPI). Four NPS subsyndromes including hyperactivity, psychosis, affective symptoms and apathy generated from NPI items were examined. Serum vitamin B12 and homocysteine (Hcy) concentrations were measured. Hierarchical linear regressions were performed to examine the relationship between vitamin B12 and NPS adjusting for demographics, cognitive functioning, socioeconomic (SES) status and Hcy levels. Multinomial regressions were additionally performed to examine the effect of vitamin B12 on different NPS severity levels: *clinically relevant NPS (NPI scores ≥ 4)*, *mild NPS (NPI scores 1-3)* and *no NPS (NPI scores = 0)*. The moderation effect of cognitive functioning, SES status and Hcy levels on the relationship between vitamin B12 and NPS was additionally explored.

RESULTS

A total of 798 dementia-free individuals (age = 69.7 ± 6.5 years old, F= 408 (51.1%)) were included in the current study. We observed 80 (10%) individuals with clinically relevant NPS. Linear regression showed a negative association between vitamin B12 levels and NPS (β [95%CI] = -1.89[-3.52, -0.27], $p=0.023$), especially with affective symptoms (β [95%CI]= -0.41[-0.80, -0.03], $p=0.034$) and apathy (β [95%CI]= -0.86[-1.46, -0.25], $p=0.005$). This association remained significant after controlling for demographics, cognitive functioning, SES status and Hcy levels. Multinomial regressions further revealed that increased vitamin B12 levels were associated with a reduced likelihood of having clinically relevant apathy,

compared to no apathy (relative risk ratio (RRR)[95%CI] = 0.04[0.003, 0.5], $p=0.013$). Moreover, moderation analyses showed that increased vitamin B12 and reduced NPS were found in individuals with low Hcy levels and high MoCA scores.

CONCLUSION

The protective effect of vitamin B12 on NPS, especially in affective symptoms and apathy, was observed in Asian dementia-free older adults. This study also provided further insights into the mechanisms between increased vitamin B12, low Hcy and early NPS, offering new avenues for therapeutic interventions for improving NPS prior to dementia onset.

KEYWORDS

Serum biomarkers, vitamin B12, neuropsychiatric symptoms

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REAL-WORLD ONE-YEAR ESTIMATION OF THE CANDIDATES FOR LECANEMAB IN A SOUTH KOREAN MEMORY CLINIC

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BACKGROUND & OBJECTIVE

Lecanemab, a new therapeutic agent anti-amyloid agent for early Alzheimer's disease (AD), has received approval from the U.S Food and Drug Administration (FDA). Therefore, there it's a time to pre-estimate the size of data on how many people can be candidates for this drug in a Korean real-world practice. This study aimed to estimate how many patients over one year could be recommended for lecanemab in a South Korean memory clinic, according to the Clarity AD study protocol, and to evaluate the most appropriate clinical criteria for prescribing lecanemab whether there is some consideration for revising the inclusion/exclusion criteria to apply in Korean clinical setting.

METHODS

We retrospectively reviewed the medical records of 6009 patients who had visited our memory clinic in 2022. This study included patients who underwent Amyloid PET in the memory clinic of Ajou University Hospital, South Korea. The inclusion and exclusion criteria were from the phase 3 trial (Clarity AD) to determine the safety and efficacy of lecanemab in participants with early AD. The evidence of amyloid was determined on ^{18}F -flutemetamol positron-emission tomography (PET). However, some components of the criteria were disregarded due to irrelevance to decision for clinical prescription of the lecanemab: presence of a study partner, exclusion for mental disorders that could interfere with the study, participation in other clinical trials, and known hypersensitivity to lecanemab. In addition, objective impairment in episodic memory was evaluated through Seoul Verbal Learning Test-Elderly version (SVLT-e) was used instead of Wechsler Memory Scale IV-Logical Memory II.

RESULTS

A total of 445 patients over one year got recommended to take amyloid PET and 318 (71.4%) of them really took out of the 6009 patients who visited Ajou University Hospital Memory clinic in 2022. 140 (44.0%) had the evidence of amyloid: 57 MCI, 74 AD dementia, and 9 other dementia. 23 MCI were considered as candidates for the lecanemab with remaining excluded due to as follows: 18 with good SVLT-e score, 4 scored <22 on Mini-Mental State examination (MMSE). Only 18 AD dementia patients satisfied all criteria: 44 were excluded only due to their MMSE score < 22. Additionally, by adjusting cutoff for the MMSE score below 21, 20, and 19, respectively baseline, the number of candidates for lecanemab among amyloid-positive and PET positive AD dementia patients increased to 26, 30, and 37 patients.

CONCLUSION

Despite a single clinic study, a total of 41 candidates for lecanemab were identified according to the Clarity AD protocol. Adjusting the MMSE score baseline increased the number of candidates for lecanemab. Therefore, this study provides insights into the real-world data one-year estimation of lecanemab candidates, and these findings could be useful in prescribing lecanemab clinically. In addition, when the lecanemab treatment is implemented in Korean real-world practices, it is proposed to reconsider cutoff for the MMSE score.

THE FREE AND CUED SELECTIVE REMINDING TEST (FCSRT) AS A SCREENING TOOL FOR MILD COGNITIVE IMPAIRMENT (MCI) IN A MULTIETHNIC POPULATION.

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BACKGROUND

The Free and Cued Selective Reminding Test (FCSRT) (Buschke, 1984) is a screening tool for neuropsychological disorders like Mild Cognitive Impairment (MCI), evaluating learning and memory retention through visual images and word coding. Despite its widespread use, its efficacy in distinguishing Cognitively Unimpaired (CU) from MCI in multiethnic populations is unclear. Our goal is to determine optimal cut-off values for the FCSRT's four subtests to improve MCI detection accuracy across diverse ethnicities.

METHOD

A total of 1,224 non-demented participants were recruited from Biomarker and Cognition Study, Singapore (BIOCIS) and underwent a series of Neuropsychological Assessments (NPA) tests (Leow et al., 2024). Participants were divided into CU and MCI groups based on Petersen and NIA-AA criteria. FCSRT test involved showing 16 pictures, four at a time, with a unique category cue for each picture, followed by three trials of immediate free recall (IFR) and cued recall (ICR) with total score of 48. Trials were separated by 20-second interference. After 20 minutes, delayed free (DFR) and cued recall (DCR) trials for all 16 items were conducted. Demographic and NPA scores distribution were analyzed by Wilcoxon rank sum test, chi-square, and Fisher's exact test. ROC analysis was utilized to assess the discriminative properties of FCSRT compared to other neuropsychological tests.

RESULTS

MCI individuals (Mean age = 63.57 years ± 10.08, Mean education = 13.85 years ± 3.66) are significantly older and have fewer years of education compared to CU (Mean age = 59.96 years ± 10.39, Mean education = 15.42 years ± 3.26). The majority are Chinese (86%) with no significant difference between groups. After adjusting for age, education, and gender, MCI participants performed worse in all NPA tests, including the 4 FCSRT subtests ($p < 0.05$). ROC analysis (Table 1) indicates that FCSRT demonstrates good discriminative ability in detecting MCI from CU, particularly in IFR (AUC = 0.96, 95% CI = 0.95-0.97, Sn = 0.96, Sp = 0.72, cut-off < 34) and ICR (AUC = 0.96, 95% CI = 0.94-0.97, Sn = 0.93, Sp = 0.78, cut-off > 14), compared to Montreal Cognitive Test (MoCA), Visual Cognitive Assessment Test (VCAT), and delayed Rey Auditory Verbal Learning Test (RAVLT).

CONCLUSION

The FCSRT proves to be a valuable MCI screening tool across diverse ethnicities. Future research should delve into item-by-item analysis and work towards developing a condensed version of the FCSRT.

KEYWORDS

Neuropsychological assessment, FCSRT, Multiethnic population

Table 1. Discriminative Properties of Neuropsychological Tests for CU and MCI

Tests	Sn	Sp	PPV	NPV	Optimal Cut-offs	AUC(95%CI)
IFR	0.96	0.72	0.54	0.67	34	0.96 (0.95-0.97)
ICR	0.93	0.78	0.55	0.67	14	0.96 (0.94-0.97)
DFR	0.74	0.98	0.55	0.63	12	0.96 (0.95-0.97)
DCR	0.65	0.98	0.55	0.63	4	0.96 (0.94-0.97)
MoCA	0.96	0.77	0.58	0.69	26	0.97 (0.96-0.98)
VCAT	0.91	0.65	0.57	0.68	27	0.92 (0.90-0.93)
RAVLT delayed	0.92	0.70	0.55	0.67	11	0.91 (0.89-0.92)

Abbreviations. CU = Cognitively Unimpaired, MCI = Mild Cognitive Impairment, MoCA = Montreal Cognitive Assessment, VCAT = Visual Cognitive Assessment Test, RAVLT = Rey Auditory Verbal Learning Test, IFR = Immediate Free Recall, ICR = Immediate Cued Recall, DFR = Delayed Free Recall, DCR = Delayed Cued Recall, Sn = Sensitivity, Sp = Specificity, PPV = Positive Predictive Value, NPV = Negative Predictive Value, AUC = Area Under the Curve, CI = Confidence Interval

AUTOMATIC BRAIN SEGMENTATION WITH AQUA: A COMPARATIVE VALIDATION STUDY IN THE SOUTHEAST ASIAN BIOCIS COHORT

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BACKGROUND

Alzheimer's disease dementia is a heterogeneous disorder that is accompanied by brain alterations, such as grey matter (GM) loss and cerebral small vessel disease burden, including white matter hyperintensities (WMH) [1,2]. Currently, classification of cognitive syndromes is largely carried out in clinic settings using neuropsychological assessments and structural MRI, where available. Current methods of interpretation and analysis of brain MRI scans include visual ratings and complex neuroimage processing which require trained professionals and are time-consuming [3-5]. To combat these challenges, recent efforts have established Artificial Intelligence (AI) techniques to aid clinicians in interpreting brain MRI scans for accurate diagnosis of neurodegenerative diseases [6]. However, these techniques need extensive validation prior to their use in clinical settings. To address this gap, the main aim of this study was to validate the use of the AI-based AQUA segmentation and WMH quantification software in a Southeast Asian community-based cohort of cognitively normal (CN), mild cognitive impairment (MCI) and dementia subjects.

METHODS

Study participants belonged to the community-based Biomarker and Cognition Cohort Study in Singapore who underwent neuropsychological assessments and structural MRI (T1-weighted and Fluid Attenuated Inversion Recovery). Participants had a research diagnosis based on their cognitive performance on the Montreal Cognitive Assessment (MoCA) - CN (MoCA 27-30), MCI (MoCA 22-26) and dementia (MoCA<22). MRI pre-processing was carried out using established SPM-based automated pipelines for WMH along with human-based visual ratings. The same images were also pre-processed through the AI-based automated AQUA pipeline. The measures obtained from these techniques were then compared using non-parametric and linear regression analyses.

RESULTS

Ninety participants (mean age 63.32±10.96 years; 70% female) were included. Dementia subjects were significantly older compared to both CN and MCI subjects. There were no differences in sex, total intracranial volume and total grey matter volume between the groups. AQUA-based visual ratings were closely associated with human-based visual ratings where a spearman-rank test showed a high correlation for total ($\rho=0.66$; $p<0.0001$), periventricular ($\rho=0.50$; $p<0.0001$) and deep ($\rho=0.57$; $p<0.0001$) WMH. Additionally, the spearman-rank test showed a high correlation between volumetric WMH obtained from AQUA and SPM software ($\rho=0.84$; $p<0.0001$). This correlation remained after controlling for age at visit, sex and diagnosis. Moreover, linear regression analyses illustrated that AQUA-derived grey matter

volumes in default mode network regions were significantly different between CN, MCI and dementia groups, where dementia groups had significant atrophy specifically in the posterior cingulate cortex compared to CN ($p=0.021$) and hippocampus compared to CN ($p=0.0049$) and MCI ($p=0.0036$) subjects.

CONCLUSIONS

In the present study we examined the usefulness of AI-based AQUA software for the automated segmentation of structural MRI in a community-based cohort from Singapore. This validation study indicates the usefulness of AQUA in a community-based research cohort on cognitive impairment with efficient and accurate quantification WMH burden and GM atrophy changes in CN, MCI and dementia subjects. AQUA software shows a high correspondence with existing established automated pipelines but is much faster and simpler in execution, thus making it a good candidate for clinical settings.

KEYWORDS

Neuroimaging, clinical validation, automated software

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DIAGNOSTIC EFFICACY OF VISUAL COGNITIVE ASSESSMENT TEST IN CEREBRAL SMALL VESSEL DISEASE AND NEUROIMAGING VALIDATION

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BACKGROUND

Vascular cognitive impairment (VCI) ranks as the second most common cause of cognitive impairment, with VCI possibly being the primary cause in Asia. Cerebral small vessel disease (CSVD) is a key symptom of VCI, characterized by cognitive impairment. Existing cognitive screening tools are mostly designed based on English and Western culture, and their translated versions in Chinese may alter the original neuropsychological properties, affecting their structural validity. The Visual Cognitive Assessment Test (VCAT) is a visual and language-neutral screening tool, potentially more suitable for multicultural, multilingual cognitive screening. Cognitive impairments in CSVD mainly involve deficits in attention and executive function, which are correlated with CSVD's radiological manifestations. However, the correlation between VCAT cognitive domains and CSVD radiological features remains unclear.

OBJECTIVES

To study the diagnostic efficacy of VCAT in identifying cognitive impairment in CSVD patients and its correlation with CSVD radiological features.

METHODS

Inclusion criteria: age 40-80 years; neuroimaging (MR) showing CSVD lesions, including recent subcortical infarcts, white matter hyperintensities, cerebral microbleeds, and enlarged perivascular spaces. Signed informed consent. Participants underwent neuropsychological assessment (NPA), including VCAT, MMSE, MoCA, CDR, Trail Making Test (TMT-A), Digit Span Test (forward and backward), Boston Naming Test (BNT), Rey Auditory Verbal Learning Test (RAVLT), Rey Complex Figure Test (RCFT), Hamilton Depression Rating Scale (HAMD), Hamilton Anxiety Rating Scale (HAMA), and Fried Phenotype Frailty Scale. Activities of daily living (ADL) were assessed. All participants underwent MRI brain scans. VCI diagnosis was made after NPA examination, comparing VCAT and MRI imaging features between two groups. Further analysis was conducted on VCI features.

RESULTS

Patients in the cognitive impairment group were older, with statistically significant differences. The cognitive impairment group had higher levels of glycated hemoglobin and lower levels of uric acid. They also exhibited lower MoCA and VCAT scores, higher anxiety levels, and greater frailty. Grip strength of the right hand was also significantly lower. VCAT showed a positive correlation with MoCA (correlation coefficient 0.73) and with immediate and delayed recall items of the RCFT, backward DSB, BNT, RAVLT, and negative correlation with TMTA, TMAB. The cognitive impairment group had larger volumes of white matter hyperintensities

and higher CSVD total burden, with significant differences. Differential analysis of subcortical nuclei volumes revealed that in the cognitive impairment group, the right thalamic volume was smaller (statistically significant). Analysis of hippocampal subfields showed that in the cognitive impairment group, the right hippocampal head volume was smaller. VCAT total score showed positive correlations with various brain regions including left and right thalamus, hippocampus, amygdala, and fornix, with the strongest correlation observed in the right thalamus (correlation coefficient 0.39). Memory domain score showed significant correlation with left and right thalamus (correlation coefficient 0.43 and 0.44 respectively). VCAT total score also showed positive correlations with various hippocampal subfields, with memory domain score showing the most significant correlation with bilateral hippocampus and its subfields. VCAT memory domain score also showed positive correlations with bilateral amygdala and its subfields, with the left subthalamic nucleus showing the most significant correlation (correlation coefficient 0.46). ROC analysis revealed an area under the curve of 0.843 for VCAT, higher than MoCA, with VCAT showing higher specificity and MoCA showing higher sensitivity. The Youden index for VCAT was 0.531, higher than MoCA.

CONCLUSION

VCAT demonstrated consistency with previous neuropsychological assessment scales, significant correlation with CSVD total burden score, and significant correlation between VCAT scores, memory domain scores, and right thalamic volume. VCAT showed superior diagnostic efficacy for cognitive impairment in CSVD patients compared to MoCA and can be considered as a screening tool for vascular cognitive impairment, especially in CSVD-related cognitive impairment.

KEYWORDS

VCAT, CSVD, cognitive impairment, neuroimaging validation.

NEUROPROTECTIVE EFFECTS OF *FICUS DELTOIDEA* ON SPATIAL MEMORY AND LEARNING IN THE ALZHEIMER'S DISEASE-LIKE RAT MODEL USING BEHAVIORAL AND HISTOLOGICAL METHODS

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BACKGROUND

Alzheimer's disease (AD) is a progressive degenerative condition of the brain characterized by a decline in cognitive function, memory loss, difficulty in performing simple tasks, and changes in mood. Studies indicated that the bioactive compounds derived from natural products not only hold promise in AD management but also exhibit a lower incidence of side effects compared to conventional treatments. Therefore, in this study, *Ficus deltoidea* (FD) as a whole offers therapeutic benefits, with its leaves being particularly rich in a wide array of phytochemical compounds. The present study was aimed at evaluating the neuroprotective effects of FD on spatial memory and learning in the aluminium chloride (AlCl₃) + D-galactose-induced Alzheimer's disease rat model using behavioral and histological indexes.

METHODS

Thirty-six adult male Wistar rats were divided into six groups (I-VI) of six rats each. Group I served as control and administered distilled water (2ml/kg) only, Groups II-VI were the treatment groups; Group II and III were administered with D-gal 60 mg/kg + AlCl₃ 200 mg/kg + Donepezil (3mg/kg); D-gal 60 mg/kg + AlCl₃ 200 mg/kg respectively while Group IV, V and VI were administered D-gal 60 mg/kg + AlCl₃ 200 mg/kg + FD 50 mg/kg; D-gal 60 mg/kg + AlCl₃ 200 mg/kg + FD 100 mg/kg and D-gal 60 mg/kg + AlCl₃ 200 mg/kg + FD 200 mg/kg respectively. All administration was done orally and intraperitoneally for the period of 10 weeks. At the end of the treatment course, the rat's behavioral performance was measured by Radial arm maze (RAM) and Novel Objective Recognition Test (NORT) to test for working, reference memory and recognition memory respectively. Subsequently, the brain samples were collected for histological studies using H&E to assess the general cytoarchitecture and Cox Golgi stain to assess neuronal fibers of the hippocampus and prefrontal cortex.

RESULT

The behavioral tests: RAM and NORT test were evaluated, along with histopathological examination of the hippocampus and prefrontal cortex. The results of the RAM test indicate that the AD-like rats treated with FD exhibit improved spatial working memory, as seen by their reduced search time for the reward compared to the AD model rats. The NORT result showed that, in comparison to the AD model rats, the AD-like rats treated with FD had better recognition memory, as evidenced by their preference for investigating the novel object. H&E results revealed cytoarchitectural changes including, necrosis, vacuolation and neuronal cytoplasmic shrinkage and remarkably decreased of pyramidal neurons in AD model rats-



treated group when compared with the FD treated groups and the control. For the Cox Golgi stain, they were less dendritic neuronal loss and damage in the hippocampus and prefrontal cortex in group IV, V, VI when compared to the AD model rats.

CONCLUSION

The findings from this study showed that FD had a neuroprotective effect against spatial learning, memory dysfunction and degenerative changes induced by AlCl₃+D-galactose in AD models of adult Wistar rats.

KEYWORDS

Alzheimer's Disease, Aluminium chloride, D-galactose, Novel Object Recognition Test, Radial Arm Maze, Hippocampus and Prefrontal cortex

THE ASSOCIATION BETWEEN LEFT VENTRICULAR GEOMETRIC PATTERNS, CORTICAL CEREBRAL MICROINFARCTS, AND COGNITION

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BACKGROUND

Left ventricular (LV) geometric patterns have been associated with cognitive impairment, while the underlying mechanisms remain unclear. The association between LV geometric patterns and cerebral small vessel disease (CSVD), such as lacunes and white matter hyperintensities, suggests that pathological changes in cerebral small vasculature may be a mechanistic link between abnormal LV geometry and cognitive dysfunction. As a novel marker of CSVD, cortical cerebral microinfarcts (CMIs) have been associated with cardiac diseases and biomarkers and are recognized as important risk factors for cognitive impairment and decline. It is worth examining the relationship between LV geometric patterns, cortical CMIs, and cognition. This study aims to investigate the associations of LV geometric patterns with cortical CMIs, cognitive function, and dementia diagnosis and the role of cortical CMIs in the relationship between LV geometry and cognition.

METHODS

LV dimensions were obtained using two-dimensional echocardiography. LV mass index and relative wall thickness were determined to categorize LV geometric patterns. Cortical CMIs were graded on 3T MRI. Cognition was assessed using neuropsychological tests and clinical diagnosis. Linear, Quasi-Poisson, and logistic regression were employed for continuous, count, and binary outcomes, respectively. Mediation analysis was used to examine the effect of cortical CMIs on the association between abnormal LV geometry and cognitive dysfunction.

RESULTS

261 patients (75.3±6.8 years) were enrolled from a memory clinic cohort. Significant associations were observed between concentric LV hypertrophy (LVH) and cortical CMI counts (RR=2.88, 95%CI: 1.07, 7.49) as well as the odds of having vascular dementia (VaD) (OR= 8.38, 95%CI: 1.65, 54.91), after adjusting for demographics, cardiovascular risk factors, and MRI markers of cerebrovascular disease. Cortical CMIs significantly mediated the association between concentric LVH and impairment in global cognition and cognitive domains of visuomotor speed and memory (**Figure 1**).

CONCLUSION

This study found significant associations of concentric LVH with increased cortical CMI counts and higher odds of dementia of VaD type. The relationship between concentric LVH and cognitive dysfunction was mediated by cortical CMIs, suggesting that LV structural abnormality may impair cognition, possibly due to vascular pathologies related to CSVD, including cortical CMIs.

KEYWORDS

Left Ventricular Hypertrophy, Cerebrovascular Disease, Dementia

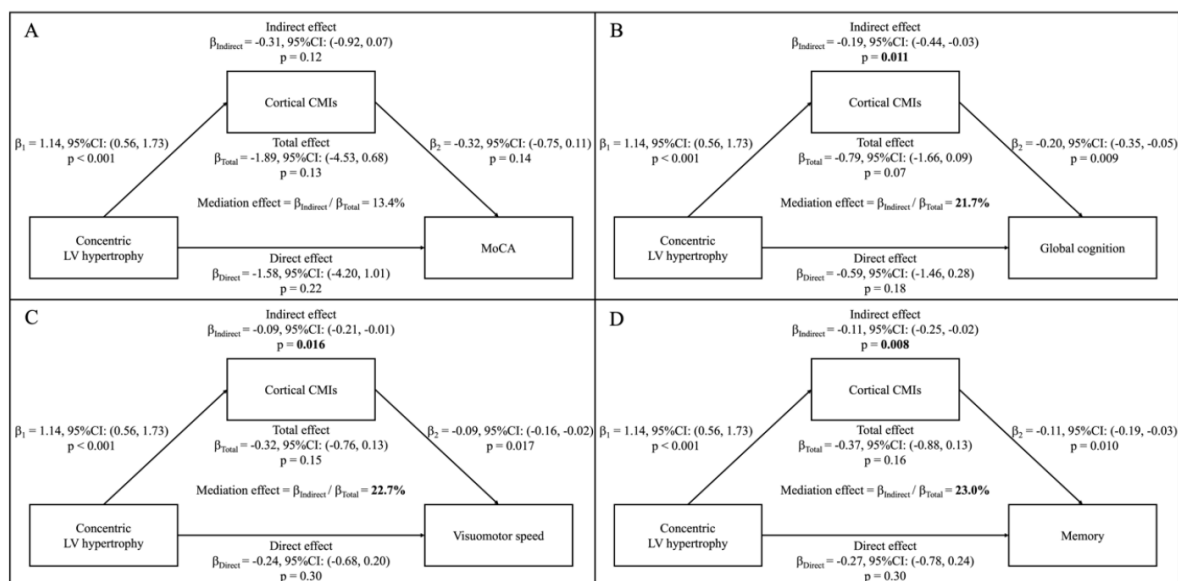


Figure 1. Mediation analysis

Mediation analysis was employed to examine the effect of cortical cerebral microinfarct (CMIs) in the relationship between concentric left ventricular hypertrophy and Montreal Cognitive Assessment (MoCA) (A), global cognition (B), as well as cognitive domains of visuomotor speed (C) and memory (D), after adjusting for age, sex, body mass index, years of education, hypertension, hyperlipidemia, diabetes, smoking status, and significant cerebrovascular disease burden. 21.7% of the association between concentric left ventricular hypertrophy and impaired global cognition was mediated by cortical CMIs.

THE ASSOCIATION BETWEEN LEFT VENTRICULAR DYSFUNCTION, CEREBRAL SMALL VESSEL DISEASE, AND COGNITIVE IMPAIRMENT

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BACKGROUND

Cognitive impairment and dementia are common in heart failure patients. Further investigation is required to determine whether brain vascular lesions serve as potential mechanisms underlying the association between left ventricular dysfunction and cognitive impairment. This study aims to examine the relationship between echocardiographic parameters of LV function, MRI markers of cerebral small vessel disease (CSVD), and cognition.

METHODS

LV ejection fraction (LVEF) and global longitudinal strain (GLS) were utilized to assess LV systolic function, while septal annular early-diastolic velocity (e'), lateral e', mitral inflow early-diastolic velocity (E) to average e' (average E/e'), tricuspid regurgitation (TR) velocity, and left atrial volume index (LAVI) were used to assess LV diastolic function. CSVD markers, including cortical cerebral microinfarcts (CMIs), lacunes, white matter hyperintensities (WMHs), and cerebral microbleeds (CMBs), were graded on 3T MRI. Cognition was assessed using neuropsychological tests and clinical diagnosis. Multivariable linear and logistic regression were employed for continuous and binary outcomes, respectively. Mediation analysis was used to examine the effect of CSVD markers on the association between LV dysfunction and cognitive impairment.

RESULTS

261 participants (75.26±6.77 years) were recruited from a memory clinic cohort. LVEF and GLS were significantly associated with presence of cortical CMIs and lacunes, in the fully-adjusted model (**Table 1**). Parameters of diastolic function, including average E/e', TR velocity, and LAVI, were also associated with cortical CMIs. GLS was significantly associated with global cognition z-scores ($\beta=-0.12$, 95%CI: -0.22, -0.01) and the odds of vascular dementia (VaD) (OR= 1.75, 95%CI: 1.25, 2.84), after adjusting for demographics and cardiovascular risk factors. These associations became nonsignificant after adjusting for cortical CMIs and lacunes. Mediation analysis showed that cortical CMIs and lacunes significantly mediated the association between GLS and global cognition.

CONCLUSION

This study found significant associations of LV systolic and/or diastolic function with presence of cortical CMIs, lacunes, global cognitive function, and dementia of VaD type. The association between decreased GLS and impaired global cognition was mediated by cortical CMIs and lacunes. These findings suggest that vascular pathologies related to CSVD may be potential mechanisms linking LV dysfunction and associated cognitive impairment.

KEYWORDS

left ventricular dysfunction, cerebrovascular disease, dementia

Table 1. Association of left ventricular systolic and diastolic function with MRI markers of cerebral small vessel disease*

Exposure variables	Cortical CMIs OR (95% CI), p-value		Lacunes OR (95% CI), p-value		Extensive WMHs OR (95% CI), p-value		CMBs OR (95% CI), p-value	
	Model 1 [†]	Model 2 [‡]	Model 1 [†]	Model 2 [§]	Model 1 [†]	Model 2	Model 1 [†]	Model 2 [#]
LV systolic function								
Presence of LV systolic dysfunction	4.63 (1.85, 11.61), p=0.001	4.97 (1.87, 13.27), p=0.001	2.68 (1.21, 6.02), p=0.015	2.64 (1.10, 6.40), p=0.029	1.25 (0.56, 2.94), p=0.59	0.72 (0.29, 1.82), p=0.48	1.24 (0.58, 2.64), p=0.57	0.85 (0.37, 1.93), p=0.70
LVEF (%)	0.92 (0.87, 0.96), p<0.001	0.89 (0.83, 0.94), p<0.001	0.96 (0.92, 0.99), p=0.028	0.95 (0.91, 0.99), p=0.010	1.02 (0.99, 1.06), p=0.16	1.05 (1.02, 1.10), p=0.006	1.01 (0.98, 1.04), p=0.56	1.03 (0.99, 1.07), p=0.12
GLS (%)	1.28 (1.11, 1.50), p<0.001	1.30 (1.11, 1.54), p=0.002	1.23 (1.09, 1.40), p=0.001	1.21 (1.06, 1.39), p=0.006	1.12 (1.00, 1.26), p=0.06	1.05 (0.92, 1.19), p=0.49	1.05 (0.95, 1.17), p=0.36	0.99 (0.88, 1.11), p=0.81
LV diastolic function								
Presence of LV diastolic dysfunction	2.90 (1.14, 7.44), p=0.025	3.41 (1.22, 9.79), p=0.020	0.64 (0.28, 1.40), p=0.28	0.52 (0.20, 1.23), p=0.15	1.00 (0.49, 2.04), p=1.00	0.96 (0.45, 2.05), p=0.92	1.17 (0.60, 2.27), p=0.63	1.16 (0.58, 2.32), p=0.67
Average E/e', per SD	1.80 (1.20, 2.71), p=0.004	1.90 (1.22, 2.97), p=0.004	0.98 (0.70, 1.35), p=0.89	0.92 (0.64, 1.30), p=0.63	1.16 (0.86, 1.60), p=0.35	1.11 (0.81, 1.55), p=0.51	0.99 (0.75, 1.32), p=0.97	0.94 (0.70, 1.26), p=0.68
Septal e', per SD	0.70 (0.45, 1.05), p=0.09	0.78 (0.50, 1.21), p=0.27	0.77 (0.54, 1.07), p=0.12	0.82 (0.57, 1.17), p=0.28	0.69 (0.50, 0.93), p=0.018	0.73 (0.53, 1.00), p=0.05	1.07 (0.81, 1.42), p=0.64	1.17 (0.87, 1.57), p=0.31
Lateral e', per SD	0.75 (0.49, 1.12), p=0.17	0.78 (0.49, 1.19), p=0.25	0.92 (0.66, 1.26), p=0.60	0.93 (0.66, 1.29), p=0.65	0.90 (0.67, 1.19), p=0.45	0.92 (0.68, 1.23), p=0.57	1.08 (0.83, 1.42), p=0.56	1.13 (0.85, 1.50), p=0.40
TR velocity, per SD	1.78 (1.21, 2.72), p=0.005	1.84 (1.23, 2.89), p=0.005	1.10 (0.81, 1.50), p=0.54	1.09 (0.79, 1.53), p=0.60	0.90 (0.67, 1.20), p=0.48	0.81 (0.59, 1.11), p=0.19	1.05 (0.80, 1.38), p=0.72	1.00 (0.75, 1.32), p=0.98
Left atrial volume index, per SD	1.52 (1.05, 2.14), p=0.020	1.52 (1.04, 2.17), p=0.022	1.18 (0.87, 1.58), p=0.26	1.08 (0.78, 1.49), p=0.62	1.03 (0.78, 1.38), p=0.82	0.94 (0.70, 1.28), p=0.70	1.32 (1.00, 1.75), p=0.05	1.27 (0.96, 1.74), p=0.11

*Results are denoted in bold if reaching statistical significance.

[†]Adjusted for demographics (age, gender, body mass index, and years of education) and cardiovascular risk factors (hypertension, hyperlipidemia, diabetes, smoking status).

[‡]Adjusted for demographics, cardiovascular risk factors, lacunes, extensive WMHs, and CMBs.

[§]Adjusted for demographics, cardiovascular risk factors, cortical CMIs, extensive WMHs, and CMBs.

^{||}Adjusted for demographics, cardiovascular risk factors, cortical CMIs, lacunes, and CMBs.

[#]Adjusted for demographics, cardiovascular risk factors, cortical CMIs, lacunes, and extensive WMHs.

Abbreviation: CMB, cerebral microbleed; CMI, cerebral microinfarct; GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; TR, tricuspid regurgitation; WMH, white matter hyperintensity.

COGNITIVE IMPAIRMENT AMONG ELDERLY PATIENTS WITH CHRONIC ILLNESS ATTENDING PRIMARY CARE AND ITS ASSOCIATION WITH CARDIOVASCULAR RISK USING THE FRAMINGHAM RISK SCORE

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BACKGROUND

Dementia is a major public health burden, particularly among the elderly population with significant implications for individuals, caregivers, and society. Identifying mild cognitive impairment early can facilitate timely intervention and care. This cross-sectional study is aimed to investigate the association between Framingham Risk Score (FRS), a widely used tool for cardiovascular disease (CVD) risk prediction with cognitive impairment among elderly patients with chronic illness in Malaysia.

METHODS

A total of 289 participants aged 60 years and above with chronic illness were recruited from Klinik Primer Hospital Tuanku Chanselor Muhriz using a computer generator simple random sampling. The Montreal Cognitive Assessment Bahasa Malaysia version (MoCA-BM) was used to assess cognitive function and FRS was calculated based on CVD risk factors

RESULTS

The prevalence of cognitive impairment among the participants was found to be 19.7%. Using Multiple Logistic Regression, age (AOR 1.101, 95%CI = 1.041, 1.163, $p < 0.001$), systolic blood pressure (AOR 1.048, 95%CI = 1.024, 1.072, $p < 0.001$) and being diabetic (AOR 2.655, 95%CI = 1.194, 5.906, $p = 0.017$) increases the odds of having cognitive impairment among elderly patients with chronic illness while having secondary education (AOR 0.087, 95%CI = 0.008, 0.963, $p = 0.047$) and higher education (AOR 0.037, 95%CI = 0.002, 0.833, $p = 0.038$) reduces the likelihood of having cognitive impairment. Individuals with higher FRS showed a greater likelihood of cognitive impairment (AOR 1.099, 95%CI = 1.049, 1.172, $p < 0.001$). The optimal cut-off point for FRS to determine cognitive impairment is 30 for males and 18.5 for females with a sensitivity and specificity of 84.4% & 51.2% for males and 76% & 63.1% respectively.

CONCLUSION

These findings suggest that FRS, originally designed for CVD risk assessment may also serve as a valuable predictive tool for cognitive impairment among elderly patients with chronic illness. Integrating FRS into routine primary care assessments could enhance the early identification of individuals at risk and enable appropriate cognitive screenings and interventions. Further research such as a longitudinal cohort study in a larger and more diverse population is warranted to validate these CVD risks' association with the development of dementia.

KEYWORDS

Framingham Risk Score, Elderly, Cognitive Impairment

COGNITIVE CARD INTERVENTION PROGRAM: A PRELIMINARY STUDY ON COGNITIVE FUNCTION, EMOTIONAL PERFORMANCE, AND QUALITY OF LIFE

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BACKGROUND

The study aims to gather concrete data on how cognitive interventions can influence cognition, emotions, and overall quality of life. It focuses on individuals with Mild Cognitive Impairment (MCI) and Subjective Cognitive Decline (SCD), conditions that may precede Alzheimer's disease (AD). While not definitive indicators of AD, MCI and SCD could serve as early alerts. In Taiwan, there's a rising interest in cognitive rehabilitation programs, though the use of cognitive cards and comprehensive case studies by healthcare professionals remains rare. This research seeks to fill that gap with solid evidence.

METHOD

Taiwan's National Palace Museum collaborated with us to develop cognitive cards. Participants were recruited from neurology clinics at Taipei Veterans General Hospital and dementia day care centers nearby. To be eligible, participants needed a score of 23-28 on the Mini-Mental State Examination (MMSE) and at least six years of education. The study involved pre- and post-tests for both the intervention group, which used the cognitive cards for a month, and the control group, which viewed a museum video. The cognitive cards, enriched with traditional Taiwanese customs, aimed to evoke personal memories and stories. Experts guided the participants through various memory-enhancing techniques like visual association and cued recall during weekly sessions. The goal was to help participants improve or sustain their memory abilities. To evaluate the intervention's impact, the study employed several assessments, including the MMSE, Wechsler Memory Scale's Logical Memory subtest (LM), Free and Cued Selective Reminding Test (FCSRT), Taiwan Geriatric Depression Scale (TGDS), and the WHO Quality of Life-BREF (WHO-QOLBREF).

RESULTS

The study involved 50 participants, split into an intervention group of 27 and a control group of 23. No significant differences were observed in Clinical Dementia Rating (CDR) and MMSE scores between the groups. The participants had an average age of 70.2 ± 9.0 years, with 40% male and 60% female representation. Statistical analysis using the paired t-test revealed significant enhancements in several memory recall tests: LM test first recall ($p = 0.04$), LM test second recall ($p = 0.02$), FCSRT-immediate recall ($p = 0.007$) and FCSRT-2nd delayed recall ($p = 0.04$). These results suggest improvements in both auditory and visual memory recall abilities. However, within the intervention group, scores for MMSE ($p = 0.07$), CDR ($p = 0.50$), TGDS ($p = 0.75$), and WHOQOL-BREF ($p = 0.89$) showed no significant post-intervention changes. The control group did not exhibit any significant alterations in psychological assessments.



CONCLUSION

The cognitive card intervention program demonstrates a beneficial effect on certain cognitive abilities. The study's robustness is evident through the use of sophisticated neuropsychological tests. These interventions are tailored and specific, blending elements of the humanities, history, art, and healthcare to create culturally resonant and age-appropriate cognitive cards for participants. Given the lack of significant changes of mood and quality of life observed within a one-month timeframe, the study suggests that a longer period of observation may be necessary to fully understand the effects of cognitive interventions.

KEYWORDS

Cognitive intervention, Subjective Cognitive Decline, Mild Cognitive Impairment, Memory capacity, Cognitive function

CHALLENGES AND EXPERIENCES IN RECRUITMENT FOR A MULTIDOMAIN LIFESTYLE INTERVENTION STUDY TO PREVENT COGNITIVE DECLINE: COMPARISON OF RECRUITMENT STRATEGIES IN A SINGLE RECRUITING SITE FOR THE SINGAPORE GERIATRIC INTERVENTION STUDY TO REDUCE COGNITIVE DECLINE AND PHYSICAL FRAILTY (SINGER) STUDY.

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BACKGROUND

Recruiting participants successfully and in a timely manner is essential for the success of randomized controlled trials [1], especially in dementia prevention studies targeting at-risk populations. Data suggests that individuals from minority and low socioeconomic settings were underrepresented in clinical research studies, which compromises the generalisability of results and widens health disparities [2]. Furthermore, there is a lack of discussion on recruitment strategies in dementia-related studies within Asian settings. To address this gap, we examined the recruitment strategies used in the SINGER study [3], a large multidomain lifestyle intervention dementia prevention trial in Singapore.

The SINGER study started recruitment in August 2021 at the National University Health System (NUHS), and later joined by a site based in Nanyang Technological University (NTU) in March 2023. NUHS, the primary recruiting site, enrolled n=921 (76%) of the total participants (n=1212). This analysis was to inform strategies for future studies using recruitment data from the primary recruiting site in NUHS. The analysis aims to identify the most effective recruitment strategy and recruitment strategies that better engage participants with higher risks and lower education attainment. We hypothesized that we will be able to observe education and risk differences in participants from the different recruitment strategies.

METHODS

The study used recruitment data to analyse the effectiveness of different strategies for recruiting participants. The strategies included recruiting from existing clinical research databases, approaching community survey participants, media coverage releases, community-based outreach, and referrals from existing participants and others.

Descriptive analyses were used to determine the number and percentage of participants recruited. The relationship of recruitment strategies with recruited participants' sociodemographic factors (age, sex, education), CAIDE score (Cardiovascular Risk Factors, Aging, and Incidence of Dementia risk score) was compared: continuous variables using ANOVA with post hoc Bonferroni comparisons where applicable, and categorical data using a chi-square test.

RESULTS

At the end of study recruitment, the NUHS site screened n=2845 community dwelling seniors, and enrolled a total of n=921, yielding an overall successful enrolment rate of 32.3%. The method with the highest yield was the referrals from existing participants (42.3%). Community related sources provided the next best yield rates, 39.6% (large community survey) and 25.8% (community outreach activities). Participants recruited from referrals were also younger, were of lower risk of

dementia (CAIDE score) and were highly educated. Participants from clinical and community settings had higher risks and lower educational attainment.

CONCLUSION

Media release, community-based activities, and outreach efforts played a significant role in the recruitment of participants, which spurred the growth of increased referrals later on. Previous studies have shown that recruitment strategies that increases the health awareness and implications were more likely to succeed [4]. Also, the success of the individual recruitment methods were also dependent on the sociodemographic factors of participants [5–7]. Careful targeting of the recruitment methods according to the population of interest need to be considered in future studies.

KEYWORDS

Multidomain trials, Dementia prevention, recruitment strategies, community-based

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PREDICTORS AND REASONS FOR NON-THROMBOLYSIS IN ACUTE ISCHAEMIC STROKE IN SEBERANG JAYA HOSPITAL

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INTRODUCTION

Stroke is the leading cause of acquired disability in adults and the second leading cause of mortality worldwide. Intravenous Thrombolysis (IVT) with tissue plasminogen activator (tPA) is a standard treatment for acute ischemic stroke, yet it remains underutilised. Understanding the predictors of non-thrombolysis can provide strategies to improve acute stroke care delivery and outcomes. Our aim is to identify reasons and barriers for non-thrombolysis in acute ischemic stroke patients who presented within 4.5-hour window to Seberang Jaya Hospital (HSJ).

METHOD

This is a retrospective cross sectional study involving stroke code activations from 1st January 2019 till 31st December 2023 in HSJ. All clinically acute stroke patients who presented to emergency department HSJ within 4.5 hours from onset of were included. Patients who were arrived outside the 4.5-hour time frame were excluded. Data were retrieved from HSJ stroke code registry Google Form and analysed using SPSS version 17.0.

RESULT

A total of 1441 stroke codes with known onset time within 4.5 hours were activated during the 5-year period. Only less than a quarter ($n = 309$, 21.4%) of them received thrombolysis. Among the main reasons for non-thrombolysis were presence of absolute contraindications (intracranial bleed: $n = 207$, 14%; stroke mimics: $n = 171$, 12%), low NIHSS score ($n = 470$, 33%), established infarct ($n = 312$, 22%), and rapid improvement in NIHSS ($n = 46$, 3%). Only 1% of the patients ($n = 19$) refused thrombolysis. Our study analysis showed that patients presented between 3 to 4.5 hours since symptom onset has significantly lower thrombolysis rate compared to their early counterpart whom presented within the first 3 hours (15.6% vs 20.5%, $p = 0.038$). Mild stroke with NIHSS score < 6 and those arrived with own transport also tend not to receive thrombolysis (95.2% vs 65.7%, $p < 0.001$; 83.1% vs 76.0%, $p = 0.043$). Gender and age, however, did not affect the thrombolysis rate in our centre.

CONCLUSION

Despite increasing use of IVT in stroke management in these recent years, there is still significant proportion of patients not receiving thrombolysis. Identification of barriers to thrombolysis is crucial in improving the delivery of timely stroke care and outcome. Improvement in awareness of stroke and utilization of EMS among public can be a stepping stone to significantly reduce the gap for better utilization of thrombolysis.

INTERPLAY OF CEREBRAL BLOOD FLOW, BRAIN VOLUME, AND COGNITIVE FUNCTION IN DEMENTIA PATHOLOGIES

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Background

Decreased cerebral blood flow (CBF), linked to early Amyloid β deposition, is a potential early biomarker for Alzheimer's disease (AD). Dementia-related brain volume (BV) reduction may obscure true CBF changes. This study investigates the interplay between CBF, BV, and cognitive function assessed by the Mini-Mental State Examination (MMSE) across various dementia pathologies.

Methods

We recruited 64 patients for a dementia screening study. The participants underwent 4D flow MRI and 3D T1WI. We quantified CBF and BV and analyzed these measures against MMSE scores. Differences in patient demographics and clinical outcomes among normal, AD, and non-AD groups were statistically evaluated using ANOVA.

Results

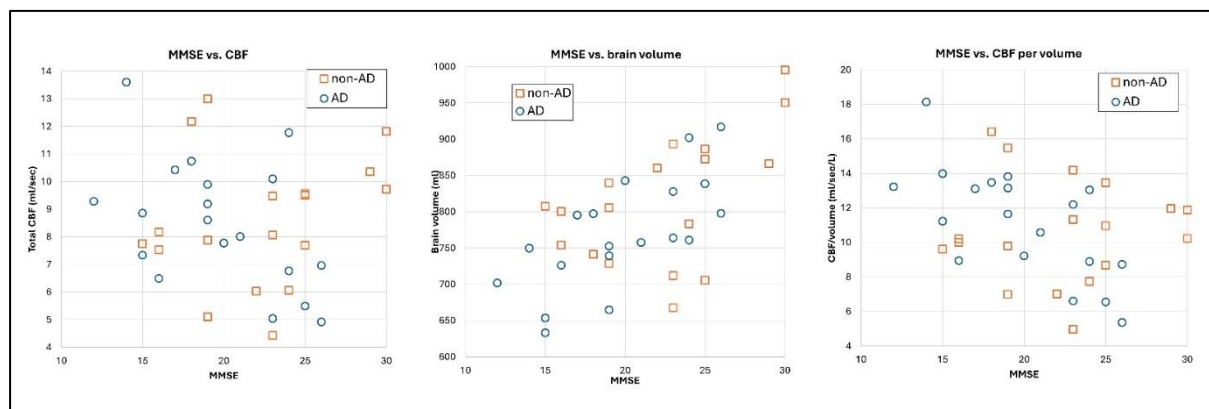
Of the original cohort, 48 patients were analyzed after excluding cases with missing data or unsuitable parameters. The analysis revealed no significant differences in age, BV, or CBF among the groups. However, MMSE scores varied significantly ($p < 0.001$), with a notable positive correlation between MMSE scores and BV in the total population ($r=0.517$), strongest in the non-AD group ($r=0.702$). Contrary to expectations, MMSE scores did not correlate positively with CBF. In the AD group, there was a significant negative correlation between CBF per BV ($r=-0.673$).

Conclusion

Our findings suggest a specific link between reduced BV and altered CBF in Alzheimer's disease, which could assist in differentiating and stratifying disease pathology. This relationship underscores the complexity of cerebral changes in dementia and the potential compensatory mechanisms that may influence disease progression and diagnosis.

KEYWORDS

Alzheimer's disease, 4D Flow MRI, cerebral blood flow



EXPLORING DEMENTIA AWARENESS IN COMMUNITY INITIATIVES: A KNOWLEDGE ASSESSMENT STUDY

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BACKGROUND

The prevalence of dementia among individuals aged 60 and above in Malaysia stands at 8.5%, and is expected to increase as Malaysia become an aged nation by 2030. However, there is lack of assessment regarding the local community's understanding of dementia. Therefore, we assessed the public basic knowledge of dementia during two community health screening projects.

METHODS

This cross-sectional study evaluated participants from two community health screening projects conducted at a local park and the main lobby of a prominent general hospital during the final quarter of 2023. We employed a validated questionnaire developed by MF Ali et al. (2023), consisting of seven true or false statements assessing basic knowledge about dementia, with Malay translations adapted for our local context. Originally derived from the Northern Ireland Life and Times (NILT) Survey 2010, this questionnaire was utilized to determine participants' awareness levels. A scoring system ranging from 0 to 4 or wrong answer for the critical statement "Dementia is a part of the normal process of aging", indicating low awareness; 5 denoting medium awareness; and ≥ 6 indicating high awareness; was applied. The cumulative score from this section was utilized to explore factors associated with awareness levels. The Mini-Cog test was used to screen for cognitive impairment (score of <3).

RESULTS

The majority of the 196 participants were female (65.3%), Malay (57.7%), with a median age of 65 (interquartile range [IQR] 8) years. A striking 91.5% of participants demonstrated a low level of awareness regarding dementia, with a median awareness score of 4 (IQR 1), and 19.3% were likely to have cognitive impairment. The statement "Dementia is a part of the normal process of aging" was the most incorrectly answered (80.9%), followed by "Dementia is another term for Alzheimer's disease" (62.6%), "Dementia can be cured" (57.8%), and "Dementia is a mental illness" (55.1%). Conversely, statements such as "People who eat healthily and exercise are less likely to get dementia" received the highest correct responses (81.1%), followed by "Dementia is a disease of the brain" (78%) and "There are many different types of dementia" (72%).

No significant associations were found between the level of dementia awareness and age, gender, race, or cognitive impairment.

CONCLUSION

The community health screening revealed that 91.5% of participants had low awareness of dementia, with 81% believing it's a normal part of aging. These figures are significantly higher than those from a 2012 survey in Northern Ireland, where only 49% had low awareness and 28% thought dementia was part of aging. Therefore, there is urgent necessity for intensified educational efforts and increased promotion aimed at fostering a deeper understanding of dementia within the community.

KEYWORDS

Dementia awareness, Dementia knowledge, Dementia Community Initiatives

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PLASMA P-TAU181 IS ASSOCIATED WITH EXECUTIVE DYSFUNCTION IN AN A β -NEGATIVE SOUTHEAST ASIAN POPULATION - BIOMARKERS AND COGNITION STUDY, SINGAPORE (BIOCIS)

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BACKGROUND

Early changes in preclinical Alzheimer's disease (AD) are detectable through cognitive tests of executive function and episodic memory as well as blood-based biomarkers. Recent research indicates that A β 42 and p-tau181 are critical for identifying A β accumulation and tau deposition, enhancing the prediction of cognitive decline and potential progression to dementia. This capability is vital for devising effective treatment strategies. This study examines the relationship between plasma P-Tau181 levels and cognitive outcomes in an A β -negative Southeast Asian cohort, thereby evaluating its predictive value for cognitive decline and its potential utility in dementia prevention strategies, independently of the traditional amyloid cascade hypothesis.

METHODS

Our sample included baseline data of 400 participants from the Biomarkers and Cognition Study, Singapore (BIOCIS). Participants underwent cognitive assessments for executive function, processing speed and visuospatial skills (WAIS-R Digit Symbol Substitution Test–DSST and WAIS-IV Block Design Task–BDN) and episodic memory (WMS-IV Logical Memory subtest–LM). Blood-based biomarkers (p-tau181, A β 42, A β 40) were assessed using Quanterix's Single Molecule Array (Simoa) technology on the HD-X Analyzer platform. All included participants were classified as A β -negative based on established clinical cutoffs (A β 42/40 $\geq$ 0.05).

RESULTS

Descriptive statistics of the sample ($M_{\text{age}}=59.84$, $M_{\text{education}}=14.20$ years, 43% male) are reported in Table 1. Regression analyses were run on all cognitive measures, while controlling for age, gender, education, and A β 42/40 ratio. P-Tau181 was found to be a significant predictor of DSST ($B=-4.00$, $t=-2.00$, $p=.0462$) and BDN ($\text{OR}_{\text{odds ratio}}=0.55$, 95% CI $(-1.13, -0.07)$, $p=.0255$), but not LM scores ($B=0.54$, $t=1.00$, $p=.3183$).

CONCLUSION

Our findings highlight a significant correlation between elevated plasma P-Tau181 levels and compromised executive function and visuospatial skills in A β -negative individuals in a prodromal Southeast Asian cohort., challenging the amyloid cascade hypothesis. This suggests that tau phosphorylation may independently influence cognitive decline. These insights

underscore the importance of further longitudinal studies to substantiate these results and refine diagnostic and therapeutic strategies for dementia.

KEYWORDS

Alzheimer's disease; plasma p-tau181, β -amyloid, plasma biomarkers, executive function

Table 1. Demographics and Descriptives

Descriptives	n = 400
Age [$M \pm SD$]	59.84 $\pm$ 10.50
Male [N , %]	171 (43%)
Education (in years)	14.20 $\pm$ 3.54
p-tau181 [$M \pm SD$]	2.87 $\pm$ 0.37
A β 42/40 [$M \pm SD$]	.0630 $\pm$.0105

Table 2. Multiple linear regression model coefficients – WAIS-R Digit Symbol Substitution Test

Predictors	B	SE	β	t	p	95% CI	
						Lower	Upper
p-tau181	-4.00	2.00	-0.09	-2.00	0.0462	-7.93	-0.07
A β 42/40	81.25	65.00	-0.05	1.25	0.2120	-46.54	209.03
Age	-0.62	0.07	-0.40	-8.39	< .0001	-0.77	-0.48
Gender	4.67	1.39	0.14	3.36	.0009	1.94	7.41
Education	1.21	0.20	0.26	5.92	< .0001	0.81	1.61

Note. CI = confidence interval

Table 3. Ordinal logistic regression model coefficients – Block Design Task

Predictors	B	Odds ratio	p	95% CI	
				Lower	Upper
p-tau181	-0.60	0.55	0.0255	-1.13	0.07
A β 42/40	-0.10	0.91	0.9911	-17.20	17.46
Age	0.01	1.01	0.1738	-0.01	0.03
Gender	-0.02	0.98	0.9343	-0.39	0.36
Education	-0.05	0.95	0.0924	-0.10	0.01

Note. CI = confidence interval

CARING FOR THE CAREGIVER: IDENTIFYING RELATIONSHIP OF SPECIFIC ITEMS ON NEUROPSYCHIATRIC INVENTORY TO CAREGIVER DISTRESS IN DEMENTIA

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BACKGROUND

Dementia represents a multifaceted neurocognitive disorder characterized by decline in cognitive functions and functional impairment including behavioral and psychological symptoms in dementia (BPSD) such as agitation, aggression, psychosis, depression, and anxiety. BPSD were identified as one of the essential variables that impact caregiver distress. This study aims to identify the relationship of specific items on Neuropsychiatric Inventory (NPI) with caregiver distress among dementia patients.

METHODS

This is a cross-sectional study. All dementia patients with BPSD aged 60 years old and above who attended Psychogeriatric clinic in Hospital Pulau Pinang between March 2023 until February 2024 were included. The types and stages of dementia were diagnosed based on Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5). Their outpatient medical records including highest NPI assessment throughout their visits were reviewed and analyzed.

RESULTS

This study included 55 patients with a mean $\pm$ SD age of 76.1 $\pm$ 7.2 years old. More than half of the patients were female 35(63.6%), majority being Chinese 43(78.2%) and two-third were living with family 37(67.3%). Amongst, the types of dementia distributions were Alzheimer disease 22(40.0%), vascular disease 19(34.5%) and mixed type 14(25.5%). It was noted that 31(56.4%) patients were in moderate stage dementia while 18(32.7%) and 6(10.9%) were in severe and mild stages of dementia respectively. The three most common BPSD reported were irritability 27(49.1%), followed by agitation 25(45.5%) as well as sleep and nighttime behavior disorders 21(38.2%); while least common BPSD were elation 1(1.8%), aberrant motor behavior 7(12.7%) and disinhibition 8(14.5%). The total NPI 12 items score has a median(IQR) of 15(12.2, 18.8). 80% of caregivers reported certain level of distress, with median(IQR) of 4(4.1, 7.3). Simple linear regression noted no significant association between sociodemographic, dementia type, dementia severity and majority of BPSD with caregiver distress, except being Chinese, hallucination, irritability and agitation. While multiple linear regression formulated a final model equation of: Total Caregiver Distress (predicted) = 3.15 + 0.49 (Hallucination) + 0.72 (Agitation) + 0.65 (Irritability), as shown in Table 1.

Table 1: Factors associated with Total Caregiver Distress among the study population (n=55)

Variables	Simple Linear Regression			Multiple Linear Regression*			
	b**	95% CI	p-value	Adj. b**	95% CI	t-stat	p-value
Chinese	-4.22	-8.07, -0.37	0.032	-	-	-	-
Hallucination	0.56	0.09, 1.03	0.021	0.49	0.10, 0.85	2.57	0.013
Agitation	1.11	0.58, 1.64	<0.001	0.72	0.20, 1.25	2.79	0.007
Irritability	0.98	0.60, 1.36	<0.001	0.65	0.25, 1.05	3.24	0.002

*The model fits well ($R^2 = 0.47$) with assumptions met. There is no interaction and multicollinearity problem.

** Crude regression coefficient; *** Adjusted regression coefficient

CONCLUSION

Our study concludes that symptoms of hallucination, agitation and irritability contributes significantly to caregiver distress among dementia patients. Therefore, focusing on symptomatic control of these symptoms would hopefully lessen the distress experienced by dementia caregivers.

KEYWORDS

Dementia, BPSD, NPI, caregiver distress

DEVELOPMENT AND VALIDATION OF THE RECOGNAIZE APP FOR DETECTION OF VASCULAR MILD COGNITIVE IMPAIRMENT USING DIGITAL GAMIFIED ASSESSMENTS

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BACKGROUND

Vascular Cognitive Impairment (VCI) is the second most common cause of dementia after Alzheimer's Disease (AD) (Gorelick et al., 2011). The coexistence of cerebrovascular pathology with AD pathology adds complexity to the diagnosis and treatment of VCI, underscoring the importance of early identification.

The growing focus on disease-specific interventions highlights the need for a deeper understanding of the underlying pathology of cognitive impairments for effective intervention (Iadecola et al., 2019). However, current tools do not cater to VCI specifically which necessitates the need for a scalable method of early diagnosis of VCI (Zygouris et al., 2020).

OBJECTIVES

1. To understand the cognitive and behavioural domain impairments manifested due to Cerebrovascular Disease (CVD)
2. Creation of digital games to assess specific cognitive and behavioural domains for CVD
3. To detect presence of VCI using a machine learning model for the digital games

METHODS

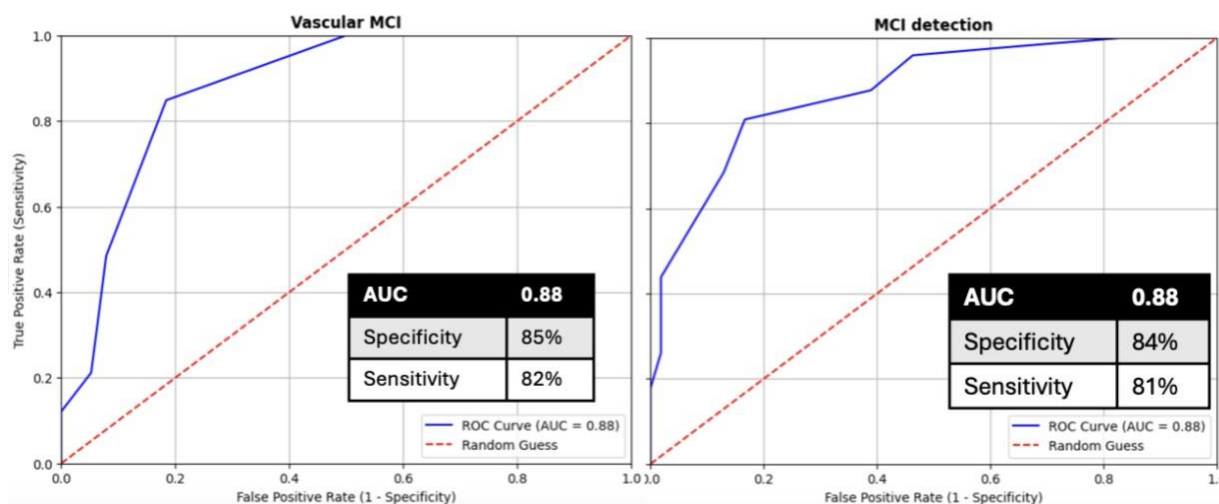
The data of 389 subjects from the Biomarker and Cognition Study (BIOCIS) at the Dementia Research Centre (Singapore), classified into Cognitively Normal (CN) and MCI, with detailed neuropsychological information and cognitive and behavioural domain impairment information was analysed. T2-weighted FLAIR imaging was used to quantify subjects' White Matter Hyperintensities (WMH) load.

Subjects with MCI and high WMH load had significantly more executive dysfunction and lower processing speed along with higher impulse dyscontrol and increased apathy. These domains were used to create 4 simplified multi-domain digital games.

140 new subjects (60 with MCI) were recruited for the validation of the developed digital games. Out of the 60 subjects with MCI, 30 had a high WMH load and they were in the Vascular MCI group.

RESULTS

A combined game score derived from the game features, was able to detect MCI from CN with an Area Under the Curve (AUC) of 0.88 as well as detect high CVD from low CVD with an AUC of 0.88 as shown in the figure below.



CONCLUSION

The ReCOGNAlze app has shown promising results in detecting MCI and CVD which can be used to screen people in the community at a higher risk of developing dementia and stroke, to be referred to specialists.

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NEUROPSYCHIATRIC AND NEUROBEHAVIORAL PROFILE OF FRAIL SE ASIANS WITH AND WITHOUT CEREBROVASCULAR DISEASE

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INTRODUCTION

In recent literature, the relationship of cerebrovascular disease and frailty has been increasingly recognised. Studies are examining how cerebrovascular disease, including stroke, white matter hyperintensities and cerebral microbleed correlates with frailty. Additionally, with decreased physiological reserves, frail individuals are found to be more vulnerable to incident cerebrovascular disease (Evans et al., 2022). Although cerebrovascular disease has been associated with a faster decline in memory and processing speed that occurs normally with age, our study shows that frailty with cerebrovascular disease, is associated with slower processing speed, independent of age.

METHODS

In our study, 221 frail participants (mean age = 62 years; males = 43.0%) with cerebrovascular disease in the Biomarkers and Cognition Study, Singapore (BIOCIS) were recruited from the Dementia Research Centre Singapore (DRCS). Participants underwent neuroimaging (MRI), comprehensive neuropsychological assessments, and lifestyle and demographic questionnaires.

Frailty was measured using the Fried frailty phenotype questionnaire, comprising of five components (weakness, slowness, unintentional weight loss, exhaustion, and low physical activity). A score of 0 on the fried phenotype questionnaire was considered non-frail, while 1 or 2 was considered as pre-frail, and 3 and above was categorized as frail. Due to the limited sample size, both pre-frail and frail participants were considered as frail for the study (Soo et al., 2023). Additionally, cerebrovascular disease was measured using the Staals criteria on the Fazekas WMH scale. Participants with a Fazekas's score of 0 were classified as CSVD-, while those who scored 1 and above were classified as CSVD+.

RESULTS

Our study showed that the performance on coding was significantly associated to frailty with cerebrovascular disease, controlling for covariates ($p < 0.05$). Fig. 1 summarises the demographic factors and tests representative of each cognitive domain.

Variables	Frail CSVD- N= 70	Frail CSVD+ N=152	P-value	Adjusted P (controlling for covariates)
Age, mean, n (%)	54.97(9.93)	65.55(9.32)	<0.001	
Sex, male, n (%)	28(40%)	67(44.4%)	0.562	
Education, mean (SD)	14.43(2.92)	13.97(3.98)	0.336	
MoCA_raw	26.19(2.85)	24.62(3.75)	0.004	0.78
Coding	75.94(15.55)	61.69(18.20)	<0.001	0.02
TMT-B	73.79(62.63)	93.75(76.94)	0.06	0.57
DS forward	11.27(2.23)	10.50(2.43)	0.03	0.80
DS backwards	9.73(2.12)	8.52(2.53)	<0.001	0.44
Story_delay	18.04(5.20)	17.49(4.69)	0.436	0.057
RAVLT delayed	10.77(3.45)	9.99(3.33)	0.11	0.91
Semantic fluency animals	19.74(5.64)	17.38(4.54)	0.003	0.45

Figure 1: Demographic and cognitive profile of frail participants with and without cerebrovascular disease

Frailty with cerebrovascular disease showed to have significantly lower completion of the digit symbol substitution test (DSST), where $p < 0.05$. This finding suggests that frailty with cerebrovascular disease is associated with slower processing speed.

DISCUSSION

Our preliminary findings provide direction to explore further underlying mechanisms that could support the relationship between frailty and cerebrovascular disease. In recent years, frailty is suggested to be representative of underlying mechanisms such as inflammation, vascular dysregulation, impaired microstructure, or functional connectivity which are common mechanisms of cerebrovascular disease (Siejka et al., 2022). A limitation of the study could be the limited sample size of frail participants with cerebrovascular disease. With the ongoing research, our increasing sample size will aid in better profiling the relationship between cerebrovascular disease.

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ALMOST CRIPPLED FOR LIFE: POST COVID-19 VACCINE CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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BACKGROUND

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) was defined as a type of autoimmune disorder characterized as relapsing-remitting or progressive immune-mediated acquired neuropathy with a gradual worsening symptoms over a period of more than eight to 12 weeks. Molecular mimicry is postulated as an important event in the occurrence of Post COVID-19 vaccine CIDP. A number of case reports and series were published wherein this is the 10th case of Post COVID 19 vaccine CIDP noted in journals.

METHODS

A 50/M known hypertensive and apparently well Filipino received his first dose of a virus vector based- vaccine against COVID-19 twenty weeks prior hospitalization. He experienced a tingling sensation and weakness in both legs accompanied by electric shooting pain twelve weeks after the vaccination. No fever, cough, dysuria, colds or diarrhea noted. At the interim, oral steroids and Vitamin B complex tablet were given; however, no relief of symptoms were noted. Neurological physical examination noted normal cognition, Intact cranial nerves, muscle strength: 5/5 both UE, 3/5 both LE; reflexes (DTR) noted +2 both UE, 0 both LE. CSF Analysis noted Albuminocytological dissociation and NCV/EMG: prolonged distal latency and decreased amplitude for bilateral median, sural and ulnar motor conduction studies.

RESULTS

Intravenous immunoglobulin (IvIg) 500 mg/day x 5 days was given with noted improvement at Day 3. Outcome Neurologic examination upon discharge noted improved muscle strength: 5/5 both UE, 4/5 both LE and Reflexes (DTR): +2 both UE, + both LE.

CONCLUSION

Post COVID-19 vaccine CIDP provides good prognosis following IvIg treatment.

KEYWORDS

COVID-19 vaccine, Chronic Inflammatory Demyelinating Polyneuropathy, Intravenous Immunoglobulin

RARE CASE OF PAROXYSMAL ENCEPHALOPATHY - NEURONAL INTRANUCLEAR INCLUSION DISEASE (NIID)

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BACKGROUND

Neuronal Intranuclear Inclusion Disease (NIID) is characterised by the presence of eosinophilic hyaline intranuclear inclusions in both the central and peripheral nervous systems. We present a rare and intriguing case of paroxysmal encephalopathy associated with NIID.

CASE REPORT

Our patient is an elderly lady who presented to us with confusion and fever over 1 day. Clinical examination initially found that she was disorientated and confused. MRI brain showed restricted diffusion involving the subcortical U fibers/corticomedullary junction highly suggestive neuronal intranuclear inclusion disease (NIID). Genetic testing done showed mutant NOTCH2NLC gene allele with expanded (GGC)>100 repeats.

DISCUSSION

The pathogenesis NIID is postulated to be due to accumulation of intranuclear inclusions in the central and peripheral nervous system, as well as visceral organs. The paroxysmal encephalopathy subtype is characterised by episodic encephalopathy with fever and eventual recovery. Diagnostic approaches encompass radiological findings, histopathological assessment, and genetic testing.

CONCLUSION

NIID represents a rare neurodegenerative condition characterized by a diverse clinical presentation and a unique radiological feature involving restricted diffusion at the corticomedullary junction. Diagnosis relies on the identification of specific histopathological characteristics and the detection of GGC trinucleotide repeat expansion within the NOTCH2NLC gene.

KEYWORDS

NIID, encephalopathy, dementia

EFFECT OF 6-WEEKS INTEGRATED ATTENTION TRAINING PROGRAM (IATP) ON COGNITIVE FUNCTION IN OLDER ADULTS WITH ANXIETY SYMPTOMS: PRELIMINARY FINDINGS

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BACKGROUND

Anxiety symptoms are common in older people and has been implicated with specific cognitive domains, including processing speed, attention shifting, and episodic memory. Older adults with anxiety symptoms are also associated with greater risk of cognitive decline and dementia. Integrated Attention Training Program (IATP) is designed to train attentional control involving the coordination of complex behaviors. The study aims to determine if a 6-week IATP will improve cognitive function in the high-risk group.

METHODS

30 individuals aged 60 years or above with anxiety symptoms participated in a 6-week single-blind randomized controlled trial (RCT) comparing IATP with health education in preservation of cognitive function. Both groups attend two 45-minute training per week for 6 weeks. Primary outcomes include attention, executive function, episodic memory, anxiety symptoms, and everyday functioning. Assessments take place at baseline (T0) and immediately after intervention (T1).

RESULTS

All the analyses are based on Intention-to-treat principle. Linear mixed effects models showed significant interactions between group and time effect in CNPI anxiety score ($p < 0.02$), sleep quality ($p < 0.018$), HK-MoCA score ($p < 0.037$), and alerting effect of the attention network ($p < 0.047$) from baseline to immediately after intervention.

CONCLUSION

Anxious older adults in the intervention group have significantly improved in anxiety level, sleep, global cognition, and attention when compared to the control group. IATP is able to offer beneficial effect on cognitive and mental health to anxious older adults. The results can have implications for the design of sustainable and low-cost health services for older people with anxiety at risk of cognitive decline.

KEYWORDS

Anxiety, Non-pharmacological Intervention, Early preventions of dementia

MODIFIABLE RISK FACTORS IN YOUNG ONSET ALZHEIMER'S DISEASE DEMENTIA: A RETROSPECTIVE CHART REVIEW

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BACKGROUND

Young onset dementia (YOD), defined by symptom onset before the age of 65, accounts for approximately six to nine per cent of all dementia cases worldwide.¹ There are multiple modifiable risk factors for YOD but relatively little is known about the role of potentially modifiable factors in the YOD. A better understanding of these risk factors is important in terms of prevention of YOD.²⁻⁴ The NUCOG scores, which correlated strongly, were highest in the control group, and lowest in the dementia group.⁵ This study aims to determine the factors associated with cognitive function in people with Young Onset Alzheimer's Disease Dementia (YOADD). This study will summarize recent findings and identify key areas in need of further research.

METHODS

The study type is an observational, retrospective chart review. We reviewed medical records for all patients aged 18 till 64 years old with YOADD attending neuropsychiatry clinic at Hospital Kuala Lumpur. Data was collected retrospectively using convenience sampling technique to determine their non-modifiable and modifiable risk factors including hypertension, diabetes, dyslipidemia, ischaemic heart disease, thyroid dysfunction, smoking status, alcohol consumption, obesity (BMI $\geq 27.5\text{kg/m}^2$) and waist circumference (males $\geq 90\text{cm}$, females $\geq 80\text{cm}$), NPI and NUCOG scores.

Confounding factors include gender, nationality, ethnicity, religion, marital status, education level and employment status were taken into account. The data analysis was done using the SPSS version 29.

RESULTS

So far 14 medical records have been reviewed. All the medical records reviewed are of age 46-64 years, where females predominate (57.1%). Most of them are Malaysian (85.7%), Malay (50%), married (64.3%), unemployed (64.3%), with highest education level up till secondary school (64.3%), living with family member(s) (92.9%) and without family history of Alzheimer's Disease Dementia (71.4%).

We have found out that alcohol consumption show statistically significant effect on NUCOG scores at the $p < 0.05$ level [$F(8,5) = 6.756$, $p = 0.025$] whereas the rest of the modifiable risk factors and non-modifiable risk factors did not show a statistically significant effect on NUCOG scores. Lower NUCOG scores in YOADD have a weak positive correlation with higher NPI scores ($r=0.16$, $n=14$), however the relationship was not significant ($p=0.585$).



CONCLUSION

There is no significant effect among non-modifiable and modifiable risk factors (except alcohol consumption) on NUCOG scores in YOADD. Low to moderate alcohol drinking has been proposed as a protective factor against the development of age-related changes in cognitive function, suggesting that protective effects are more likely with wine consumption and the absence of an APOE e4 allele.⁶⁻⁸ There is a weak association between lower NUCOG scores and higher NPI scores in YOADD.

KEYWORDS

Young Onset Dementia, Young Onset Alzheimer's Disease Dementia, Alzheimer's Disease Dementia, Neuropsychiatry Unit Cognitive Assessment Tool, Neuropsychiatry Inventory

TASTELESS THALAMUS: AN ISOLATED CASE OF DYSGUESIA POST THALAMIC STROKE

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INTRODUCTION

Dysgeusia or altered sensation of taste is a rare cause of ischemic stroke. We report a case of a young gentleman with dysgeusia post a minor infarct.

CASE DESCRIPTION

A 33-year-old healthy gentleman, active smoker presented with a 12-hours history of left sided weakness and facial asymmetry upon waking. His assessment showed right sided third-cranial nerve palsy with contralateral mild motor and sensory impairment with appendicular ataxia. He scored 3 points on National Institute of Health Stroke Scale. A non-contrast CT brain shows an established right thalamus infarct without large vessels occlusion on CT angiogram. He did not complaint of dysgeusia on primary event nor was it explored. He subsequently returned to work after intense rehabilitation for one month with minimal residual diplopia. He expressed dysgeusia involving both the tongue only 3 months post the index event but recalled to experience it from the stroke onset. Objective testing with sweet, sour and bitter food were negative but he was able to differentiate hot and cold sensation. No other new or residual deficits were noted. His blood investigations were within normal limits including young stroke workup.

DISCUSSION

Even though dysgeusia is a rare form of stroke presentation, there are several case reports documented it post infarct in specific locations. Thalamic infarct in particular was documented less commonly compared to cortical infarcts as a cause of dysgeusia. Despite dysgeusia has many factors associated with it, our patient was a healthy young male with no other confounding factors except the thalamic infarct.

CONCLUSION

Clinicians tend to underscore the importance of taking a focused history during the primary event especially those with minor neurological deficit. A minor thalamic infarct alone can be considered as the primary source of dysgeusia once other causes are ruled out.

KEYWORDS

Dysgeusia, Thalamus, Stroke

A DEEP DIVE INTO THE NEUROPSYCHOLOGICAL IMPACTS OF COVID-19 INNON-HOSPITALIZED PATIENTS WITH LONG COVID AND BRAIN FOG

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BACKGROUND

Coronavirus disease 2019 (COVID-19) causes persistent symptoms, including brainfog. We investigated which cognitive functions were most affected by COVID-19 innon-hospitalized Asian patients with long COVID and subjective cognitive complaints.

METHODS

We investigated the cognitive characteristics of participants diagnosed with COVID- 19 who developed brain fog that persisted for at least two months and occurred withinthree months of the initial infection. The neuropsychological assessment included screening tests for overall cognition and comprehensive tests for memory, executive function, processing speed, and subjective emotional and disease symptoms.

Cognitive test scores were converted into Z-scores, and principal component analysis(PCA) was employed to define cognitive domains across subtest scores.

RESULTS

We recruited 55 non-hospitalized patients with long COVID and brain fog (24 malesand 31 females, mean age: 45.6 ± 14.6 years, mean duration of education: 14.4 ± 3.0 years). Comprehensive assessments revealed cognitive impairments in 69.1% of the patients. Processing speed (27.3%), memory recall (21.8%), memory learning (20.0%), and inhibitory control (20.0%) were the most affected areas. Self-reported anxiety and depression were observed in 35% and 33% of the patients, respectively. Furthermore, the degree of anxiety could predict their performances on learning.

CONCLUSION

Nearly 70% of patients with subjective cognitive complaints and long COVID had objective cognitive impairments, including slow processing speed, memory loss, and executive dysfunction. A comprehensive evaluation is essential for patients with longCOVID with brain fog, including those with mild disease.

KEYWORDS

long COVID, brain fog, neuropsychology.

ESTIMATING THE ECONOMIC BURDEN OF ALZHEIMER'S DISEASE IN RAPIDLY AGING SOCIETIES: INSIGHTS FROM SOUTH KOREA AND TAIWAN

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BACKGROUND

Alzheimer's disease is the most common form of dementia, characterised by memory loss and a decline in cognitive abilities that significantly interferes with social and occupational functioning. Alzheimer's disease profoundly impacts patients and caregivers and poses significant economic challenges to healthcare systems and societies globally.

South Korea and Taiwan are among the fastest aging countries worldwide, with South Korea reporting 880,371 diagnosed dementia cases and Taiwan over 300,000 cases. These rapid demographic shifts are expected to drive an increase in prevalence of dementia, including Alzheimer's disease. Despite this, research on the economic burden of Alzheimer's disease in the Asia-Pacific region, especially in rapidly aging countries like South Korea and Taiwan, remains limited.

METHODS

A structured review of the literature was conducted to identify cost-of-illness studies related to dementia in South Korea and Taiwan, with a specific focus on Alzheimer's disease and its subtypes. Studies reporting cost estimates, encompassing direct and indirect costs, were included in the analysis.

RESULTS

Among the 83 studies reviewed, five met the inclusion criteria. All studies examined the costs of dementia, with none evaluating Alzheimer's disease specifically. Notably, only two of these studies were published within the last five years.

The annual costs of dementia in South Korea varied widely, ranging from US\$1.3 billion to US\$10.9 billion, and an average annual cost per patient ranging from US\$3,986 to US\$44,121. These costs were influenced by factors such as the utilization of long-term care facilities and the level of impairment in daily activities. In Taiwan, no population level estimate of overall costs was identified, however, the mean annual direct cost per patient with dementia ranged from US\$6,840 to US\$7,830 for mild to severe cases, respectively. Informal care contributed significantly to the total cost across all levels of dementia severity.

The proportional contribution of indirect costs to total costs varied widely, ranging from 11.2% to 55%, with significant variability in evaluation methods. Most studies considered caregiver productivity and income loss, but some also assessed paid caregiving, unpaid family care burden, and productivity loss due to medical care, treatment, premature death, and opportunity costs.



CONCLUSION

Studies indicate the economic burden of dementia in South Korea & Taiwan is significant, though there are few up to date estimates available, and limited research specifically on Alzheimer's. There is a clear need for updated, consistent, and comprehensive estimates of economic impact. Future studies should incorporate the most recent costs and epidemiological data, encompassing all aspects of direct and indirect costs incurred by Alzheimer's patients and their caregivers.

KEYWORDS

cost-of-illness, economic burden, societal costs, dementia, Alzheimer's disease

UNDERSTANDING DEMENTIA THROUGH AN ETHNOGRAPHIC EXPLORATION OF LOCAL PERSPECTIVES AND EXPERIENCES IN KUANTAN, PAHANG

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OBJECTIVES

This ethnographic study explores the experience and perspective of dementia among Malaysians who live in Kuantan, Malaysia.

METHODS

Fieldwork spanning two years included visits to diverse community sites such as qigong courts, religious centres, and community organizations. Participant recruitment depended on community outreach initiatives and a mix of semi-formal and informal interviews, totalling 18 sessions.

FINDINGS

Study revealed the complexities of cultural values, familial responsibilities, and community dynamics in providing care. Metaphors used by caregivers and community members provided valuable insights into the societal attitudes towards dementia. Caregivers face challenges balancing formal and informal care.

DISCUSSION

Cultural competence is essential in dementia care and community-based initiatives must be established to support individuals with dementia and their caregivers. The concept of utilizing traditional coffee shops, or *kopitiams*, as informal spaces for community interaction and support emerges as a promising avenue for enhancing dementia care in Kuantan. Malaysia's senior centre (PAWE) also needs additional broadening, oversight, and inspiration to help caregivers and people experiencing dementia.

IMPLICATIONS

Informal care is preferred in Malaysia, even though informal carers experience challenges because of their lack of resources and education. Long-term caregiving is made more difficult by dementia, which points towards the importance of early diagnosis to enhance quality of life and caregiver outcomes. The government should provide oversight, inspiration, and correction for organizations who do not meet the demands of the National Policy on Older Persons (2011).



LIMITATIONS

Although this study provides insightful information about the experience of dementia care for the people who live in Kuantan, Malaysia, it could be difficult to extrapolate outside of this setting. Broader application may be limited by sampling bias resulting from recruitment through community programmes and other factors such as context, language limitations between cultures, and subjective interpretation of metaphors and cultural traditions.

ACKNOWLEDGEMENTS

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KEYWORDS

Dementia, Ethnography, Malaysia, Informal Care, Caregiving

CURRENT PRACTICES IN THE DIAGNOSIS AND MANAGEMENT OF MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE: FINDINGS FROM THE ASIA PRIME PROJECT

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BACKGROUND

Cognitive impairment and Alzheimer's disease (AD) are increasingly considered major global public health concerns because of the risk of progression to dementia and increased mortality. While mild cognitive impairment (MCI) as a symptomatic prodromal phase of AD has historically been difficult to diagnose, recent progress in the clinical use of advanced diagnostic markers of AD neuropathology has given clinicians greater confidence in differential diagnosis. Such diagnostic tools may also permit the use of disease-modifying treatments (DMTs) once made available in this region. The Asia PRIME project was thus designed to understand the current status and anticipate the future landscape of the AD care pathway, including that of MCI due to AD, following the launch of anti-amyloid therapies in Asian countries.

METHODS

Between October 2022 and October 2023, 44 physicians comprising neurologists and psychiatrists from Hong Kong, India, Indonesia, Malaysia, the Philippines, Singapore, South Korea, Taiwan, and Thailand participated in one-to-one consultations. The interviews sought insights into the assessment, diagnosis, treatment, and follow-up of patients with MCI due to AD.

RESULTS

For patients in Asia with suspected MCI due to AD, cognitive screening is done using short neuropsychological assessments like the Mini-Mental State Exam or Montreal Cognitive Assessment; in South Korea, physicians employ additional comprehensive test batteries, such as the Seoul Neuropsychological Screening Battery. The diagnosis of MCI due to AD typically takes 1–6 months from initial visit, with magnetic resonance imaging being the mainstay first-line diagnostic modality coupled with routine laboratory tests. *APOE* genotype tests, while not routinely conducted, are frequently ordered in South Korea, Thailand, India, and the Philippines. Except in South Korea, amyloid positron emission tomography is only conducted upon request or typically reserved for patients with atypical MCI due to its high cost and limited access. Cerebrospinal fluid sampling is considered invasive, and the use of blood-based biomarkers is rare and mostly occurs in research settings. While individuals with MCI in South Korea are stratified by etiology, the majority of the treaters in Asian countries stratified patients



by disease severity. The treatment goal in MCI is to delay progression to AD while maintaining quality of life (QoL). Most patients with MCI due to AD (96% in South Korea versus 69% in other Asian countries) are on medication, with nootropics and cholinesterase inhibitors (primarily donepezil) most frequently prescribed. Non-pharmacological interventions include hospital-based psychosocial activation and physical exercise programs. Follow-up visits are scheduled every 3–6 months to assess for cognition, functioning, disease progression, QoL measures, and comorbidities, with neuropsychological tests repeated every few months, annually, or when needed.

CONCLUSION

The advent of DMTs for early AD in Asia means that the AD patient journey is evolving. An accurate diagnosis and detection of amyloid pathology with imaging and fluid biomarkers are imperative in identifying candidates with mild AD or MCI due to AD who may benefit from anti-amyloid treatments. As such, providing guidance on a roadmap for assessment, diagnosis, treatment, and follow-up can help standardize management and set expectations for patients navigating the early course of AD.

KEYWORDS

Mild cognitive impairment; Alzheimer's disease; patient journey.

COGNITIVE ACTIVITY PARTICIPATION ON STRUCTURAL BRAIN CHANGES

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BACKGROUND

Our randomized controlled trial (RCT), funded by the Research Grants Council in Hong Kong (reference number: 24114519), demonstrated that cognition was maintained and the functional connectivities of the default mode network (DMN) were strengthened at 6 months among participants with increased cognitive activity participation. We conducted a secondary analysis on the neuroimaging data to investigate the effect of engaging more in cognitive activities on structural brain changes. This secondary analysis could potentially provide additional insight into its neuromodulatory effect.

METHODS

In our RCT, community-living Chinese older adults with prior Chinese calligraphy handwriting practice and subjective cognitive decline (but without mild cognitive impairment or dementia) were randomly assigned to either the control group (where they continued their usual practice of calligraphy) or the intervention group (where they doubled their amount of practice) for 6 months. Changes in structural MRI data (measured by the Alzheimer's Disease-Resemblance Atrophy Index, AD-RAI, an MRI-based machine learning-derived biomarker of brain atrophy in AD) were compared using repeated measures analysis of variance.

RESULTS

By 6 months, the control group showed a larger increase in the AD-RAI compared to the intervention group, though the between-group difference did not reach statistical significance. The control group also had a greater AD conversion rate than the intervention group (6% vs 0%; $p = 0.08$).

CONCLUSION

The control group's larger increase in AD-RAI and higher AD conversion rate might indicate AD progression not effectively mitigated in the absence of new interventions. The smaller changes in the intervention group might suggest a slowing of disease progression, which could potentially have substantial implications over an extended period. Future studies with larger sample sizes or longer follow-up durations may reveal statistically significant protective effects on structural brain changes by adopting a more cognitively active lifestyle.

KEYWORDS

Cognitive activities, brain atrophy, structural brain volume, Alzheimer's Disease-Resemblance Atrophy Index, dementia prevention

MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE IN ASIA: CURRENT BARRIERS ALONG THE PATIENT JOURNEY

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BACKGROUND

Mild cognitive impairment (MCI) due to Alzheimer's disease (AD) is a state of impaired cognition that does not meet the criteria for dementia and is associated with markers of underlying AD neuropathology. While MCI as a symptomatic prodromal phase of AD has historically been difficult to diagnose, early diagnosis and intervention are nonetheless critical in ameliorating downstream pathological processes and preventing further decline. While the differential diagnosis of MCI is becoming easier, owing to continued advances in biomarkers of AD neuropathology, patients with MCI due to AD still face barriers to timely diagnosis and optimal interventions. The Asia PRIME project aimed to determine current challenges in the assessment, diagnosis, and management of MCI due to AD, in order that treating physicians can determine the optimal care pathway for patients in the region.

METHODS

Between October 2022 and October 2023, 44 physicians comprising neurologists and psychiatrists from general and tertiary hospitals in Hong Kong, India, Indonesia, Malaysia, the Philippines, Singapore, South Korea, Taiwan, and Thailand participated in one-to-one interviews. Consultations addressed current assessment and diagnostic pathways for patients with MCI due to AD, treatment patterns, and anticipated changes following future launches of amyloid-targeting disease-modifying treatments (DMTs).

RESULTS

In South Korea, the detection rate of MCI due to AD was high due to active screening tests in public dementia centers. In contrast, detection rates in other Asian countries were poor, with low patient awareness cited as a major factor in Hong Kong, India, Indonesia, and the Philippines. Patients in Hong Kong, India, Malaysia, the Philippines, and Thailand faced difficulty obtaining an initial hospital consultation due to backlogs in scheduling and insufficient manpower for performing detailed assessments. Following an initial consultation, diagnosis may take 1–6 months, with delays caused by backlogs in brain imaging in Indonesia, Malaysia, and Thailand, and neuropsychological assessment in South Korea and Taiwan. The limited use of biomarker tests to investigate AD neuropathology may reflect regional difficulties in access. While over one-third of patients in South Korea underwent amyloid positron emission tomography, this was used in only 5% of clinical assessments overall in other



countries because of its high cost and limited access, being completely unavailable in Indonesia, India, and Malaysia. Except in Thailand, cerebrospinal fluid tests were either rarely ordered (India and South Korea) or unavailable in clinical settings. Blood-based biomarker tests were recently introduced in Taiwan (used in <1% of assessments) but were otherwise unavailable in clinical settings in the region, being used only for research purposes in several centers. Beyond limited biomarker test availability, barriers to the future uptake of amyloid-targeting DMTs included the presumed high cost of treatment, reimbursement, monitoring side effects, especially amyloid-related imaging abnormalities, regular follow-ups, multiple stakeholder engagement, and centers' limited readiness for infusion facilities.

CONCLUSION

To harness the benefits of amyloid-targeting DMTs becoming available in the future, standardization of practices and an optimal path for the assessment and diagnosis of MCI due to AD in Asia must be established, prioritizing access to timely biomarker tests.

KEYWORDS

Mild cognitive impairment; Alzheimer's disease; patient journey.

CLINICAL CHARACTERISTICS OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS IN PATIENTS WITH DRUG-NAÏVE ALZHEIMER'S DISEASE

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BACKGROUND

Behavioral and psychological symptoms of dementia (BPSD) are less well-defined aspects of Alzheimer's disease (AD). We designed this study to explore the followings: 1) the clinical profiles of BPSD 2) the clustered-groups domains of the Korean-Neuropsychiatric Inventory (K-NPI) assessment of BPSD 3) the clinical characteristics of the clustered-groups of BPSD in patients with drug-naïve probable AD.

METHODS

Descriptive and cluster analyses of the 12 K-NPI domains were done in 220 patients with drug-naïve probable AD. After clustering these domains, characteristics of these positive symptoms clustered-group of patients were compared with the negative symptoms groups of patients.

RESULTS

The mean Korean-Mini Mental Status Examination (K-MMSE), Clinical Dementia Rating (CDR) scale, and K-NPI scores were 15.0, 1.6, and 14.2, respectively. The CDR and K-MMSE scores correlated with total K-NPI scores, and depression was the most common symptom. According to cluster analysis, five major clusters were identified. Using the associated neuropsychological dysfunctions, characteristics of each group were defined.

CONCLUSIONS

This study identified the clustered-domains for K-NPI, and suggested the possible anatomical substrates for these groups in drug-naïve AD patients. These attempts may clarify the complex and bizarre behavioral and psychological symptoms as more neurologically relevant symptoms.

KEYWORDS

BPSD, Drug-naïve, Alzheimer's disease, Cluster analysis

SERVICE EVALUATION OF CAREGIVERS' FOR PERSONS WITH DEMENTIA SUPPORT GROUP AT PANTAI JERUDONG SPECIALIST CENTRE, BRUNEI DARUSSALAM

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BACKGROUND

Family caregivers of persons with dementia are exposed to unique stressful situations and care demands where they might not be fully equipped to cope with. This group of individuals are at risk of various physical and mental health burdens, yet formal services benefiting caregivers are particularly lacking for the population of Brunei Darussalam. The caregivers' support group program was thus formed with the goal of providing psychosocial support for caregivers whose challenges can often feel very isolating, with the hypothesis that implementing this may help to reduce perceived care burden.

METHOD

This is done through an eight-week program delivered in the didactic form of psychoeducation on dementia illness trajectory and caregiving skills as well as providing an emotional outlet for caregivers. At present, two separate cohorts ($n = 15$) had undergone the program, made up of family caregivers of persons with dementia. A paired-samples t-test was conducted to explore the changes in pre- and post- program data, as well as evaluation of attendance rate.

RESULTS

They completed informant ratings with mean scores indicating significant decline in cognitive functions observed in their family members with dementia ($M = 4.01$). On a scale measuring caregiver burden, the first cohort maintained a stable range ($p > 0.05$) at Low burden both pre ($M = 1.16$) and post program ($M = 1.20$) whereas the second cohort started off with an average of Moderate burden ($M = 2.07$) with post-program data being omitted due to effect of higher attrition rate (54%).

CONCLUSION

This calls for further evaluation of the format and content of the program material, as well as study on determinants of care demands to better capture the caregiving journey. The implication of this evaluation is that a focus on creating safe space for emotional support may take precedence over didactic topics as the first stage in improving the quality of life for the caregivers, and subsequently, their relationships with the persons living with dementia.

KEYWORDS

Dementia, caregivers, support group, perceived burden, caregiving skills, interventions.

DEMENTIA CARE IN MALAYSIA: THE INFORMAL CARE PARTNERS' NARRATIVE

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BACKGROUND

Living with dementia impacts both the person and their unpaid care partners who are usually their family or relatives. Their needs, perceptions, and how they experience the condition at different levels should be considered. The aim of this review is to understand Malaysia's unpaid care partners' perspective in living with dementia.

METHODS

A scoping review and narrative synthesis were used where articles relevant to the search criteria for the Malaysian context from CINAHL, Scopus, MEDLINE, PubMed and APA PsycInfo were reviewed.

RESULTS

A total of 10 studies were included in the review. Acceptance, coping, self-management, integration, and adjustment were key attributes identified from the perspective of these unpaid care partners in the process of living with dementia. Different mechanisms that could empower them in this process include the awareness towards a changed situation, personal networks, access to information and education, personal conditions, and attitude to life and communication.

CONCLUSION

Unpaid care partners to those living with dementia share the same attributes to the ones they are caring for although manifested differently. Building their narrative helps in planning supportive services that could help them build resilience. Language used to describe these care partners also played an important part in empowering them through this process.

KEYWORDS

Dementia, informal care, resilience-building

MAPPING COGNITIVE RESERVE: A RESTING-STATE FUNCTIONAL CONNECTOME APPROACH IN SUPERAGERS

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BACKGROUND

Cognitive reserve denotes the brain's capacity to endure and adapt to age-related alterations and neurological impairments, serving as a safeguard against cognitive deterioration and dementia among older individuals. Utilizing functional neuroimaging offers the potential for direct and precise quantification of cognitive reserve, holding significant clinical promise. This investigation aimed to establish a metric for cognitive reserve using data from resting-state functional brain connectomes and validate this model among SuperAgers, defined as older adults exhibiting memory performance akin to that of cognitively healthy middle-aged individuals.

METHOD

We collected resting-state functional MRI (rsfMRI) scans, cognitive assessments employing the Seoul Neuropsychological Screening Battery, and cognitive reserve index (CRI) data from 74 older adults with intact cognitive function. Employing the Automated Anatomical Labeling (AAL) atlas, we extracted representative signals from 90 nodes through singular value decomposition of voxel-wise signals. Functional connectivity between node pairs was estimated via partial correlation computation.

RESULTS

Utilizing connectome-based predictive modeling, we forecasted CRI, adjusting for age, sex, and years of education, revealing a robust correlation with observed CRI (correlation coefficient: 0.952, mean absolute error: 3.723 ± 0.436). Predicted CRI also exhibited positive associations with cognitive abilities, encompassing memory and frontal executive functions.

CONCLUSION

Application of the model to external data from SuperAgers showcased a higher actual CRI compared to predicted CRI. This study underscores the feasibility of utilizing rsfMRI-derived functional connectivity data to predict clinically pertinent measures of cognitive reserve.

KEYWORDS

Machine Learning, Cognitive Reserve, Functional Connectome, Superagers

INTERACTION BETWEEN THYROID FUNCTION, APOE E4, AND COGNITIVE FUNCTION IN COGNITIVELY NORMAL ELDERLY

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BACKGROUND

The interaction between the thyroid-related hormones, apolipoprotein E ϵ 4 (APOE ϵ 4) and cognitive function has been reported despite controversial results. This study was aimed to investigate this correlation among cognitively normal elders.

METHODS

This study assessed 495 cognitively normal elders aged over 65 who underwent comprehensive hematological and neuropsychological assessments including the quantification of serum free thyroxine and thyroid stimulating hormone (TSH) as well as the Korean version of the Consortium Establish a Registry for Alzheimer's disease (CERAD-K). The Korean version of Geriatric Depression Scale (GDS-K) was also employed to evaluate the severity of depression. Age, gender, education, and the presence of APOE ϵ 4 were considered as covariates.

RESULTS

There was a significant positive association between verbal fluency test (VFT), Word List Memory Test (WLMT), and Word List Recall Test (WLRT) score and serum TSH levels ($p=0.005$, 0.032 , and 0.027 respectively). However, the further analysis adding the interaction between APOE ϵ 4 and TSH level revealed only VFT score was significantly influenced by this interaction ($p=0.029$).

CONCLUSION

Lower serum TSH levels had impacts on both semantic memory (VFT) and episodic memory (WLMT, WLRT) among cognitively normal elders, whereas the interaction of TSH and APOE ϵ 4 influenced only the task of semantic memory (VFT) in this group.

KEYWORDS

Thyroid hormones, APOE, Cognitive function

COMPARING EFFICACY OF PLASMA PHOSPHORYLATED TAU 181 AND 217 ON PREDICTING AMYLOID PET POSITIVITY

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BACKGROUND

Plasma phospho-tau (p-tau) biomarkers are considered as useful blood-based biomarkers of AD. Among p-tau biomarkers, plasma p-tau217 demonstrated equivalent diagnostic performance to CSF p-tau217 in detecting amyloid PET positivity, whereas p-tau181 did not in previous report. This study aimed to determine the efficacy of plasma phosphorylated tau (p-tau)217 and p-tau181 for detecting positive amyloid PET in two independent Asian cohorts.

METHODS

Plasma p-tau217 and 181 were measured using a single-molecule array (Simoa) in cognitive unimpaired individuals (CU, n=121), patients with mild cognitive impairment (MCI, n=102) and those with dementia (n=75) from two independent cohorts (cohort 1 and cohort 2). All participants underwent amyloid PET.

RESULTS

In total participants of cohort 1, both plasma p-tau181 ($P < 0.001$) and p-tau217 ($P < 0.001$) were higher in A β ⁺ group than A β ⁻ group. Plasma p-tau217 (AUC = 0.938 [CI 0.899–0.976], $P < 0.001$) outperformed p-tau181 (AUC = 0.857 [CI 0.797–0.917], $P < 0.001$) to detect amyloid PET positivity (P -value for difference < 0.001). Also, in total participants of cohort 2, both plasma p-tau181 and p-tau217 were higher in A β ⁺ group. But efficacy of p-tau217 and p-tau181 to detect amyloid PET positivity was not statistically significant.

CONCLUSIONS

Both plasma p-tau217 and 181 showed a high performance in determining A β -PET positivity. Plasma p-tau217 might have more predictive value.

KEYWORDS

P-tau181, P-tau217, Alzheimer's disease, Amyloid PET

BIOLOGICAL POTENTIAL OF ATRACTYLODIN FOR THEIR EFFECTS ON INFLAMMATION-RELATED NEURODEGENERATIVE DISEASES WITH THEIR UNDERLYING MOLECULAR MECHANISMS

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BACKGROUND

Atractylodes lancea contains numerous phytochemicals, including atractylodin which attracts most of the research interest in the scientific field. *Atractylodes lancea* has anti-oxidant, anti-bacterial, anti-fungal properties and used against gastrointestinal diseases. Atractylodin was found to be effective in intestinal inflammation, intestinal motility, and dysmotility in rats. Atractylodin also improve the delay of gastric emptying time in Sprague Dawley rats.

METHODS

Here in the present work, biological effect of atractylodin for their anti-neuroinflammatory properties has been investigated with their underlying molecular mechanisms through scientific data analysis of different research of scientific field. Detailed pharmacological potential of atractylodin has been investigated in the present work in order to know its health beneficial aspects in the medicine. Other pharmacological activities of atractylodin have been also investigated in the present work through scientific data analysis of different scientific research work.

RESULTS

Biological potential of atractylodin for their anti-neuroinflammatory properties has been investigated through scientific data analysis with their underlying molecular mechanisms and found that it significantly inhibited the production of inflammatory factors which signified its therapeutic potential for the treatment of inflammation-related neurodegenerative diseases. Further, in another scientific study, atractylodin significantly inhibited N-acylethanolamine-hydrolyzing acid amidase signified its importance in the treatment of neurodegenerative diseases. Other pharmacological studies also signified its positive effect in neurodegenerative diseases.

CONCLUSION

Present work scientific data analysis signified biological potential of atractylodin for their effects on inflammation-related neurodegenerative diseases with their underlying molecular mechanism.

KEYWORDS

Atractylodin, Neurodegenerative diseases, Molecular mechanisms

THERAPEUTIC POTENTIAL OF IRISFLORENTIN IN THE BRAIN DISORDERS AS AN ANTI-PARKINSONIAN DRUG CANDIDATE WITH THEIR MOLECULAR MECHANISM

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BACKGROUND

Flavonoids are found to be present in numerous medicinal plants and scientific study revealed the biological potential and therapeutic benefit of flavonoidal compounds in the brain functions and related disorders such as Parkinson's disease. Irisflorentin is a flavonoidal compound found to be present in the roots of *Belamcanda chinensis* well known medicinal plant in the traditional Chinese medicine.

METHODS

In order to know the biological potential of irisflorentin in the medicine and other allied sectors, effectiveness of irisflorentin for the treatment of Parkinson's disorder has been studied in the present investigation through scientific data analysis of different research work of scientific fields. Effectiveness of irisflorentin on acetylcholinesterase (AChE) activity has been also investigated in the present investigation through scientific data analysis of current scientific research works. Molecular mechanisms have been also investigated through scientific data analysis of current scientific research works to know the biological importance of acetylcholinesterase in the brain complication.

RESULTS

Scientific data analysis of different research work revealed the biological importance of irisflorentin in the treatment of Parkinson's disorder as it improves dopaminergic neuron degeneration and signifying their potential to treat Parkinson's disease. Scientific study revealed the biological importance of irisflorentin on acetylcholinesterase enzymes as it showed significant effect on acetylcholinesterase enzyme. Molecular study signified the biological importance of acetylcholinesterase enzyme in the Parkinson's disease.

CONCLUSION

Scientific data analysis of current research work revealed the biological potential of flavonoidal compounds in the medicine including irisflorentin for the treatment and development of better medicine against Parkinson's disorders.

KEYWORDS

Irisflorentin, Anti-Parkinsonian, Flavonoid, Brain Disorders

VENTRICULAR ARRHYTHMIA ASSOCIATED WITH CHOLINESTERASE INHIBITOR USE AMONG PATIENTS AT A FALLS AND SYNCOPE SERVICE

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BACKGROUND

In January 2024, the Malaysian National Pharmaceutical Regulatory Agency (NPRA) issued alerts on QT prolongation and torsade de pointes for rivastigmine and donepezil, two commonly prescribed cholinesterase inhibitors. We interrogated registry data from a Falls and Syncope Service to determine cases with potential ventricular arrhythmia related to cholinesterase inhibitor use.

METHODS

The Falls and Syncope Service, Universiti Malaya Medical Centre (UMMC), registry contains information on sociodemographics, falls history, associate symptoms, precipitating factors, medical history, medications used, social circumstances, investigations and diagnosis of all consecutive new patients seen at the clinic from its inception 2015. Patients were referred from the emergency department, primary care clinics, hospital inpatients and outpatients within the UMMC and other hospitals throughout Malaysia. Data obtained up to 2020 were available for analysis at the time of this study.

RESULTS

Of the 850 patients recorded in the registry, dementia was present in 5.5% (n=47). Dementia medications prescribed were memantine 19.1% (n=9), rivastigmine 10.6% (n=5), and donepezil 6.4% (n=3). Overall, orthostatic hypotension (n=6, 13%), gait instability (n=4, 8.5%), vasovagal syncope (n=3, 6.4%), cardiac syncope (n=2, 4.2%) and hypoglycemia (n=1, 2.1%) were diagnosed in all individuals with dementia. Of those with cardiac syncope, one individual had bradycardia and one had prolonged QT.

CONCLUSION

QT prolongation may lead to Torsades de Pointe a form of ventricular arrhythmia which could present as unexplained falls or syncope. Prolonged QT was present in one of the eight patients treated with cholinesterase inhibitors at the Falls and Syncope Service. Only 17% of patients with dementia were treated with cholinesterase inhibitors suggesting that physicians avoided the drug in those with falls risk. 12-lead ECG should be recommended in persons living with dementia prescribed cholinesterase inhibitors, as syncope from arrhythmia, either prolonged QT or bradycardia, is known to occur.

KEYWORDS

Dementia, cholinesterase inhibitors, older persons

MISPLACEMENT OF SOMETHING INSIDE THE REFRIGERATOR IS NOT AN EARLY SIGN OR WARNING SIGNAL OF DEMENTIA

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BACKGROUND

The purpose of this study is to explore the clinical implications of the 'fridge sign,' an atypical behavior characterized by the misplacement of items in unconventional locations, such as storing remote controls and mobile phones within a refrigerator.

METHODS

We analyzed patients who presented with memory impairment as their primary complaint and inquired about the presence of the 'fridge sign.' A total of seventy-nine patients underwent detailed neuropsychological testing for analysis. We investigated the cognitive profiles of 'fridge sign'-positive patients and performed follow-up evaluations with neuropsychological tests or telephone interviews. We compared the cognitive profiles and the clinical progression of 37 'fridge sign'-positive mild cognitive impairment (MCI) patients and 74 'fridge sign'-negative MCI patients.

RESULTS

Among 4559 individuals reporting memory complaints, 104 (2.28%) exhibited 'fridge sign' symptoms. Detailed neuropsychological analysis was conducted on 79 of these patients. The 'fridge sign' predominantly appeared in those diagnosed with subjective cognitive decline (SCD, 44.3%) or MCI (46.8%), often accompanied by a depressive mood, and was comparatively rare in dementia (5.0%). None of the 'fridge sign'-positive patients demonstrated significant cognitive deterioration throughout the follow-up. 'Fridge sign'-positive MCI patients scored higher on the geriatric depression scale compared to 'fridge sign'-negative MCI patient.

CONCLUSION

The 'fridge sign' does not serve as an early or progressed indicator of dementia. Instead, it appears to be more closely associated with depression.

KEYWORDS

Fridge sign, Depression, Mild cognitive impairment, Subjective cognitive decline

A NORMATIVE STUDY OF THE MONTREAL COGNITIVE ASSESSMENT-BASIC VERSION (MOCA-B) IN COMMUNITY-DWELLING INDIVIDUALS IN TAIWAN

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BACKGROUND

The Montreal Cognitive Assessment (MoCA) is a standard tool for evaluating cognitive abilities. The Montreal Cognitive Assessment-Basic (MoCA-B) was developed to reduce the impact of education on psychometric tests. It has also been translated and published in Taiwan. The MoCA-B, however, lacks normative data and psychometric properties. This study aims to define norms for the Taiwanese MoCA-B and explore its psychometric characteristics along with demographic associations.

METHODS

The study included 76 healthy participants aged 63 to 88, comprising 24 males and 52 females with an average age of 71.8 ± 4.5 , and educational backgrounds ranging from 0 to 6 years. Multiple regression analysis was employed to assess and adjust for demographic factors affecting MoCA scores.

RESULTS

The regression analysis indicated that both age ($r = -0.164$, $p < 0.05$) and education ($r = 0.681$, $p < 0.001$) significantly correlated with the total and domain scores of the MoCA-B. Notably, the verbal fluency domain exhibited gender-based disparities, with females performing more advantageously on this subtest. A correction formula has been formulated to derive the standardized individual MoCA-B score. Additionally, a clinical reference cut-off point has been established at an adjusted total score of 15.89.

CONCLUSION

The study's objective was to offer impartial assessments of cognitive abilities by calibrating the MoCA-B's total and domain scores based on age and educational background. It also examined the influence of education levels ranging from 0 to 6 years on the MoCA-B's outcomes. Moreover, establishing normative data for the Taiwanese demographic is expected to enhance the MoCA-B's efficacy and practicality within Taiwan significantly.

KEYWORDS

Montreal Cognitive Assessment, Montreal Cognitive Assessment -Basic, neuropsychological assessment, normative data, demographic variables.

TRANSITION IN COGNITIVE FRAILTY AND ITS ASSOCIATION WITH DEPRESSION, ANXIETY AND STRESS OVER A 7-YEAR PERIOD IN THE MALAYSIAN ELDERS LONGITUDINAL RESEARCH STUDY

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BACKGROUND

Cognitive Frailty (CF), linked to detrimental health outcomes in the elderly, has raised interest in its potential reversibility amidst the backdrop of rapid aging. While current factors that elevate CF risk predominantly revolve around physiological aspects, the exploration of psychological contributors remains relatively limited. This objective of this study was, therefore, to examine the association between depression, anxiety and stress with CF transition over seven years.

METHODS

The Malaysian Elders Longitudinal Research (MELoR) study enrolled participants aged above 55 years through stratified random sampling from electoral rolls of three parliamentary districts within the Klang Valley in 2013. In 2020, follow-up data were collected using virtual surveys due to the COVID-19 pandemic. CF was gauged using the Cardiovascular Health Study index and the Fatigue, Resistance, Ambulation, Illness, and Loss of Weight index at baseline and follow-up respectively. Mild cognitive impairment (MCI) was assessed using the Montreal Cognitive Assessment. CF was characterised based on frailty and MCI outcomes. Depression, anxiety, and stress were evaluated via the 21-item Depression, Anxiety and Stress scale.

RESULTS

Incorporating data from participants aged (mean $\pm$ SD) = 76.03 $\pm$ 13.3 years, 56.9% female, analysis revealed CF among 6 (1.1%) participants at baseline and 16 (2.8%) at follow-up. The trajectory of CF transition over seven years indicated improvement in 93 (16.79%) participants and deterioration in 461 (83.21%). Differences in education, asthma and cancer were observed between those whose CF improved and worsened. Improvement in CF were observed among 92 (100%), 88 (97%) and 91 (100%) of those with normal to mild symptoms of depression, anxiety and stress respectively, compared to those with moderate to severe symptoms. Presence of moderate to severe anxiety was associated with worsening in cognitive frailty transition.

CONCLUSION

The findings underscore the fluctuating nature of CF over the course of seven years. Importantly, the study suggests that increased depression, anxiety and stress were associated with worsening in CF transition. The study delves into the interconnection between psychological states and the evolution of cognitive frailty, revealing the potential for psychological interventions to mitigate CF progression.

KEYWORDS

Cognitive frailty transition, psychosocial factors, aged

EXPLORING THE PSYCHOSOCIAL FACTORS ASSOCIATED WITH GOOD QUALITY OF LIFE AMONG FAMILY CAREGIVERS OF DEMENTIA PATIENTS IN MALAYSIA

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BACKGROUND

Dementia is a worldwide issue and Asia is currently experiencing a rapid rise in cases. The role of family caregivers is significant in providing the high demands of care and maintaining the quality of life for dementia patients, but they are often disregarded. Hence, it is important to understand their experiences and needs, so that negative outcomes such as abuse can be prevented and effective support and care can be provided to improve the quality of care and overall quality of life for both caregivers and dementia patients. With that, this study aimed to explore the psychosocial factors associated with good quality of life among the family caregivers of dementia patients in Malaysia through qualitative research.

METHODS

The study employed a phenomenological design with qualitative research methodology, originally planning to involve 20 participants, but data saturation was achieved after 7 participants. Purposive sampling was used to select participants, and data collection was conducted through questionnaires and semi-structured interviews. The data were analyzed using descriptive and thematic analysis techniques.

RESULTS

Three themes were identified and generated from the interviews with participants: caregiving experience, coping strategies used, and support and intervention. Early-stage dementia caregiving can cause psychological distress, anger, social isolation, and job issues, primarily due to a lack of knowledge. Even if participants report a good quality of life, recognizing and addressing these challenges is crucial to providing support to caregivers. Over time, the caregiving experience can transition from negative to positive as caregivers gain more experience and knowledge, potentially leading to an improved quality of life. Coping strategies play a significant role in this transition, with effective coping mechanisms such as spiritual coping, social support, resilience, active coping, distraction, planning, and acceptance being common among Malaysian caregivers. Supportive interventions like emotional and practical support are the most common and helpful interventions for dementia caregivers in Malaysia. However, the lack of support and interventions remains a critical issue as most of the caregivers still have limited or no access to support and intervention, highlighting the need for broader and more accessible interventions.

CONCLUSION

Despite initial challenges due to a lack of knowledge and experience, caregivers can still maintain a good quality of life through various psychosocial factors such as the adoption of various coping strategies and access to support and interventions. The study emphasizes the necessity of culturally sensitive and knowledge-based support interventions and the promotion of available community services to ensure family caregivers are well-equipped to manage their roles effectively and subsequently enhance their quality of life.

KEYWORDS

Dementia, Family Caregiver, Quality of Life, Dementia Caregiver, Psychological Well-being

PROSPECTIVE CHANGES IN ANTICHOLINERGIC COGNITIVE BURDEN IS ASSOCIATED WITH CHANGES IN PHYSICAL PERFORMANCE IN MELOR STUDY

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BACKGROUND

Exposure to anticholinergic medications is associated with increased risk of dementia, cardiovascular outcomes and mortality in older persons. We aimed to determine the prospective relationship between changes in anticholinergic cognitive burden (ACB) over time with changes in physical performance.

METHODS

Medication and physical performance data were obtained at baseline (2013-2015) and wave 4 follow-up (2020-2022) from the Malaysian Elders Longitudinal Research (MELoR) study. Participants were classified into absence of, no change, increased and reduced ACB groups. Physical performance was determined through survey questions on upper limb strength, walking ability, chair-bed transfer ability and stair climbing.

RESULTS

Follow-up ACB and physical performance data were available for 751 individuals aged 67.82 (SD=6.91) years at recruitment, 59.7% of whom were women. Compared to individuals with no ACB exposure, individuals with reduced ACB were more likely to have persistent or new impairment in upper limb strength, chair-bed transfer and stair-climbing. In addition, persistent or new impairment in ability to walk across a small room, chair-bed transfer and negotiate stairs were also more likely in individuals with increased ACB over time.

CONCLUSION

Both increased and decreased anticholinergic exposure over nine-year follow-up is associated with reduced physical performance. Causal evidence for the deleterious effect of anticholinergic exposure on physical performance and indicate the impact of exposure may not be reversible. Intervention studies to reduce inappropriate anticholinergic use and to prevent physical deterioration in at risk individuals are now indicated.

KEYWORDS

Changes, Anticholinergic Cognitive Burden, Physical Performance.

RELATIONSHIP BETWEEN LONG-TERM CARE INSURANCE SERVICE UTILIZATION PATTERN AND CLINICAL FACTORS INCLUDING THE SEVERITY OF DEMENTIA

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BACKGROUND

After the opening of the Dementia Prevention Center at Ilsan Hospital in Korea, we plan to produce basic data for establishing a strategy for providing long-term care benefits for dementia patients by analyzing the use of medical and long-term care services according to various clinical factors including the severity of Dementia.

METHOD

Information on patients who received cognitive function tests such as K-MMSE and neuropsychological test battery was collected at Ilsan Hospital. Based on this patient group, the National Health Insurance service's customized DB and the elderly's long-term care DB information were joined to verify the patient's medical records and investigate the use of the elderly's long-term care benefits.

RESULT

A total of 1921 patients people were diagnosed with dementia at Ilsan Hospital in Korea, from 2011 to 2018, and 391 patients (20.35 %) were classified as long-term care rating judges, 76 patients (3.96%) were undecided, and 1454 patients (75.69 %) were not applied. Statistically significantly, the number of patients diagnosed with dementia in Ilsan Hospital also increased from 2016 to 2023, and the number of dementia rating groups increased continuously, especially after the introduction of the special dementia grade in 2019. 75.69 % of the patients diagnosed with dementia at Ilsan Hospital are not applied for long-term care insurance for the elderly, and they are showing a relatively young age and high level of education. Cognitive function tests in hospitals also reflect the severity and frequency of patients and the suffering of their guardians when assessing neurological behavioral abnormalities. However, currently, the evaluation score for long-term care service for the elderly are judged only by the presence or absence of symptoms, so it is considered necessary to take countermeasures as it shows differences in hospital examination results and the results of long-term care service evaluation.

CONCLUSION

It is necessary to identify the long-term care benefits required for each characteristic of dementia patients, to indirectly verify the validity of the current benefit system by current status, and to develop policies to establish long-term care benefit types and service strategies for individual characteristics of dementia patients

KEYWORDS

Dementia, Long-term care, National Health Insurance

ESTIMATION OF LONG-TERM CARE UTILIZATION AND LIFETIME DISTRIBUTION OF MEDICAL COST FOR DEMENTIA IN KOREA

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BACKGROUND

To investigate the current status of long-term care services for patients with dementia and lifetime medical costs for dementia in South Korea.

METHOD

This study utilized the National Health Insurance Service-National Health Information Database (NHIS-NHID) from January 2017 to December 2021. The prevalence and incidence of dementia was estimated by extracting people who were diagnosed and treated with dementia (age ≥45 years) from the database. The use of long-term care services for the elderly with newly diagnosed dementia was also investigated. Additionally, the lifetime medical expenses for dementia were estimated using data on single year's medical costs, population data, and a life table from Statistics Korea.

RESULT

The prevalence of dementia increased over three years from 2015 to 2017, while the incidence of dementia gradually decreased. Among the patients with newly diagnosed dementia, approximately 30% used the long-term care services, while 4th graders accounted for the highest proportion every year. The older the age and the lower the income quartile, the shorter the time it took to apply for long-term care services after diagnosis of dementia. The total medical expenses per capita increased steadily every year, and the lifetime medical expenses were higher for females than males. Half of the lifetime medical costs of dementia occurred after 67 years of age for males and 83 years for females.

CONCLUSION

This study suggests that medical, social, and political measures are needed to effectively manage long-term care service recipients and prepare for rising medical costs for dementia.

KEYWORDS

Dementia, Long-term Care, National Health Insurance, Medical cost

CHARACTERISTICS OF PATIENTS ATTENDING MEMORY CLINIC AT A TEACHING HOSPITAL IN EAST COAST MALAYSIA

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BACKGROUND

Malaysia has a growing ageing population¹ with a national prevalence of dementia of 8.5%². However, the data that describes the characteristics of dementia patients in the East Coast of Peninsular Malaysia is scarce. This study aims to highlight the epidemiological data and clinical characteristics of patients attending the memory clinic at Sultan Ahmad Shah Medical Centre@IIUM (SASMEC@IIUM), a major teaching hospital in the East Coast of Peninsular Malaysia.

METHODS

This is a cross-sectional study that involved data collection from the electronic medical record of all 17 patients who attended the memory clinic from January 2022 until March 2024. Basic demographic trends, subtypes of cognitive impairment, dementia severity Functional Assessment Staging (FAST) scale, neuropsychiatric symptoms, Clinical Frailty Scale (CFS), polypharmacy and history of falls were recorded.

RESULTS

52.9% of the patient samples were males. Age was 75 ± 8.3 years (mean $\pm$ SD). The types of cognitive impairments were vascular dementia (41.8%), Alzheimer's disease (29.4%), mixed type of vascular and Alzheimer's disease (17.6%) and mild cognitive impairment (11.8%). FAST scale was 4 ± 1 (mean $\pm$ SD) and CFS was 5 ± 0.6 (mean $\pm$ SD). Most patients did not have neuropsychiatric symptoms (64.7%) at the time of diagnosis. 58.8% of the attendees had polypharmacy while 47.1% had at least 1 history of fall within 12 months of diagnosis.

CONCLUSION

The small sample of patients reflects the underutilization of this service in the East Coast and further study is necessary to explore the contributing factors. This study illustrates that most patients who attended the memory clinic at SASMEC@IIUM were in the mild stages of dementia with mild frailty and a low rate of neuropsychiatric symptoms. Almost half of the patients had other geriatric issues (falls and polypharmacy) and this indicates that multidisciplinary intervention in the form of a comprehensive geriatric assessment is paramount in the management of dementia.

KEYWORDS

dementia, frailty, geriatric syndromes, memory, comprehensive geriatric assessment

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**CLITORIA TERNATEA ROOT FRACTION ALLEVIATES
NEUROINFLAMMATION AND OXIDATIVE STRESS IN CHRONIC CEREBRAL
HYPOPERFUSION RAT**Wei Chun Lim¹, Murugaiyah Vikneswaran^{1,2}, Hassan Zurina¹¹ Centre for Drug Research, Universiti Sains Malaysia, 11800 Penang, Malaysia² Discipline of Pharmacology, School of Pharmaceutical Sciences, Universiti Sains Malaysia,
11800 Penang, Malaysia**BACKGROUND**

Chronic cerebral hypoperfusion (CCH) is a major cause of vascular dementia and is caused by reduced blood flow to the brain which leads to neuronal damage. *Clitoria ternatea* (CT) has been widely used as an herbal plant to alleviate inflammation. However, the exact mechanism remains unclear. This study aimed to determine the neuroinflammation and oxidative stress effects of CT root fraction (CTRF) in the CCH rat model using the in-vitro and in-vivo approaches.

METHODS

Column chromatography was used to extract CTRF and Clitorienolactone A (CLA). The anti-inflammatory properties of indomethacin, CLA, and CTRF were assessed using denaturation inhibition and membrane stabilization assays. The CCH model was developed with the two-vessel occlusion (2VO) method, while the sham group underwent the identical surgical procedure without ligation. After a 4-week post-surgery period, both CCH and sham rats were administered either a vehicle, CTRF (10, 20, and 40 mg/kg), or 10 mg/kg of indomethacin orally. The brain was extracted for protein analyses.

RESULTS

CTRF exhibited anti-inflammatory effects in the hypotonia-induced membrane stabilization and BSA denaturation inhibition assay, as compared to CLA and indomethacin. In rats treated with CCH+vehicle and CCH+CTRF (40 mg/kg), the expressions of the TLR4/NF κ B signalling pathway were increased. This led to an increase in oxidative stress, as evidenced by decreased levels of GSH, GPx, and catalase. Additionally, there was a shift in microglia regulation from M2 to M1 polarization, characterized by increased expressions of pro-inflammatory cytokines TNF- α and IL-1 β , and decreased expressions of anti-inflammatory cytokines IL-10 and TGF- β . Meanwhile, the administration of CCH+CTRF at a dosage of 10 and 20 mg/kg and CCH+indomethacin (10 mg/kg) expressed inversely compared to CCH+vehicle. Among all treatment groups, only the CCH+vehicle group exhibited an elevation in malondialdehyde levels. Conversely, the sham group did not exhibit any negative consequences from any of the interventions.

CONCLUSION

In conclusion, our data suggest the CTRF effects via inhibiting the TLR4/NF κ B signalling pathway, reducing oxidative stress, and increasing microglia M2 polarization. The finding suggested that CTRF (10 and 20 mg/kg) has shown potential as a therapeutic target in the treatment of vascular dementia.

KEYWORDS

Clitoria ternatea root, Chronic cerebral hypoperfusion, Neuroinflammation, Oxidative stress

**CLARITY AD: ASIA REGION ANALYSIS OF A PHASE III TRIAL OF
LECANEMAB IN EARLY ALZHEIMER'S DISEASE**

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BACKGROUND

Across Asia, Alzheimer's disease (AD) prevalence is expected to rise dramatically due to rapidly aging populations, among other factors. AD pathology may be initiated by the accumulation of soluble and insoluble aggregated A β peptides (oligomers, protofibrils, and fibrils). Lecanemab is a recently approved humanized IgG1 monoclonal antibody that preferentially targets soluble aggregated A β species (oligomers, protofibrils), with activity at insoluble fibrils. In the recent 18-month phase 3 Clarity AD study, lecanemab demonstrated a consistent slowing of decline in clinical (global, cognitive, functional, and quality of life) outcomes, and reduction in brain amyloid in early AD. Lecanemab was well tolerated in Clarity AD, with an increase in incidence of amyloid-related imaging abnormalities (ARIA) versus placebo. Herein, we present the results for the Asia region population from Clarity AD. These results exclude the participants from China, which will be published separately as part of the Clarity AD China Cohort study.

METHODS

Clarity AD was an 18-month treatment (core study), multicenter, double-blind, placebo-controlled, parallel-group study in patients with early AD. Eligible patients were randomized across 2 treatment groups (placebo and lecanemab 10 mg/kg biweekly) according to a fixed 1:1 schedule. The primary efficacy endpoint in the core study was change in the Clinical Dementia Rating-Sum-of-Boxes (CDR-SB) from baseline at 18 months. Key secondary endpoints include change from baseline at 18 months in amyloid PET standardized uptake value ratio (in patients participating in the amyloid PET sub-study), AD COMposite Score (ADCOMS) and AD Assessment Scale-Cognitive Subscale 14 (ADAS-Cog14). Safety was monitored throughout the study in a blinded manner by the sponsor and in an unblinded manner by an independent data safety monitoring committee.

RESULTS

Of the total of 1795 subjects were randomized in Clarity AD, 294 subjects were in the Asia region (Japan:152 subjects; Korea:129 subjects; Singapore:13 subjects). For the primary endpoint, there was a slowing decline of 25% with lecanemab in CDR-SB at 18 months compared to placebo in the Asia region (adjusted mean difference: -0.349; 95% confidence intervals: -0.773, 0.076). Results for the secondary efficacy endpoints favored lecanemab versus placebo in the Asia region. Efficacy of lecanemab was generally consistent with the overall population. Lecanemab was well tolerated in Asia subjects, with safety profile in Asia subjects similar to the overall Clarity AD population. The most common adverse effects of special interest were ARIA-H (lecanemab:10.3%; placebo:14.9%), ARIA-E (lecanemab:6.2%; placebo:1.4%), and infusion-related reactions (lecanemab:12.3%; placebo:1.4%). Incidence of



adverse events leading to study drug dose interruption or withdrawal, infusion-related reactions and ARIA-E was lower for the lecanemab treated group in the Asia region relative to the overall Clarity AD population. Results from quality of life and biomarker assessments in the Asia region were also generally similar to the overall Clarity AD population.

CONCLUSION

In the Clarity AD Asia region, lecanemab was as efficacious and safe with manageable risks as in the overall population, with a favorable risk-benefit profile.

KEYWORDS

Alzheimer's disease; lecanemab, disease modification



ASSOCIATION BETWEEN ANTICHOLINERGIC BURDEN WITH NEUROPSYCHIATRIC SYMPTOMS AND RISK OF HOSPITALIZATION IN MILD COGNITIVE IMPAIRMENT OR DEMENTIA

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BACKGROUND

Anticholinergic burden is the cumulative usage of multiple drugs with anticholinergic effects. Anticholinergic burden has been associated with symptomatic deterioration and further disruption to cognition, and increased risk of neuropsychiatric disturbance among both mild cognitive impairment and dementia individuals. Despite this, anticholinergic medicines are commonly used to treat various health conditions in these populations. This study aims to investigate the association of anticholinergic burden on hospitalization and neuropsychiatric symptoms among PLWD attending the memory clinic of a teaching hospital in Kuala Lumpur, Malaysia.

METHOD

This cross-sectional observational study included individuals with mild cognitive impairment or dementia attending the memory clinic between January to December 2022. Collected data includes sociodemographic information, comorbidities, cognitive and functional assessment, neuropsychiatric symptoms and medication history. Anticholinergic burden was assessed using the Anticholinergic Cognitive Burden (ACB) score. The association between neuropsychiatric symptoms were compared against the different ACB scores. Cox proportional hazard analysis was used to assess the risk of hospitalization in all participants.

RESULTS

Of 657 older adults recruited, with mean age of 80.66 (SD 7.39) years old. 35.5% of participants were exposed to anticholinergic drugs with mean ACB score of 0.8 (SD 1.3). Those with ACB score of ≥ 3 were associated with nursing home residency, neuropsychiatric symptom clusters (hyperactivity, psychosis and physical behaviour), number of prescribed medications and dependency on activities of daily living. Older adults with ACB scores of 1-2 had increased risk of hospitalization (Hazard Ratio (HR) = 1.84, 95% CI: 1.17-2.90) on univariate Cox regression analysis. However, the significance was diminished with the inclusion of confounders.



CONCLUSION

One in three persons living with mild cognitive impairment or dementia had exposure to drugs with anticholinergic properties. High anticholinergic burden is associated with neuropsychiatric symptoms but not hospitalization. These findings evaluate the necessity of each anticholinergic drug to minimize harm in this population.

KEYWORDS

anticholinergic burden; mild cognitive impairment; dementia; neuropsychiatric symptoms; hospitalization.

Asian Society Against Dementia

PD-ASAD-36

RANDOMIZED CONTROLLED TRIAL OF THE EFFECT OF INTEGRATED CARE FOR DEMENTIA (ICD) IN PERSONS WITH DEMENTIA (PWDs) AND THEIR CAREGIVERS

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Ministry of Health Malaysia

BACKGROUND

Dementia poses a significant public health challenge globally, affecting millions of individuals and their families. Integrated Care for Dementia (ICD) aims to enhance the quality of life for PWDs and alleviate caregiver burden. This abstract outline the findings of a randomized controlled trial (RCT) assessing the effectiveness of ICD on persons living with dementia (PLWD) and their caregivers.

METHODS

A randomised controlled trial among PWDs and their caregivers attending psychogeriatric clinics was conducted among PWDs undergoing follow-up in Hospital Kuala Lumpur, Hospital Tuanku Jaafar Seremban, Hospital Permai Johor Bahru and three district health clinics in Negeri Sembilan (Klinik Kesihatan Seremban 2, and Klinik Kesihatan Senawang). The eligible participants were randomised into intervention and control groups. The randomisation sequence was generated by Random Allocation Software version 2.0 using the block randomisation method.

Participants in the intervention group (n=46) received Cognitive Stimulation Therapy (CST) for PWDs and psychoeducation (total of 5 modules) for their caregivers, while those in the control group (n=39) received standard of care. Sociodemographic profiles and outcome indicator assessments via Mini Mental State Examination (MMSE), Zarit Burden Inventory (ZBI), and Quality of Life- Alzheimer's Disease (QOL-AD) were taken at baseline and 14 weeks post-intervention. The psychoeducation knowledge scores were also recorded within each module. The repeated measures ANOVA was used to assess the effect over time (within group) and effects in between-groups.

RESULTS

Out of 85 participants enrolled at the start of the project, 67 of them completed all the assessments, given the attrition rate of 21%. Statistically, the baseline for MMSE, ZBI and QOL-AD in between intervention and control group were comparable. After 14 weeks post-intervention, there were no significant changes observed on MMSE over time ($F=1.949$, $P=0.167$) and in between group ($F=2.131$, $P=0.149$). There were also no significant changes for ZBI over time ($F=2.895$, $P=0.094$) and in between group ($F=1.558$, $P=0.216$). However, there are significant differences for QOL-AD ($F=4.045$, $P=0.048$) over time, but no significant changes observed in between groups ($F=0.708$, $P=0.403$). Finally, the overall psychoeducation

knowledge scores were significantly improved ($t=4.058$, $P<0.001$) among intervention group participants.

CONCLUSION

The current findings suggest that ICD has improve Quality of Life (QOL) for PWDs but other indicator such as MMSE and ZBI show insignificant results. The enhancement in the QOL for PWDs attributed to CST, alongside the integration of psychoeducation within the ICD program has collectively contributing to a more dignified and self-esteemed life for PWDs. In extrapolating applicability, our conclusion indicates that the ICD program is not only effective for persons with dementia but also recommends its application to other older people populations.

KEYWORDS

Dementia, Integrated care, Randomised-controlled Trial, effectiveness

EVALUATION OF THE BLOOD-BRAIN BARRIER FUNCTION AND NEUROINFLAMMATORY RESPONSE IN THE CONDITIONS OF PROLONGED EXPOSURE TO MITRAGYNA SPECIOSA (KETUM) ALKALOIDS AND DECOCTION IN RATS

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BACKGROUND

Mitragyna speciosa or *ketum* has gained a lot of attention in recent years. Therapeutic benefits were reported but so did potential health risks and abuse. *M. speciosa* principal alkaloid mitragynine is known to permeate the blood-brain barrier (BBB), the brain microvascular endothelium that tightly regulates molecular traffic at the blood-brain interface to maintain optimal environment for neuronal function. Altered BBB function leads to development and progression of CNS diseases. Putting this together, this study is designed to evaluate the BBB function in the conditions of prolonged exposure to mitragynine and *M. speciosa* decoction.

METHODS

1, 5 and 10 mg/kg mitragynine HCl were administered to male Sprague dawley rats intraperitoneally (i.p), and *ketum* decoction standardised to 10 mg/kg mitragynine content was given orally (p.o) for 14 days, a duration that represents 1 year of human consumption. 1 mg/kg methadone HCl, a commercially used drug for opioid substitution therapy was also included in this study. Hot-plate test was performed at day 1 to evaluate the therapeutic effectiveness of all test compounds given. As drugs of abuse are often linked with neuroinflammation and addiction, neurobehavioral study of Novel-object recognition task (NORT) was performed at day 13 and 14 to evaluate cognitive performance and potential withdrawal signs was access on the last day of treatment. The effect of test compounds on BBB tight-junction was evaluated via spectrophotometric quantification of Evans blue dye perfused through femoral vein 24-hour after the last dose administration. The presence of CD4+, ICAM-1 and VCAM-1 were investigated using Western blot to probe for potential induction of neuroinflammation and the presence of albumin in parenchyma was examined to strengthen the evaluation of tight-junction function. Junctional protein claudin-5, P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), multidrug resistance proteins (MRPs) and glucose transporter 1 (GLUT1) mRNA expression that affect drug deposition were inspected using quantitative real-time PCR.

RESULTS

Results show that compounds administered successfully reached the brain by demonstrating significant analgesic effect in hot-plate test. There is a significant withdrawal effect as evaluated by global withdrawal scoring (GWS) in 5 and 10 mg/kg (i.p) mitragynine HCl dosage. There is no cognitive impairment observed in all test groups excluding methadone that responses negatively to the NORT test. The observation correlates to negative detection of CD4+ in brain parenchyma and absence of ICAM-1 and VCAM-1 in microvessels. Prolonged administration of all test groups do not cause BBB tight-junction leakage in all brain region. The observation was supported by no significance upregulation of albumin protein in brain parenchyma. The

mRNA expression of claudin-5, BCRP, MRPs, and Glut-1 transporters were not altered in all treatment group. However, there is a significance upregulation of 11.78 ± 2.3 -fold P-gp efflux transporter expression in 10 mg/kg mitragynine HCl dosage while other treatment groups do not show altered expression of this transporter.

CONCLUSION

Findings of this study contribute to safety data of *M. speciosa* which are urgently needed to weigh the balance between therapeutic benefits and potential health risks of the plant; and to aid evidence-based decision on the future of *M. speciosa*.

KEYWORDS

Mitragyna speciosa, blood-brain barrier, addiction

Asian Society Against Dementia

PD-ASAD-39

THE TRIGLYCERIDE-GLUCOSE INDEX AND ALTERED MENTAL STATUS ARE ASSOCIATED WITH EARLY NEUROLOGICAL DETERIORATIONS IN ACUTE ISCHEMIC STROKE PATIENTS

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BACKGROUND

Triglyceride-glucose (TyG) index has been proposed as a novel biomarker for insulin resistance. Previous studies showed its ability to predict the incidence of acute ischaemic stroke and its long-term prognosis. Early neurological deteriorations (ENDs) in ischaemic stroke contribute to the high burden of stroke and are becoming one of the therapeutic parameters. Whether the TyG index was associated with ENDs needs further investigation.

METHODS

We recruited and retrospectively analyzed all patients with acute ischaemic stroke who were admitted to the Stroke Unit of Dr. Sardjito General Hospital Yogyakarta during the year 2023. Baseline laboratory data were obtained within 24 hours after admission. TyG index was calculated by $\text{Ln}[(\text{fasting triglyceride (mg/dl)} \times \text{fasting blood glucose (mg/dl)})/2]$. ENDs were determined by at least a 2-point increase of the National Institute of Health Stroke Scale (NIHSS) within 7 days of admission. Altered mental status was defined as cognitive disturbances, decreased level of consciousness, or delirium. Univariate analysis was performed and then the patients were grouped based on ENDs occurrence. The association between the TyG index and ENDs was analyzed and its predictive ability was determined with the receiver operating characteristic (ROC) curve. Multivariate logistic regression analysis was performed to determine other confounding factors.

RESULTS

There were 309 patients included in the study. Baseline characteristics showed 53.07% was male, the mean age was 62.7 ± 12.2 years old and the baseline NIHSS score was 7.9 ± 7.2 . The TyG index of all patients had a median of 8.79 (IQR=0.84). There were 43 patients suffering ENDs (13.9%). ROC curve analysis showed TyG index of 8.66 had the best predictive cut-off value for ENDs with the area under the curve (AUC) being 0.586 (0.49-0.68) with sensitivity and specificity values of 74.4% and 44.5%, respectively. Among patients with ENDs, those with higher TyG index ($n=32$; 10,35%) were significantly more common ($p=0.02$). Bivariate analysis showed higher TyG was associated with ENDs (OR=2.33, 95% CI 1.13-4.82, $p=0.02$). Multivariate analysis showed that higher TyG index (OR 2.5; 95%CI 1.18-5.32; $p=0.017$) and altered mental status at admission (OR=4.1; 95% CI 1.73-9.69; $p=0.001$) were associated with ENDs.

CONCLUSION

Our study revealed that higher TyG index and altered mental status in acute ischaemic stroke patients were associated with an increased risk of early neurological deteriorations.

KEYWORDS

Acute ischaemic stroke, TyG index, Altered mental status, Early neurological deteriorations

Asian Society Against Dementia
PD-ASAD-40

PLASMA P-TAU181 AND OTHER BLOOD-BASED BIOMARKERS CAN BE USED TO PREDICT AMYLOID PET POSITIVITY

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BACKGROUND

This study aimed to determine the efficacy of combining plasma phosphorylated tau (p-tau)181, amyloid beta (A β)42/A β 40, neurofilament light (NfL), and apolipoprotein E (APOE) genotypes for detecting positive amyloid positron emission tomography (PET), which is little known in the Asian population, in two independent cohorts.

METHODS

Biomarkers were measured using a single-molecule array (Simoa) in a cohort study (Asan). All participants underwent amyloid PET. Significant changes in the area under the curve (AUC) and Akaike Information Criterion values were considered to determine the best model. The generalizability of this model was tested using another cohort (KBASE-V).

RESULTS

In the Asan cohort, after adjusting for age and sex, p-tau181 (AUC = 0.854) or APOE ϵ 4 status (AUC = 0.769) distinguished A β status with high accuracy. Combining them or adding NfL and A β 42/40 improved model fitness. The best-fit model included the plasma p-tau181, APOE ϵ 4, NfL and A β 42/40. The models established from the Asan cohort were tested in the KBASE-V cohort. Additionally, in the KBASE-V cohort, these three biomarker models had similar AUC in cognitively unimpaired (AUC = 0.768) and mild cognitive impairment (MCI) (AUC = 0.997) participants.

CONCLUSION

Plasma p-tau181 showed a high performance in determining A β -PET positivity. Adding plasma NfL and APOE ϵ 4 status improved the model fit without significant improvement in AUC.

KEYWORDS

APOE; Alzheimer's disease; amyloid beta; amyloid positron emission tomography; neurofilament light; p-tau181

LOW-INTENSITY ULTRASOUND IMPROVES COGNITIVE FUNCTION IN PATIENTS WITH ALZHEIMER'S DISEASE

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BACKGROUND

This study aims to explore whether employing low-intensity ultrasound in individuals on the Alzheimer's disease (AD) continuum, specifically those with mild cognitive impairment or early-staged dementia, leads to beneficial cognitive outcomes via neuromodulation induced by ultrasound.

METHODS

Before undergoing ultrasound therapy, positive results were observed in the 18F-florbetaben amyloid PET scans of all subjects. To confirm the safety of the ultrasound procedure, brain MRIs were performed both pre- and post-treatment. Our approach utilized a low-intensity ultrasound system equipped with four separate transducers operating at a base frequency of 250kHz. Treatments were carried out three times weekly, spanning a total of four weeks, with each treatment session lasting 30 minutes of sonication.

RESULT

Quantitative analysis revealed that the scores for the Trail Making Test-Black and White (TMT-BW) following a four-week ultrasound therapy period were lower than the initial baseline (TMT-BW A, from 115.6 ± 70.1 to 87.3 ± 56.2 , $P=0.017$; TMT-BW B, from 316.2 ± 160.6 to 231.3 ± 64.3 , $P=0.044$). When



comparing FDG PET scans before and after treatment, there was a notable increase in FDG PET uptake in the frontal and parietal regions of the early-onset group versus the late-onset group. Furthermore, post-treatment Brain MRIs showed no signs of cerebral microbleeds or edema, indicating the safety of the ultrasound therapy.

CONCLUSION

Our research verifies the safety of employing low-intensity ultrasound therapy in early-stage Alzheimer's disease patients. Additionally, it provides evidence that ultrasound treatment can facilitate clinical enhancements within the AD continuum.

KEYWORDS

Alzheimer's disease, Low intensity Ultrasound, Neuromodulation

Asian Society Against Dementia

PD-ASAD-42

PRELIMINARY STUDY OF VALIDITY AND RELIABILITY OF THE FRONTAL ASSESSMENT BATTERY IN VASCULAR COGNITIVE IMPAIRMENT: A CROSS-SECTIONAL STUDY IN INDONESIAN TERTIARY CARE HOSPITALDiba Anindhita Nandawardhani, MD¹, Amelia Nur Vidyanti, MD, PhD¹, Astuti Prodjohardjono, MD, PhD¹, Cempaka Thursina Srie Setyaningrum, MD, PhD^{1*}¹*Department of Neurology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/ Dr. Sardjito General Hospital, Yogyakarta, Indonesia***BACKGROUND**

The Frontal Assessment Battery (FAB) is one of the most widely used executive functioning screeners worldwide in clinical settings. Deficits of executive function are the very first symptoms of vascular cognitive impairment (VCI) involving frontal lobe function. There has never been an Indonesian adaptation of the FAB. This preliminary study aimed to measure validity and reliability of the FAB in VCI in Indonesia and to measure the correlation between FAB test with Trial Making Test B (TMT B) and Clock Drawing Test (CDT).

METHODS

This study used a cross-sectional design. 40 people consist of 20 VCI group and 20 healthy people group in neurology clinic of Dr. Sardjito General Hospital Yogyakarta during the year 2024 included in this study. The FAB-INA test was conducted first, followed by TMT B and CDT. The FAB-INA items were divided into six items: (1) concept formation and abstract reasoning (similarities); (2) mental flexibility (phonemic verbal fluency); (3) motor programming (Luria motor sequences); (4) sensitivity to interference (conflicting instructions); (5) inhibitory control (go-no-go); (6) environmental autonomy (prehension behaviour). Pearson's correlation and confirmatory factor analysis were employed for validity test. Cronbach's alpha coefficient was performed to determine internal reliability.

RESULTS

The results of validity testing from 40 respondents showed that all items in the FAB-INA were moderately valid with correlation coefficients (r) of > 0.3 ($p < 0.01$). Confirmatory factor analysis showed a convergence with the variance explained more than 50% for all items, which also indicated that FAB-INA had acceptable construct validity to measure executive function in VCI. Cronbach's alpha values (α) were 0.756, 0.708, 0.741, 0.725, 0.775, 0.789 for similarities, phonemic verbal fluency, motor programming, conflicting instructions, inhibitory control, and environmental behaviour, respectively. The FAB-INA and its items were strongly related to TMT B and CDT measures with correlation coefficients (r) of > 0.6 ($p < 0.01$). The strongest association being found with TMT B with correlation coefficients (r) of -0.814 ($p < 0.01$) which indicated that the higher the FAB score, the lower the TMT B score. Meanwhile, correlation coefficients (r) of 0.732 ($p < 0.01$) were found in CDT.

CONCLUSION

Our study reveals that FAB-INA had good validity and reliability to measure executive function in VCI. Moreover, the FAB-INA had strongest correlation with TMT B for executive function in VCI. Further study of the reliability in VCI is still needed.

KEYWORDS

Frontal assessment battery, trial making test B, clock drawing test, vascular cognitive impairment, validity study, reliability study

Asian Society Against Dementia
PD-ASAD-43

CHARACTERIZING MEMORY CLINICS IN SINGAPORE: THE SINGAPORE MEMORY CLINIC COLLABORATION SURVEY

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BACKGROUND

Memory clinics (MC) are described as multidisciplinary centres that offer a highly specialized and comprehensive approach in the assessment, diagnosis, treatment, care and support of people with mild cognitive impairment (MCI) and dementia. They play a crucial role in the early diagnosis of dementia with a goal of preserving independent function. There is limited data regarding current practices of memory clinics in Singapore. The study aims to characterize the current practices of Singapore memory clinics.

METHODS

This is a cross-sectional study conducted using a voluntary, self-administered questionnaire sent via e-mail from June to August 2023. The questionnaire was based on the one used in a memory clinic survey in Australia for the Australia Dementia Network (ADNeT) Memory and Cognition Clinic Guidelines.

RESULTS

We received a total of 11 responses from public institutions (10 hospital based and 1 polyclinic). Among the respondents, 5 were geriatricians, 4 were neurologists and 2 were family physicians. Despite the availability of technology, only 8 (66.7%) clinics used telemedicine as a mode of assessment and this is mainly limited to follow-up visits. While wait-times varied, only 63.6% of clinics were able to offer an appointment within 30 days for HIGH priority referrals. Wait-times for ROUTINE priority referrals were within 60 days in 45.5% of the clinics. All clinics offer follow-up visits but the wait-times for these is every 6 months. All clinics provide advice on pharmacologic treatments whilst 90.9% offer neuropsychological services.

CONCLUSION

Wait-times and post-diagnostic services for Singapore MCs are comparable to what is being seen in MCs from other countries. However, there is still a need for a guideline to standardise memory clinic services in Singapore so as to manage the rising number of dementia cases in the country and new developments in management.

KEYWORDS

Memory clinic, Singapore, Memory clinic survey, current clinical practice

Asian Society Against Dementia

PD-ASAD-44

EXPLORING THE ASSOCIATION BETWEEN COGNITIVE IMPAIRMENT AND CHRONIC KIDNEY DISEASE: A SCOPING REVIEWChing Ching Hii¹, Aznida Firzah Abdul Aziz¹, Mohd Fairuz Ali¹, Teh Rohaila Jamil¹, Ahmad Hazri Ilyas¹¹*Department of Family Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia***BACKGROUND**

Chronic kidney disease and cognitive impairment are both significant global health issues. It is increasingly recognized that individuals with chronic kidney disease (CKD) are at higher risk of developing cognitive impairment compared to general population. The intersection of chronic kidney disease and cognitive impairment presents challenges to both patients and healthcare providers. There is no definite cure for both chronic kidney disease and dementia. Understanding the multifaceted associations contributing to cognitive impairment in chronic kidney disease is crucial for effective management and intervention strategies. This scoping review aims to comprehensively map the existing literature on factors associated with cognitive impairment in chronic kidney disease.

METHODS

A systematic search was conducted across three major electronic databases which are PubMed, Web of Science and Scopus, to identify relevant studies published from year 2015 to 2024. Search string "chronic kidney disease" AND (cognitive impairment OR dementia OR neurocognitive) was used. Studies investigating the associations between cognitive impairment and CKD were included. Following the removal of duplicates and initial screening, eligible studies were subjected to full text assessment. Total of 20 studies met the inclusion criteria. The review followed the Arksey and O' Malley framework and adhered to PRISMA-ScR guidelines. Data extraction and synthesis were performed to identify common themes and factors associated with cognitive impairment in chronic kidney disease.

RESULTS

The identified factors associated with cognitive impairment in chronic kidney disease encompassed a wide range of domains, including demographic factors i.e., older age and lower education level, disease related variables such as lower calculated glomerular filtration rate (eGFR), albuminuria, factors specifically associated with renal issues like uraemia, anaemia and renal replacement therapy, comorbid conditions like diabetes mellitus, hypertension, stroke, as well as dietary influence.

CONCLUSION

This scoping review provides an overview of the factors associated with cognitive impairment in chronic kidney disease, highlighting the multifactorial nature of this condition. Patients with chronic kidney disease appear to have cumulative risk factors associated with cognitive impairment. Targeted screening for cognitive impairment should be considered in these patients. Future research should focus on interventions to prevent or ameliorate cognitive impairment in this susceptible population. (349 words)

KEYWORDS

Chronic kidney disease, cognitive impairment, dementia, neurocognitive disorder

POSTERIOR CORTICAL ATROPHY: CHALLENGING RARE DIAGNOSIS

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INTRODUCTION

Posterior Cortical Atrophy (PCA) is a rare, debilitating clinico-radiological syndrome characterized by progressive loss of higher order visuospatial, visuoperceptual and other posterior cortical functions which includes space and object perception deficits due to occipito-parietal and occipito-temporal atrophy. PCA is among of the major atypical AD phenotypes and designation as visual-variant, biparietal, or visual-spatial AD. Here, we present to you, a case of PCA.

REPORT

A 59 year old gentleman was premorbidly active and excellent sports and science teacher. Presented with progressively worsening of visuospatial and visuoperceptual disturbances. It started in 2021 and noted by his wife, he experienced inability to assess the distance of cars during driving which resulted in emergency brake, associated with worsening imbalance gait and giddiness. The symptoms then persisted till 2023, when he had a decline in cognitive functions - more forgetful, misplacing his personal items and shorter attention span.

He was assessed by Psychiatric team which revealed impaired functions in three areas including language, executive functioning and depth perceptions. His score in Colorado Posterior Cortical Questionnaire is 32/60 and shown positive findings Constructional apraxia, Letter Cancellation Test and Facial recognitions. MRI brain shown posterior cortical atrophy. The diagnosis was made based on the findings coupled with MRI Brain result and he is scheduled for PET Scan.

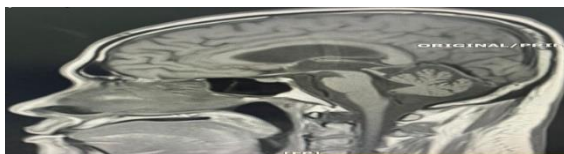


Figure 1: MRI BRAIN: Brainstem atrophy with flattened pons

Posterior cortical atrophy (PCA) is a clinico-radiological syndrome characterised by the progressive loss of higher order visuospatial, visuoperceptual and other posterior cortical functions consistent with occipito-parietal and occipito-temporal atrophy. Main features of this illness comprised of space and object perception deficits, constructional dyspraxia, environmental agnosia, dressing apraxia, alexia, elements of Gerstmann syndrome with sparing of other cognitive domains (1). The clinical progression of PCA started with early deterioration in space perception, object perception and calculation followed by decline in language, executive and episodic memory functions (2). PCA is a diagnosis of exclusion which requires exclusion of other causes of visual impairment (cortical and ocular) - stroke, which can be



distinguished from the insidious and progressive PCA course, lack of acute presentation and imaging appearances (1).

CONCLUSION

Diagnosis of PCA is remain a challenge as it is typically delayed due to misdiagnosis with an ocular or psychological illness. Establishing diagnosis promptly will provide opportunities for accurate multidisciplinary managements.

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EXPLORING THE INFLUENCE OF AGE AND EDUCATION ON VISUAL COGNITIVE ASSESSMENT TEST (VCAT) COGNITIVE PERFORMANCE IN MALAYSIAN COGNITIVELY HEALTHY ELDERLY

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INTRODUCTION

The global phenomenon of population aging presents a significant challenge in the realm of neurodegenerative disorder prevention and detection. As such, the need for effective cognitive assessment tools becomes paramount. The Visual Cognitive Assessment Test (VCAT) emerges as a promising solution due to its language-neutrality, making it suitable for diverse multilingual populations. This study aims to investigate the correlation between age, education, and cognitive performance as measured by the VCAT, offering valuable insights into potential risk factors for cognitive decline and dementia.

METHODS

Data for this study were obtained from the Validation of the VCAT for the Early Diagnosis of Cognitive Impairment in a Multilingual Population in Malaysia Study, conducted between May 2018 and December 2019 across five hospitals in Northern Malaysia. Cognitively healthy individuals were defined as having no dementia complaints and a Clinical Dementia Rating (CDR) score of zero. Participants aged 50 years and above, with a minimum of six years of formal education, were recruited. Participants were categorized into three education groups: 6-9 years of formal education (n=7), 10-13 years (n=39), and more than 13 years (n=33). Additionally, participants were divided into seven age brackets ranging from 50 to above 80 years. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 22. Parametric One-way ANOVA or non-parametric Kruskal-Wallis tests were employed to compare VCAT performance across age groups and schooling levels. Spearman's correlation coefficient was utilized to explore relationships between VCAT scores and VCAT cognitive domains.

RESULTS

Analysis of data from 79 cognitively healthy elderly participants revealed an average VCAT score of 25.1 ± 3.09 , ranging from 17 to 30. Significant associations were observed between age and total VCAT scores ($p = 0.001$) as well as memory ($p = 0.004$), while education correlated significantly with visuospatial ($p = 0.001$) and executive ($p = 0.003$) domains. Notably, VCAT scores demonstrated a correlation with age but not educational level (correlation analysis: $r = 0.094$, $p = 0.412$), with higher scores evident among younger age groups (correlation analysis: $r = -0.336$, $p = 0.002$).

CONCLUSIONS

In conclusion, our study sheds light on the influence of age and education on the cognitive performance of healthy elderly individuals, as assessed by the VCAT. By elucidating these relationships, we contribute to a deeper understanding of the factors underlying cognitive aging and dementia risk. Moving forward, targeted interventions aimed at promoting cognitive health and preventing dementia may benefit from considering age and education as key determinants of cognitive resilience in older adults. However, future research endeavours should focus on longitudinal studies to elucidate the trajectory of cognitive decline over time and validate these findings in larger, more diverse cohorts.

KEYWORDS

VCAT, cognitively healthy participants, age, education

Asian Society Against Dementia
PD-ASAD-47

COGNITIVE IMPAIRMENT AMONG ELDERLY WITH DIABETES AND ITS ASSOCIATION WITH DIABETES CONTROL. A CROSS-SECTIONAL STUDY AT A UNIVERSITY-BASED PRIMARY CARE CLINIC

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BACKGROUND

The rise in diabetes and the shift in aging population increases the prevalence of cognitive impairment among elderly with diabetes which contributes to significant health challenges. It is increasingly recognized that diabetes has significant effect on cognitive decline, together with the aging population. The relationship between diabetes control and cognitive impairment is important to identify early detection of cognitive impairment for effective management, improve quality of life and reduce health care burden.

OBJECTIVES

This scoping review summarizes of existing literature on the prevalence of cognitive impairment among elderly with diabetes, the association between diabetes control and cognitive impairment, factors associated with cognitive impairment among elderly with diabetes, and the correlation of diabetes control (HbA1c) with cognitive impairment in elderly with diabetes.

METHODS

A systematic search was conducted via multiple electronic databases to identify relevant studies from PubMed, Web of Science and Scopus that has been published between the year 2015 and 2024. Studies that demonstrated association between cognitive impairment and diabetes among elderly were included. Those studies that met the inclusion criteria were analysed for key findings, methodologies and limitations. A total of 12 relevant studies were included after removal of duplicates. Data retrieval and synthesis was conducted to identify the association factors between diabetes control and cognitive impairment among elderly and its associated factors.

RESULTS

Based on the review, studies from various regions were identified which includes China, India, Sweden and Malaysia, demonstrating varied prevalence rates of cognitive impairment among elderly with diabetes. Conflicting evidence in regards of association between cognitive impairment and diabetes control was observed, with factors such as HbA1c level, age, education level, ethnicity and comorbidities emerging as significant determinants of cognitive impairment in elderly with diabetes.

CONCLUSION

This scoping review encompasses the complexity of the relationship between diabetes control and cognitive impairment among elderly populations. Diabetes control poses cumulative risk factor in association with cognitive impairment. Early screening for cognitive impairment in elderly with diabetes should be performed. Some of the studies demonstrated discrepancies in findings suggest the influence of diverse demographic, cultural and methodological factors. Further studies are needed to elucidate this relationship and tailored care intervention for managing cognitive decline in elderly with diabetes populations. (363 words)

KEYWORDS

Diabetes Control, HbA1c, cognitive impairment, elderly, dementia

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MITRAGYNINE (KRATOM)-WITHDRAWAL BEHAVIOUR AND COGNITIVE IMPAIRMENTS CAN BE AMELIORATED BY AN EPIGENETIC MECHANISM

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BACKGROUND

Kratom is a preparation from *Mitragyna speciosa*, which is used as a natural drug preparation for many purposes in the world. However, an overdose of Kratom may cause addiction-like problems including aversive withdrawal resulting in cognitive impairments via unknown mechanisms. Its main psychoactive alkaloid is mitragynine, showing opioid-like properties.

AIMS/METHODS

By comparing the neuropharmacological effects of mitragynine and morphine withdrawal in rats, we aimed to identify a potential pharmaceutical treatment that could alleviate the cognitive impairments that are commonly associated with withdrawal.

RESULTS

We discovered that dose-dependent behavioural withdrawal symptoms after a 14-day treatment with mitragynine (1–10 mg/kg) resembled those of withdrawal from morphine (5 mg/kg). However, mitragynine (5 and 10 mg/kg) also induced impairments in a passive avoidance task. Mitragynine withdrawal not only reduced hippocampal field excitatory postsynaptic potential (fEPSP) amplitudes in basal synaptic transmission and long term potentiation (LTP) but also reduced epigenetic markers, such as histone H3K9 and H4K12 expression. At the same time, it up-regulates HDAC2 expression. Targeting the epigenetic adaptations with the HDAC inhibitor, SAHA, reversed the effects of mitragynine withdrawal on epigenetic dysregulation, hippocampal input/output curves, paired-pulse facilitation, LTP and attenuated the cognitive deficit.

CONCLUSION

The data from this work show that SAHA can attenuate cognitive impairments and hippocampus transmission deficit induced by mitragynine withdrawal. Thus, it may provide a new treatment approach for aversive Kratom/mitragynine withdrawal and addiction.

KEYWORDS

cognitive deficits, histones, Kratom, LTP, mitragynine, morphine withdrawal, SAHA

UNDERSTANDING THE PERCEPTIONS OF INFORMAL CAREGIVERS REGARDING RESPITE CARE: A SCOPING REVIEW

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BACKGROUND

Respite care is crucial for providing temporary relief to informal caregivers, yet it remains underutilized and poorly understood, particularly among Asian populations. Understanding the impact of respite care is crucial for enhancing caregiver well-being and improving care recipient outcomes. This scoping review aims to explore the perceptions of respite care among informal caregivers, identifying gaps in the literature to enhance support systems for this population.

METHODS

A comprehensive search strategy using the term "respite AND (carer OR carers OR caregiver OR caregivers)" was employed to identify relevant literature. Peer-reviewed articles, grey literature, and policy documents published from 2000 onwards were included. Eleven databases, including Web of Science, Scopus, ScienceDirect, and PubMed, were searched. The review followed the Arksey and O'Malley framework for scoping reviews and adhered to PRISMA-ScR guidelines.

RESULTS

Originally, 1,892 sources were retrieved, with 1,541 being excluded due to duplication or based on title/abstract. This left 351 references that were reviewed and categorized. Among these, 37.6% focused on older adults, stroke survivors, dementia, and Alzheimer's, while 26.5% pertained to children. The remaining 126 references provided general descriptions of respite care, of which 65 met the inclusion criteria. The literature notably highlighted caregiving within older adult and stroke and dementia populations, emphasizing the positive impact of respite care on caregiver well-being. In Asian contexts, significant gaps were identified, with many caregivers being unaware of respite care services. Of those aware, only a minority utilized the service, citing barriers such as transportation issues, negative experiences, financial constraints, family disagreements, and distrust of outsider care quality. Qualitative analysis underscored intergenerational dynamics, emphasizing filial attitudes and behaviors.

CONCLUSION

This scoping review sheds light on varied perspectives of informal caregivers, revealing insights into their experiences and awareness regarding respite care. Overcoming barriers related to low awareness and utilization is crucial for improving caregiver support. Recognizing intergenerational dynamics in caregiving suggests the need for culturally appropriate approaches to providing respite care. Tailored services can align with individual preferences and boost caregiver satisfaction. Future research efforts should prioritize understanding the long-term impact and exploring innovative strategies for delivering respite care.

KEYWORDS

Respite care, informal caregivers, caregiving, well-being, support services.

SECRETOME HYPOXIA MESENCHYMAL STEM CELL INJECTION AS A POTENTIAL THERAPY IN ISCHEMIC STROKESisca Silvana^{1,2}, Iskandar Japardi³, Muhammad Rusda³, Rini Savitri Daulay³, Agung Putra⁴,
Irawan Mangunatmadja⁵¹*Doctoral Program Department of Paediatric, Faculty of Medicines, Universitas Sumatera Utara, Indonesia*²*Staff of Paediatric Department, Faculty of Medicines, Universitas HKBP Nommensen Medan, Sumatera utara, Indonesia*³*Staff of Paediatric Department, Faculty of Medicines, Universitas Sumatera Utara, Indonesia*⁴*Stem Cell and Cancer Research (SCCR), Faculty of Medicine, Universitas Islam Sultan Agung (Unissula), Semarang, Central Java, Indonesia*⁵*Paediatric Department, Faculty of Medicines, Universitas Indonesia***INTRODUCTION**

Ischemic Stroke is a sudden neurological deficit that result from a blockage in blood vessels of the brain that causing brain damage, disability and death. Secretome hypoxia mesenchymal stem cells (SH-MSCs) is a potential therapy to improve the neurological deficit by increasing the expression of VEGF (Vascular Endothelial Growth Factor) and CD31. Vascular Endothelial Growth Factor is a specific mitogen from endothelial cell which has the strongest specificity in angiogenesis, so does the CD31 in endothelial vessel making an interaction and homophylic function to keep the barrier of vascular permeability. Neurogenesis and angiogenesis effect from VEGF and CD31 activity by SH-MSCs causing brain cells regeneration and giving neurological improvement.

METHODS

The method used in this study was laboratory true experimental post test only control group design. Sampel was taken with non-probability sampling with consecutive sampling which uses 24 Rattus novergicus rats as object of this research were divided into 3 groups, there are sham, control, P1 (MCAO + 150 ul secretome) group. Rats in control and P1 group were made in stroke condition with Middle Cerebral Artery Occlusion methods by clamping Common Carotid Artery. Rats neurological evaluation measured by modified Neurologic Severity Scores (mNSS).

RESULTS

Mean value of VEGF expression in P1 is $(3,37 \pm 1,94)$ ng/ml that get higher result than control group $(0,46 \pm 0,21)$ ng/ml and sham group $(1,00 \pm 0,14)$ ng/ml. Mean value of CD31 expression in P1 is $(7,05 \pm 2,82)$ % that get higher result than control group $(5,58 \pm 1,51)$ %.

CONCLUSION

SH-MSCs can induce cell proliferation, neuron cell survival, angiogenesis, vascularization, neurogenesis and blood-brain-barrier integrity recovery in rats brain through the increases of VEGF and CD31 expressions and lead to neurological function and clinical improvement in ischemic stroke in rats.

KEYWORD

Mesenchymal Stem Cell, VEGF, CD31, Ischemic Stroke

SPHEROID FORMATION INCREASED CD133-POSITIVE CANCER STEM CELLS IN NON-SMALL CELLS LUNG CANCER CELL LINES: IMPLICATIONS FOR ADVANCED PROGNOSTIC ASSESSMENTKhadijat Abubakar Bobbo^{1,2*}, Kamal Shaik Fakiruddin³, Chau De Ming⁴, Norshariza Nordin⁴, Syahril Abdullah^{1,4,5*}¹*UPM-MAKNA Cancer Research Laboratory, Institute of Bioscience, Universiti Putra Malaysia, 43400 UPM, Selangor, Malaysia*²*Department of Human Anatomy College of Medical Sciences, Faculty of Medicine, Gombe State University 760253 GSU, Gombe State-Nigeria*³*Haematology Unit, Cancer Research Centre, Institute for Medical Research (IMR), National Institute of Health (NIH), Ministry of Health Malaysia, 40170 Shah Alam, Selangor, Malaysia*⁴*Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM, Selangor, Malaysia*⁵*Malaysia Genome and Vaccine Institute, National Institutes of Biotechnology Malaysia, Jalan Bangi, 43000 Kajang, Selangor, Malaysia.***BACKGROUND**

Cancer stem cells (CSCs) are believed to be the culprit behind drug resistance, metastasis and tumor relapse. These cells are hypoxic stem cell-like subunit, constituting a negligible percentage of heterogenic tumour. The CSCs show the propensity to migrate, symmetrical and asymmetrical replicate, and differentiate; hence, repopulating tumor. These cells express transcription factors; SOX2, OCT4, and NANOG enhancing stemness properties. They also express unique CSC surface biomarkers such as ALDH, CD44, and CD133. Here we use the CD133, which is one of the most established CSCs markers in several types of cancers, especially non-small cell lung cancer (NSCLC), to analyse the CSCs levels in parent and the fourth generation (G₄) spheroid.

METHODOLOGY

To increase the CD133-positive CSCs' population in NSCLC (A549, H460 & H2170) cell lines underwent four cycles/generations (G₄) spheroid formation. For each cell line, 1000 cells/well were seeded in 96-well ultralow attachment plates in low-serum medium supplemented with B27. After 14 days, spheroids were dissociated and reseeded for four more cycles. The spheroid sizes, CD133-positive CSCs' population, clonogenicity, chemoresistance, death receptors and stemness transcription factors were analysed.

RESULT & DISCUSSION

A significant increase in the spheroid size and CD133⁺ expression were observed in G₄ cells. This supports studies in breast, colon and prostate cancer cell lines. Furthermore, a higher cisplatin resistance (IC₅₀) was demonstrated by both monolayer and 3-D cultures of G₄ cells. An increase in the number of CD133⁺ CSCs and poor drug penetration in the case of the spheroids, might be associated with these higher drug resistances. Additionally, the G₄ cells formed larger spheroids and more colonies. Furthermore, death receptor four (DR4) and decoy receptor two (DcR2) were significantly increased and decreased respectively. These both are

indicators of tumor aggression and higher drug resistance. Finally, a significantly increase in the stemness genes were observed in the G₄ cells. Previous studies have shown that CSCs express more of the factors than the non-CSC cancer cells. Through the JAK/STAT and Wnt/ β -catenin signaling pathways, these transcription factor have been demonstrated to generate stemness, self-renewal, metastasis, invasion, and chemoresistance in cancer stem cells.

CONCLUSION

This study demonstrates that 3D culture successfully enhances the population of CD133⁺ CSCs in NSCLCs cell lines. Significantly upregulating stemness transcription factors, and certain death receptors resulting to tumor prognostic advancement in the enhanced CSCs cells lines. This is essential for targeted therapeutic strategies, and improving clinical management for advanced cancer.

KEYWORDS

Cancer stem cells, non-small cell cells, CD133, spheroid formation, stemness transcription factors

ACKNOWLEDGMENT

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A CASE OF HUNTINGTON DISEASE PRESENTING AS DEMENTIA

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INTRODUCTION

Huntington's disease (HD) is an autosomal dominant neurodegenerative disease with anticipation phenomenon seen in families due to CAG trinucleotide repeat expansion located in the first exon of the HD gene. The CAG repeat is highly polymorphic and varies from 6 to 37 repeats on chromosomes of unaffected individuals and from more than 30 to 180 repeats on chromosomes of HD patients.

CASE REPORT

A Malay man, ex-hotel staff with underlying history of left lung benign tumor post left lung lobectomy and renal calculi presented initially on the age of 33 years old with memory issues, difficulty in recall, repeating same questions, slowness in answering questions, slow movements, depression, and anxiety. He was dismissed from his work due to his behaviour during employment. There was a strong family history of maternal Parkinson-like disease symptoms whereby his mother, an aunt and uncle were affected at approximately 40 years old.

Subsequently, at age 40 years, he developed chorea of bilateral upper and lower limbs, facial dystonia, and difficulty in ambulation. On examination, there was stereotypic jerky facial movement with mouth twitching. His MMSE score was 24 while MOCA score was 26. Brain MRI showed cerebral atrophy with associated volume loss at bilateral caudate nuclei and putamen. Genetic molecular testing showed a full expanded allele with 47* $\pm$ 2 CAG repeats in the HD gene.

CONCLUSION

Huntington disease can mimic neuropsychiatric symptoms such as dementia. Additional movement disorder symptoms such as parkinsonism and chorea which can manifest later in the disease progression are important clues for HD diagnosis.

HEMOLYTIC UREMIC SYNDROME: ATYPICAL YET TYPICAL

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INTRODUCTION

Hemolytic uremic syndrome is characterized by classic triad of microangiopathic anemia, thrombocytopenia, and acute kidney injury. About 20% of cases sometimes presented with seizure and extrapyramidal symptoms. Central nervous system manifestation in hemolytic uremic syndrome still remain enigmatic, hence treatment usually empiric.

REPORT

We hereby discussed a case of a 3-years-old boy with underlying steroid sensitive nephrotic syndrome. He developed diarrhea (non-bloody) and fever for a day. He was presented to us with hypovolemic shock and acute encephalopathy. He developed generalized tonic seizure within 24 hours of admission.

He had mild acute kidney injury with proteinuria and hematuria; multiple electrolyte imbalances; and also transaminitis. He had persistent thrombocytopenia ranging from 24,000 to 90,000 /unit with elevated LDH and presence of schistocytes on the peripheral blood film, suggestive of possible thrombotic microangiopathies. Stool culture grew salmonella and enteropathogenic E.coli.

Neurologically, he was persistently encephalopathic with absent menace reflex and bilateral upper motor neuron signs, i.e. spasticity, hyperreflexia and clonus.

He underwent total plasma exchange (TPE) followed by iv human immunoglobulin infusion (1g/kg total 2g/kg). With just 2 sessions of TPE, his hematological abnormalities, transaminitis, and acute kidney injury had resolved with less encephalopathy and pyramidal signs. After extubation, he was noted to have extrapyramidal manifestation such as orobuccal dyskinesia and choreoathetosis as well as cerebellar ataxia which reduced over the hospital stay.

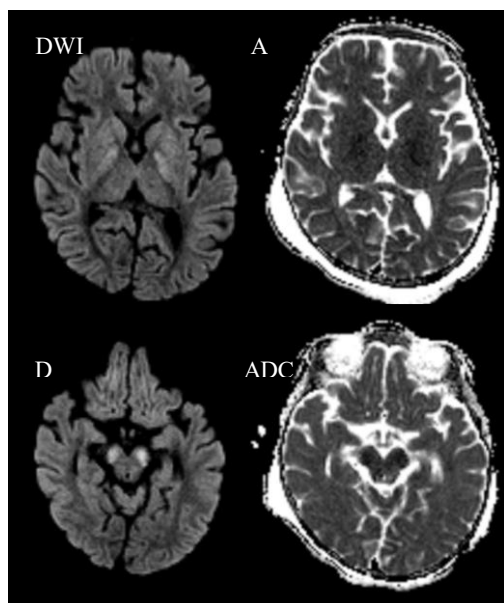


Figure 1: Axial T2W & ADW: Bilateral near symmetrical restricted diffusion of cerebral peduncles of the midbrain, and to a lesser extent at the basal ganglia, internal capsules, thalami and cerebellum.

During the clinic follow up, he was verbal and not encephalopathic with bilateral positive menace reflex. Assessment during clinic showed he had excellent cognitive recovery but relatively slower motor recovery with modified Rankin score of 4.

CONCLUSION

MRI is the modality of choice, better done in acute phase, for diagnostic or prognostic of the disease. TPE should be considered early in patients with HUS and neurological complications. Prognosis was favorable even with severe CNS involvement.

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Asian Society Against Dementia
PD-ASAD-54**ANOSOGNOSIA OF APATHY IN THREE MAJOR NEURODEGENERATIVE DEMENTIA: A CROSS-SECTIONAL STUDY**Hideki Kanemoto,^{1,2} Takashi Suehiro,² Daiki Taomoto,² Yuto Satake,² Kenji Yoshiyama,²
Manabu Ikeda²¹ *Health and Counseling Center, Osaka University, Japan*² *Department of Psychiatry, Osaka University Graduate School of Medicine, Japan***BACKGROUND**

Apathy appears early and frequently in patients with various dementia including Alzheimer's disease (AD), Lewy body disease (LBD), and frontotemporal lobar degeneration (FTLD). Because apathy in patients with dementia affects the burden of caregiving and mortality, intervention in apathy is one of important issues for patients with dementia. Apathy is often associated with lack of awareness of cognitive impairment, which is a barrier to treatment adherence, decreases quality of life, and increases the caregiver burden. However, there are few reports about lack of insight for apathy, i.e. anosognosia of apathy, in patients.

METHODS

We collected the data of patients who visited our clinic from January 2010 to March 2024 and diagnosed with AD, LBD, or FTLD according to international diagnostic criteria. To assess apathy and awareness of apathy, we used apathy subitem of Neuropsychiatric Inventory (NPI) and three apathy items of Geriatric Depression Scale, respectively. We determined that apathy was objectively present by the apathy score of three or more in NPI and judged that patient was aware of the own apathy if the GDS-3A score was two or higher. Participants divided into three groups; those who are aware of their own apathy (APA_{INS+}), those with apathy objectively who are unaware of their own apathy (APA_{INS-}), and those without apathy. Firstly, to evaluate the difference in prevalence of lack of the insight into apathy by the type of dementia, we compared the number of APA_{INS+}, APA_{INS-}, and CONT between AD, LBD and FTLD using Chi square test. To investigate the factors involved in the lack of insight for apathy, stepwise multivariate logistic regression analysis was conducted with whether the patient is in APA_{INS+} or APA_{INS-} as dependent variables and with sex, age, MMSE, clinical dementia rating (CDR), discrepancy of everyday memory checklist scores between patients and family caregiver (deltaEMC), and all subitem scores in NPI as explanatory variables in each of AD, LBD, and FTLD.

RESULTS

We collected data of 778 with AD, 240 with LBD, and 103 with FTLD. While there were no significant differences in MMSE (mean [SD] = AD 20.5 [4.9] vs LBD 21.4 [5.3] vs FTLD 20.1 [6.9]) and CDR between diseases, those with FTLD were significantly younger than the others (mean [SD] = AD 75.9 [8.8] vs LBD 77.3 [6.8] vs FTLD 69.2 [8.5]). APA_{INS-} was more common in AD than in LBD (AD 24.9% vs LBD 15.4% vs FTLD 26.2%). Lack of insight for apathy was significantly related with following variables: age, higher deltaEMC score, as well as higher apathy and aberrant motor behaviors scores in NPI in AD; lower NPI depression score in LBD; and lower CDR and higher delta EMC score in FTLD.

CONCLUSION

Anosognosia of apathy was common in AD and FTLD compared with LBD. Anosognosia of apathy was related to anosognosia of memory impairment, but not to cognitive dysfunction.

KEYWORDS

apathy, anosognosia, Alzheimer's disease

THE IMPACT OF SOCIAL ISOLATION AND LONELINESS ON PSYCHIATRIC SYMPTOMS IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT

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BACKGROUND

Social isolation and feelings of loneliness, which do not always coincide, are known risk factors for psychiatric symptoms such as psychotic symptoms, depression, and anxiety in older people. These symptoms are also common in people with mild cognitive impairment (MCI). This study examines the relationship between isolation, loneliness, and psychiatric symptoms in people with MCI.

METHODS

Data were collected from patients over 60 years of age diagnosed with MCI based on Petersen's criteria, who visited our institution between April 1, 2021, and March 31, 2024. The study included patients without lack of data necessary for analysis. Living status whether they live alone or not was used as a surrogate marker for social isolation, and the UCLA Loneliness Scale was utilized to measure loneliness. Patients' characteristics were compared between those living alone and those not living alone. Multiple regression analysis was conducted with the scores of delusions, hallucinations, depression, and anxiety of Neuropsychiatric Inventory (NPI) as well as Geriatric Depression Scale (GDS) as objective variables and age, sex, living status, UCLA Loneliness Scale scores, and the Mini-Mental State Examination (MMSE) scores as explanatory variables.

RESULTS

The study included 183 MCI patients (mean MMSE score 26.8, mean age 75.6 years, 113 females, 41 living alone). Those living alone had significantly higher age, and predominantly female, with significantly fewer years of education. Psychiatric symptoms, including NPI scores for delusions and hallucinations, and total scores, were significantly higher in those of living alone. Multiple regression analyses showed the following relationships: NPI delusions were positively correlated with living alone; NPI depression were positively correlated with the UCLA Loneliness Scale; NPI anxiety was negatively correlated with age and positively correlated with living alone and the UCLA Loneliness Scale; and GDS scores were positively associated with the UCLA Loneliness Scale and sex. No significant associations were found with NPI hallucinations.

CONCLUSION

In MCI patients, delusions were associated with isolation, anxiety with both isolation and loneliness, and depression primarily with loneliness. While no significant association were observed with hallucinations. These findings suggest that interventions targeting social isolation and loneliness contribute in different manners to improvement of psychiatric symptoms in patients with MCI. Further research is needed to explore the underlying conditions in these cases.

KEYWORDS

mild cognitive impairment, psychosis, depression, anxiety, social isolation, loneliness

PREVALENCE OF COGNITIVE IMPAIRMENT AND THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) TOWARDS COGNITION AMONG PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA (OSA)

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BACKGROUND

It was reported that OSA patients had higher risk to develop cognitive impairment. This study aimed to look for the prevalence of cognitive impairment and domains affected in OSA patient and to explore the effect of continuous positive airway pressure (CPAP) towards cognition among OSA patients with cognitive impairment.

METHODS

A single-centre, cross sectional study was conducted among OSA patients attended Respiratory clinic, Universiti Teknologi MARA (UiTM). Selected patients had cognitive assessment done using Malay version Montreal Cognitive Assessment (MMoCA). Those with MMoCA < 22 were labelled to have cognitive assessment and counselled for CPAP. We further explored the effect of CPAP in this particular groups after 3 months.

RESULTS

Out of 76 patients, 17 patients (22.4%) had cognitive impairment. The mean age (SD) of participants was 52.16 (8.438) years. Those with cognitive impairment had significantly higher apnoea-hypopnea index (AHI) [mean (SD) of 69.4 (19.81), p value < 0.001] and lower oxygen saturation (SPO2) nadir [median 62 (IQR 62-68), p value < 0.001]. The most affected cognitive domains affected among OSA patients with cognitive impairment were attention and memory. On exploratory analysis, the cognitive function improved significantly after CPAP treatment to median (IQR) MMoCA score of 25 (23-28) from 20.5 (19.8-21).

CONCLUSION

22.4% of OSA patients had cognitive impairment. SPO2 nadir was the only factor associated with cognitive impairment in OSA patient after multiple regression. The most affected cognitive domains involved were attention and memory. CPAP was found to improve cognitive function in OSA patients.

KEYWORDS

Obstructive sleep apnoea, cognitive impairment, continuous positive airway pressure

Asian Society Against Dementia

PD-ASAD-57

ATN CLASSIFICATION AND CLINICAL PROGRESSION OF THE AMYLOID-NEGATIVE GROUP IN ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE PARTICIPANTS

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BACKGROUND

Alzheimer's disease has recently been classified using three biological markers (amyloid [A], tau [T], and neurodegeneration [N]) to help elucidate its progression. We aimed to investigate whether there were differences between cognitive function and the clinical dementia symptoms over time relative to the ATN classification in the amyloid-negative group.

METHODS

In the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort, 310 participants who underwent all the tests required for ATN classification were enrolled. The cognitive function score differences (Alzheimer's Disease Assessment Scale-Cognitive Subscale 13 [ADAS-Cog 13], Clinical Dementia Rating Sum of Boxes [CDR-SOB], and Mini-Mental State Examination [MMSE]) between the groups were analyzed using the analysis of covariance and score changes over time with a linear mixed-effects model.

RESULTS

In the cross-sectional analysis, ADAS-Cog 13 scores were higher for A-T-N+ and A-T+N+ than for A-T-N- ($p < 0.001$) and A-T+N- ($p < 0.001$). In the longitudinal analysis, CDR-SOB scores for A-T+N+ deteriorated faster than A-T-N- ($p < 0.001$), A-T+N- ($p < 0.001$) and A-T-N+ ($p < 0.001$). Hippocampal atrophy progressed faster in A-T-N+ ($p < 0.001$) and A-T+N+ ($p = 0.02$) than in A-T-N-.

CONCLUSION

Through this study, we discovered that even in individuals classified as amyloid negative, neurodegeneration with tau deposition exacerbates cognitive decline and worsens clinical symptoms, underscoring the need for continuous monitoring and observation.

KEY WORDS

ATN Classification; Amyloid PET Negative; SNAP; PART

Asian Society Against Dementia

PD-ASAD-58

SUBCUTANEOUS INJECTION OF D-GALACTOSE AT 500MG/KG INDUCES DEMENTIA-LIKE CONDITIONS IN AN8-WEEKS OLD SWISS ALBINO MICE MODELWan Mohd Norsyam^{1,2}, Anis Nabilah Mohammad Naser¹, Shazlin Shaharudin³, Amirah Azmi⁴, Musfirah Zulkurnain⁵, Yong Foo Wong⁶ & Azim Patar¹¹ *Department of Neuroscience, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia*² *Faculty of Sports Science and Recreation, Universiti Teknologi MARA Cawangan Pahang, 26400 Bandar Tun Abdul Razak Jengka, Pahang, Malaysia*³ *Exercise & Sport Science Programme, School of Health Science, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia*⁴ *School of Mathematical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia*⁵ *Food Technology Division, School of Industrial Technology, Universiti Sains Malaysia, 11800 Penang, Malaysia*⁶ *Centre for Research on Multidimensional Separation Science, School of Chemical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia***BACKGROUND**

Prolonged lifespan is associated with an increased incidence of age-related conditions such as dementia. It causes memory decline, language impairment and behavioural issues, impacting both social skills and physical abilities. This study was utilized a D-galactose-induced aging model in mice to ascertain the optimal dosage for inducing aging phenotype in 8-weeks old Swiss albino mice.

METHODS

Twenty-eight male mice were further divided into four groups, receiving either normal saline or three different doses of D-galactose (50mg/kg, 200mg/kg and 500mg/kg) for 10-weeks intervention. All mice underwent daily subcutaneous injections of D-galactose. Behavior analysis including elevated plus maze test, open field test, and novel object recognition test, were conducted during the final week of the intervention. The mice were euthanized via carbon dioxide inhalation. Blood samples were collected for biochemical analysis, and the brain tissues were collected for histological analysis. To further identify the presence of amyloid plaques or neurofibrillary tangles, Congo red staining was used for this purpose.

RESULTS

Administration of D-galactose at a dose of 500 mg/kg had profound changes on the impairment of the behaviour in mice in all behavioural tests ($p < 0.05$). There are significant alterations in levels of inflammatory markers (IL-2, IL-6, IFN- γ & TNF- α) ($p < 0.05$). We found significant changes histologically including neuronal damage, changes morphologically in the hippocampus and cortex. The presence of the amyloid plaques in brain tissues indicated the presence of protein aggregates after 10 weeks of consuming 500 mg/kg of D-galactose compound.



CONCLUSION

D-galactose injection with 500mg/kg altered behaviorally 8-weeks Swiss albino mice, changes the levels of inflammatory as well as brain histology. Further research exploring the underlying mechanisms maybe contribute to the development of effective therapies for combating dementia.

KEYWORDS

Dementia, D-galactose, dosage, mice model, subcutaneous injection



PREDISPOSING AND PRECIPITATING FACTORS FOR DELIRIUM AMONG OLDER HOSPITALIZED ADULTS: A PROSPECTIVE CROSS-SECTIONAL STUDYShin Wuei Tan¹, Jun Ni Keng¹, Siew Im Khoo¹, Stephenie Ann Albart²¹ *Department of Geriatric, Hospital Seberang Jaya, Malaysia*² *Clinical Research Centre, Hospital Seberang Jaya, Penang, Malaysia***BACKGROUND**

Delirium is a serious neuropsychiatric condition characterized by acute and fluctuating inattention, change in cognition and disturbance in awareness. Delirium is a common, costly, and potentially devastating condition for older hospitalized adults, unfortunately it is often unrecognized. We aimed to identify predisposing and precipitating factors associated with delirium in acutely admitted older adults.

METHODOLOGY

We performed a cross-sectional prospective study on patients aged 65 years and above who admitted to the medical wards from 1st January to 31st March 2018. Subjects were recruited by convenience sampling within 48 hours of admission. All patients were screened for presence of delirium using the Short Confusion Assessment Method (CAM-S) form, further confirmed by the gold standard DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) criteria.

RESULTS

Twelve patients (9%) out of 131 patients screened and recruited had prevalent delirium. The predisposing factors were being oldest old (≥ 80 years old), having lower education levels, and frail older adults, which were found to be statistically significant (p value <0.05). Precipitating factors for having a prevalent delirium were hypoxia, physical restraint, iatrogenic events, electrolyte imbalance, hip fracture, immobility, and sleep disturbance (p value <0.05). Based on simple logistic regression, the predisposing factors of oldest age (odd ratio (OR), 19.29; 95% confidence interval (CI) 2.13–174.11), nursing home residence (OR 7.73; 95% CI 1.15–51.82), and frail older adult (OR 5.925; 95% CI 1.52–23.11) are associated with an increased risk of developing delirium. While malnutrition (OR 26.37, 95% CI 6.43–108.12), dehydration (OR 14.36, 95% CI 3.02–68.42), physical restraint (OR 23.60, 95% CI 1.93–283.46), iatrogenic event (OR 11.7, 95% CI 1.486–92.129), electrolyte imbalance (OR 3.54, 95% CI 1.02–12.27), immobility (OR 14, 95% CI 3.49–56.15) and sleep disturbance (HR 11.43, 95% CI 2.88–45.36) were associated with precipitating delirium in older hospitalized patients. However, after multiple logistic regressions, only immobility (OR 11.18, 95% CI 1.26–99.01, p value: 0.03) was the only factor that associated with increased the risk of delirium.

CONCLUSION

Identification of the predisposing and precipitating factors allows prevention, early detection and appropriate management of delirium to prevent morbidity and mortality of older hospitalized patients.

KEYWORD

Delirium, Precipitating, Predisposing

UNVEILING NEURODEGENERATIVE DISORDERS THROUGH COGNITIVE DEFICITS: A CASE SERIES OF HUNTINGTON'S DISEASE

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INTRODUCTION

Huntington's disease is a rare, autosomal dominant neurodegenerative disease. Typically, its onset is during adulthood, characterized by dysfunctional movement, personality and cognition. While the motor signs are dramatic and classically lead to its clinical suspicion, a large proportion may have features suggestive of dementia that predate the clinical signs. We illustrate a series of cases of Huntington's disease, initially presenting with cognitive deficits.

REPORT

36-year-old Chinese gentleman, with history of generalized anxiety disorder five years ago, presented with executive dysfunction characterized by difficulty in organizing, impulsivity, poor planning and prioritization. This was first noticed eight months ago, followed by a significant weight loss. He appeared irritable, constantly tapping his arms and had a compulsion to spit. Otherwise, there were no neurological deficits and his baseline blood investigations were normal. CT brain showed bilateral caudate atrophy. Genetic testing demonstrated 46 CAG repeats, and he was diagnosed with Huntington's disease. He was started on an atypical antipsychotic to manage his behavioural symptoms.

44-year-old Malay lady, with background history of dyslipidemia, complaint of involuntary movement for one year. She had generalized choreiform movement over her extremities and trunk. Further history suggested disorganized thinking, issues with attention, depressive symptoms and insomnia five years ago, preceding choreiform movement. Clinical examination demonstrated forehead and facial chorea, motor impersistence, milkmaid's grip, truncal instability and slow saccades. Blood investigation were within normal limits. MRI Brain showed bilateral caudate atrophy with mild cerebral atrophy. Huntington gene testing was positive for 42 CAG repeat. She showed slight clinical improvement with tetrabenazine and antipsychotics.

50-year-old Malay lady, was referred for gait instability for the past three years. History suggested excessive daytime sleepiness and impaired memory, particularly sensory and working memory, years prior to her motor symptom. Similar issues were observed in first-degree relatives. Clinically, she had prominent facial twitching and generalized chorea, truncal ataxia, dysarthria and irregular gait. Her MMSE score was 19, scoring lower in orientation, attention, registration, and recall. Blood investigations were within normal. MRI brain showed



generalized cerebral atrophy, particularly over bilateral caudate. Huntington gene testing showed an expansion of >40 CTG repeats.

Traditionally, the diagnosis of Huntington's disease is based on the presence of involuntary choreiform movements and a positive genetic test for the CAG-expanded allele gene. Although the diagnosis focuses on the motor signs of the triad, there is increasing evidence that both cognitive and neuropsychiatric symptoms can, and often do, present decades before the onset of motor symptoms. Neuropsychiatric symptoms include depression, anxiety, apathy, irritability, psychosis, disinhibition, and hostility, while cognitive deficit involves impairment in attention, working memory, episodic memory, language, recognition of facial emotion, and empathy.

CONCLUSION

Cognitive deficits and changes in personality are potential early manifestations of Huntington's disease. Identification of these deficits allows prompt diagnosis and planning of treatment strategies to improve quality of life and identify family members at risk.

CHARACTERIZING EARLY- VS LATE-ONSET VASCULAR COGNITIVE IMPAIRMENT FEATURES IN INDONESIAN POPULATION: A CROSS-SECTIONAL STUDY

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BACKGROUND

Vascular cognitive impairment (VCI) is one of the most common types of cognitive disorder in Indonesia. Although the distinct features of early-onset (EO) and late-onset (LO) cases in Alzheimer's disease and frontotemporal dementia have been widely studied, these differences are less well-characterized in VCI. This study aimed to investigate the clinical and cognitive profile of patients with EO (age at onset < 65 years) and LO (age at onset ≥ 65) VCI.

METHODS

This is a retrospective study with data obtained from the Cognitive Clinic Registry of Prof. Dr. dr. Mahar Marjono National Brain Center Hospital, Jakarta, Indonesia (March 2022-2024). All patients with VCI, further classified into VCI-non-dementia (VCI-ND) and vascular dementia (VaD), were included. Comprehensive neuropsychological tests, including Montreal Cognitive Assessment (MoCA), The Consortium to Establish a Registry for Alzheimer's Disease neuropsychological battery (CERAD-NB), Clock Drawing Test (CDT), and Trail Making Test (TMT) A and B, along with neuroimaging examinations, were performed in each patient.

RESULTS

A total of 801 VCI patients were included, with the majority (63.7%) being EO cases. VCI-ND (n=606, 75.7%; EO: 67%, LO: 33%) were more prevalent than VaD (n=195, 24.3%; EO: 53.3%, LO: 46.7%). EO VCI group had a significantly higher proportion of smoking history (EO vs LO VCI: 14.9% vs 3.4%), whilst the opposite was true for cardiovascular disease (LO vs EO VCI: 22.3% vs 13.9%). Hypertension prevalence was higher in LO VaD patients compared to EO (79.1% vs 60.6%).

History of ischemic stroke predominated in all groups; however, hemorrhagic stroke was more frequently found in EO cases, both for VCI-ND and VaD. For concomitant neurological deficits, EO VCI had a higher proportion of aphasia (11.8% vs 6.5%, $p=0.017$) and motor deficits (41.8% vs 29.6%, $p=0.001$). Meanwhile, coordination/balance impairment was more commonly found in LO VCI (12% vs 3.3%, $p<0.001$).

VCI LO patients had significantly worse performances in recent memory ($p=0.007$), recall ($p=0.0001$), and recognition ($p=0.002$) tests, as well as TMT A ($p=0.02$); similar results were also found in VCI-ND subgroups. Meanwhile, EO VCI group had a higher proportion of attention impairment (30.5% vs 23.2% $p=0.03$), especially in VaD patients ($p=0.002$). Other CERAD-NB, MoCA, CDT, and TMT B results were similar between EO and LO cases within VCI-ND and VaD groups.



CONCLUSION

There was a higher burden of EO cases, both in VCI-ND and VaD populations. Cardiovascular risk factors might contribute differently to VCI in different age groups and disease severity. LO cases, especially in VCI-ND, had worse memory functions and recognition; accompanying coordination/balance disorder was also more common. Meanwhile, EO VCI patients displayed a higher number of attention impairments, aphasia, and motor deficits. Our findings suggested that age at onset is an important determinant of the clinical and cognitive features of VCI.

KEYWORDS

vascular cognitive impairment, early-onset, late-onset

THE LACK OF AWARENESS OF DEPRESSIVE SYMPTOMS AND THE NEUROANATOMICAL DIFFERENCES BETWEEN DEPRESSION WITH AND WITHOUT AWARENESS AMONG EARLY-ONSET ALZHEIMER'S DISEASE.

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BACKGROUND

Although the patients with Alzheimer's disease (AD) sometimes show the lack of awareness of depression as well as cognitive impairment, the frequency of the lack of the awareness has not been well known in early-onset AD (EOAD). Moreover, the neuroanatomical differences between depression with and without awareness are also unclear. The aim of this study is to compare the prevalence of the lack of the awareness of depressive symptoms between EOAD and late-onset AD (LOAD) and to explore the brain region related to the awareness of depression in EOAD.

METHODS

Analysis 1: We collected the data of mild cognitive impairment and mild dementia ($CDR \leq 1$ and $MMSE$ score ≥ 22) due to EOAD and LOAD who visited our clinic from 4/2009 to 3/2024. Objective depression and subjective depression were assessed using Neuropsychiatric Inventory (NPI) depression subitem and geriatric depression scale-15 (GDS-15), respectively. NPI depression score ≥ 1 indicates objective depressive symptoms and GDS score ≥ 5 indicates subjective depressive symptoms. Awareness of cognitive impairment were assessed using everyday memory checklist (EMC). To assess the severity of anosognosia of cognitive impairment, we calculated delta EMC by subtracting the caregivers' EMC scores from the patients' EMC scores. Chi-square test was preformed to compare the ratio of objective depressive symptoms without awareness (NPI depression score ≥ 1 and GDS score < 5) among EOAD and LOAD.

Analysis 2: We extracted the data of EOAD patients with objective depressive symptoms (NPI depression score ≥ 1) whose MRI were preformed from 4/2009 to 1/2024. We divided the data into Awareness+ and Awareness- group, using the cutoff score of GDS, 4/5. Brain structures were compared between two groups, using voxel-wise regression in SPM12. Age, sex, MMSE, delta EMC and NPI depression scores were used as the covariates.

RESULTS

Analysis 1: Eighty-one EOAD (Age: 62.7 (7.2), 38 females) and 369 LOAD patients (Age: 78.7 (5.4), 43 females) were included. EOAD group showed significantly higher NPI depression score and lower GDS score than in LOAD group (NPI: 1.21 (1.9) vs 0.69 (1.6),

$p < 0.001$; GDS: 3.21 (2.7) vs 4.59 (3.4), $p = 0.001$). There were no significant differences of MMSE, EMC scores and delta EMC. The ratio of depressive symptoms without awareness was significantly higher in EOAD than in LOAD (22.2% vs 7.3%).

Analysis 2: In Awareness+ group ($n=14$), MMSE score was significantly lower than in awareness- group ($n=10$). There were no significant differences of age, sex, EMC scores and delta EMC among two groups. Awareness+ group showed lower gray matter volume in left angular gyrus compared with Awareness- group ($k=1045$, $p_{FWE}=0.008$).

CONCLUSION

This study indicated EOAD may have less awareness of depressive symptoms than LOAD, despite severer objective depression symptoms. The severity of cognitive impairment may correlate with subjective depression in EOAD. Moreover, the finding that angular gyrus atrophy, which is common in AD, was associated with objective depression symptoms with awareness may indicate some degree of the progression of the disease requires to feel subjective depressive symptoms in EOAD.

KEYWORDS

Early-onset Alzheimer's disease, Awareness of depression, left angular gyrus

Asian Society Against Dementia

PD-ASAD-63

THE ASSOCIATION BETWEEN APOE GENOTYPES, GUT MICROBIOTA, AND COGNITIVE FRAILTY AMONG THE AGELESS COHORT

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INTRODUCTION

Cognitive frailty, characterised by the concurrent presence of physical frailty and mild cognitive impairment, poses a substantial challenge to ageing populations. Recent studies underscore the intricate interplay between gut microbiota and APOE, particularly in neurodegenerative diseases like Alzheimer's. However, investigations into the associations of cognitive frailty, gut microbiota and APOE genotypes cumulatively remains unestablished.

OBJECTIVE

This study aims to examine the relationship between gut microbiota, cognitive frailty, and APOE genotypes in shaping CF progression among community-dwelling older adults.

METHODS AND RESULTS

Blood samples from 1200 participants of the Transforming Cognitive Frailty into Later-Life Self-Sufficiency (AGELESS) cohort will be utilized. Data and samples have been obtained from community-dwelling older participants either first recruited for the Malaysian Elders Longitudinal Research (MELoR) and Towards Unusual Ageing (TUA) cohorts which started in 2013 or as new recruits to replace loss-to-follow up in 2021-22. In addition, stool samples were obtained from 200 consenting participants.

All 1200 blood samples will APOE genotyped for APOE2, E3 and E4 through PCR amplification targeting specific SNPs, to obtain more accurate allele frequencies at a population level which is validated through Sanger sequencing for accuracy. Concurrently, gut microbiota profiling will encompass alpha and beta diversity assessments, providing insights into microbial abundance and diversity dynamics. Subsequently the APOE genotypes will be compared to gut diversity and abundance statistical analyses, comprising ANOVA, principal component analysis, correlation analyses, and various R packages, will scrutinize the relationships between APOE genotypes, gut microbiota composition, and cognitive frailty scores. Expected outcomes include elucidating the intricate interplay among gut microbiota composition, APOE genotypes, and cognitive frailty progression.

CONCLUSION

Insights gleaned from this study hold promise for informing targeted intervention strategies, particularly in mitigating the deleterious effects of APOE E4 on cognitive health. This will contribute to the expanding discourse surrounding the gut-brain axis and its implications for cognitive health within aging populations. The findings have potential implications for tailored interventions and healthcare strategies, especially in lower-middle-income countries like Malaysia.

KEYWORDS

cognitive frailty, gut microbiota, APOE genotype, AGELESS, and Malaysia

Asian Society Against Dementia

PD-ASAD-64

INVESTIGATING STRUCTURAL NEUROIMAGING VARIANCES USING VOXEL-BASED MORPHOMETRY (VBM) BETWEEN BEHAVIORALLY IMPAIRED AND NON-IMPAIRED INDIVIDUALS - BIOMARKERS AND COGNITION STUDY, SINGAPORERasyiqah Binte Shaik Mohamed Salim¹, Yi Jin Leow¹, Ashwati Vipin¹, Nagaendran Kandiah^{1,2}¹ Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore² Duke-NUS Medical School, National University of Singapore, Singapore**BACKGROUND**

Mild Behavioural Impairment(MBI) is a neuropsychiatric syndrome in older adults that could reflect an at- risk state for developing neurodegenerative disorders like Alzheimer's disease[1,2]. Voxel-based morphometry(VBM) is a neuroimaging analysis technique that identifies localised differences in gray matter(GM) volume, revealing structural changes associated with various neuropsychiatric conditions[3,4].

Past research suggests changes in GM volume(GMV) in the prefrontal cortex, frontal, temporal, limbic, and cerebellar regions are associated with behavioural symptoms[5]. Hence, this study aims to quantitatively define regions-of-interest associated with MBI by analysing GMV differences between MBI-positive and negative individuals.

METHODS

Effects of MBI status on differences in GMV were investigated using VBM(uncorrected $p < 0.001$, minimum cluster size=100voxels) for 824 non-demented individuals(109 MBI-positive(cut-off 5.5)), from Biomarkers and Cognition Study, Singapore. A two-sample t-test, controlled for age, gender, and education, was conducted to identify voxel-wise GMV differences. Effects of A β 42/40 ratio(cut-off 0.05, $n=64$), and cerebral small vessel disease(CSVD) status(modified Fazekas white matter hyperintensity cut-off 5, $n=109$), on GMV was assessed.

Brain T1-weighted MRI scans were performed on a 3T Siemens Prisma Fit scanner with the following parameters: TR/TE/TI=2000/2.26/800ms, flip angle=8°, matrix size=256×256, voxel size=1.0×1.0×1.0mm³.

T1-weighted scans were normalised to MNI space, then segmented to calculate GM, white matter, and cerebrospinal fluid volumes by voxel intensities using the MATLAB2022b SPM CAT12 toolbox.

RESULTS

The cohort consists of 824 non-demented individuals, with 109 (59.6% male, age=56.9±10.8, education=14.0±3.82 years, MBI-score=11.6±7.46) MBI-positive, and 715 (59.3% males, age=60.3±10.4, education=14.6±3.64 years, MBI-score=0.9±1.41) MBI-negative individuals.

VBM analyses of the MBI cohorts showed decreased GMV in MBI-positive individuals, as compared to MBI-negative, in the frontal, occipital, insular, temporal, parietal, medial temporal (MT)lobes, and cerebellum (Table 1). The largest cluster spans the occipital, cerebellum, temporal, and MT lobes.

Analysis of MBI-positive individuals(n=109) based on CSVD status revealed increased GMV in CSVD- negative individuals, in the frontal, temporal, MT, parietal, and occipital lobes, basal ganglia, cerebral cortex, forebrain, cerebellum, and insula. Analysis based on A β 42/40 ratio showed increased GMV in A β 42/40- negative individuals was found in the frontal lobe.

CONCLUSION

The study illustrates significant decreases in GMVs in MBI-positive as compared to MBI-negative individuals, predominantly in frontal, temporal, and cerebellar regions. These findings underscore the potential of VBM in identifying at-risk individuals for neurodegenerative disorders by detecting subtle neuroanatomical changes linked to behavioural symptoms.

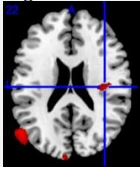
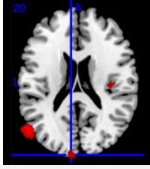
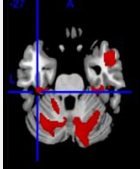
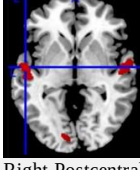
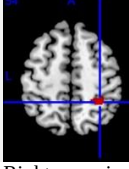
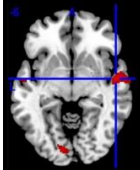
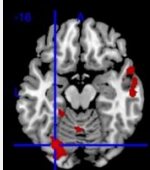
KEYWORDS

Voxel-based morphometry (VBM), Mild Behavioural Impairment (MBI), Gray Matter Volume

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Table 1: Table summarising cluster coordinates, regions, and size

CONTRAST	REGIONS	MNI COORDINATES(X, Y, Z)	CLUSTER SIZE (VOXELS)
MBIpos – MBI _{neg} *refer below for visualisations of clusters	Right Rolandic operculum, Right Insula 	38, -18, 22	146
	Left Cuneus, Left Superior occipital gyrus, Left Calcarine fissure and surrounding cortex 	-8, -98, 20	224
	Left Fusiform gyrus, Left Inferior temporal gyrus, Left Lobule VI of cerebellar hemisphere, Left Lobule IV, V of cerebellar hemisphere 	-40, -30, -34	271
	Left Superior temporal gyrus, Left Middle temporal gyrus 	-56, -9, -2	328
	Right Postcentral gyrus, Right Inferior parietal gyrus (excluding supramarginal and angular gyri), Right Superior parietal gyrus 	32, -45, 54	349
	Right superior temporal gyrus, Right temporal pole: middle temporal gyrus, Right middle temporal gyrus, Right temporal pole: superior temporal gyrus, Right inferior temporal gyrus 	52, -6, 6	2083
	Left/Right Lobule VI of cerebellar hemisphere, Left/Right Crus I of cerebellar hemisphere, Left/Right Fusiform gyrus, Left/Right Crus II of cerebellar hemisphere, Left/Right Lobule IV, V of cerebellar hemisphere, Left Lingual gyrus, Right Lobule VIII of cerebellar hemisphere, Left Calcarine fissure and surrounding cortex, Left/Right Lobule VII B of cerebellar hemisphere, Lobule VIII, VI of vermis, Vermis_4_5_7, Left/Right Parahippocampal gyrus, Right Inferior temporal gyrus 	-28, -74, -16	7773

A CASE OF PROBABLE DEMENTIA WITH LEWY BODIES PRECEDED BY FUNCTIONAL NEUROLOGICAL DISORDER

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INTRODUCTION

Lewy body dementias comprise Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB). DLB is characterized by fluctuating cognition, visual hallucinations, rapid eye movement sleep behaviour disorder (RBD), and parkinsonism. It is not uncommon but remains underdiagnosed since recognition is mainly clinical; its features typically overlap with those of Alzheimer's or idiopathic Parkinson's disease.

REPORT

We report an 80-year-old gentleman who has underlying ischaemic heart disease, hypertension, benign prostatic hyperplasia, atrial fibrillation, and hyperthyroidism. He has been suffering from psychiatric illnesses such as primary insomnia and anxiety since 2009, as well as a history of functional neurological disorder (FND) from 2012 until 2021. He experienced body tremors at certain times every day, with the condition being most severe on Fridays. The movement disorder usually aborted by distraction.

In 2022, he experienced recurrent fluctuations in cognition, exhibiting episodic unresponsiveness and confusion, which resolved spontaneously after a few minutes each time. In 2023, he was admitted for displaying irrelevant speech and memory impairment lasting for 3 days. Assessment did not reveal infective or other potential underlying causes contributing to the symptoms of delirium. For both episodes, he had worsening of his anxiety condition prior to the fluctuations. Further history revealed he experienced postural dizziness with episodes of falls, and history of constipation requiring casualty visits. There was no history to suggest REM sleep behaviour disorder, hallucination, delusion, hypersomnia, and fatigue.

Examination showed normal range of eye motion with saccadic intrusion on smooth pursuit and saccadic hypometria. There was rigidity of upper limbs more at left side and decremental bradykinesia on finger tapping. There was no tremor and postural hypotension. Gait examination showed reduced arm swings. Tandem walking exhibited some degree of instability. Olfactory examination with Sniffin' Sticks test revealed lower border of hyposmia, nearing anosmia. His MoCA score was 22 out of 30. NUCOG indicated scores below 2 standard deviations for domains other than language. Interval EEG was normal and MRI brain showed relative atrophy of parietal lobes with normal hippocampal and brainstem volumes, and non-specific subcortical white matter lesions.

CONCLUSION

With two clinical core features, namely fluctuating cognition and parkinsonism, this patient was diagnosed with probable DLB. This diagnosis was made according to the revised consensus



criteria established by the DLB Consortium in 2017 for the clinical diagnosis of probable and possible cases. Cognitive decline, especially in the case of acute presentation, rarely warrants clinicians to suspect neurodegenerative disorders. The transition from functional neurological symptoms to DLB highlights the diagnostic complexities and the need to identify early stages in neurodegenerative diseases.

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EGB761 IN AMNESTIC TYPE OF MILD COGNITIVE IMPAIRMENT AND MILD DEMENTIA: EXPERIENCE FROM SINGE CENTER IN THAILAND

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INTRODUCTION

Egb761 is indicated to slow down cognitive deterioration in both amnesic type of mild cognitive impairment (aMCI), mild Alzheimer's disease (AD), and mixed AD with cardiovascular risk (CVD) dementia. Egb761 also possibly improves behavioral disturbances, but clinical data, especially in Asian population, are sparse. This study aimed to report behavioral outcomes in patients with aMCI, mild AD, and mixed AD and CVD dementia who received Egb761.

METHODS

This retrospective study collected data from patients who visited the neuropsychiatric clinic and received Egb761 at Khon Kaen University from January 2020 – June 2023. Clinical characteristics and demographic data were retrieved. Severity and burden of behavioral and psychological symptoms of dementia (BPSD) were measured by Neuropsychiatric inventory (NPI). Cognitive measurements were measured by either Thai Mental State Examination (TMSE) or Montreal Cognitive Assessment Scale Thai Version (MOCA-Thai).

RESULTS

We identified a total of 36 patients, 26 female (66.7%), who received either Egb761 at 120 mg/day (n = 9) or 240 mg/day (n = 27). Thirty patients (83.3%) had either mild AD or mixed AD with CVD dementia with the mean TMSE of 20.5 ± 4.4 , and 7 patients (16.7%) had aMCI with the median of MOCA of 21.8 ± 4.1 . There were 14 patients (38.9%) of patients who had behavioral disturbances (NPI FxS > 0) at the baseline. After following up for the mean duration of 7.4 ± 2.9 months, there were no statistically significant changes ($p > 0.05$) in the mean TMSE of 20.85 ± 5.6 and the mean MOCA-Thai of 22.3 ± 4.6 . Within 14 patients with behavioral disturbances at the baseline, improvement of NPI FxS and burden scores were noted in 12 patients (85.7%) and 10 patients (71.4%), respectively. The mean improvement of NPI FxS and burden scores were -15.5 ± 17.7 , and -6.6 ± 8.1 , respectively. Fifteen of 22 patients (68.2%) who had no behavioral disturbances at the baseline remained stable during the follow up, with 7 patients (31.8%) developed mild – moderate behavioral disturbances (NPI burden < 4 in every domain).

CONCLUSION

Our clinical experience with Egb761 in aMCI and mild dementia was favorable and the results align with previous studies that the treatment is beneficial in slowing down cognitive deterioration. It was likely to be beneficial in alleviation of behavioral disturbances and prevention of emergent BPSD.

KEYWORDS

Egb761, dementia, mild cognitive impairment

DEMOGRAPHIC, CLINICAL, AND NEUROPSYCHOLOGICAL PROFILES OF URINE AMYLOID TEST KIT POSITIVITY

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BACKGROUND

With Alzheimer's Disease (AD) being progressively prevalent worldwide, methods of earlier detection are more vital than ever to facilitate early intervention. It is normal for urine to contain soluble Amyloid-beta¹, and it has been shown that it is a reliable diagnostic tool for individuals with MCI or AD². In light of this, Qankorey has developed a novel test kit to detect fragments of Amyloid Precursor Proteins in urine³.

OBJECTIVE

To supplement this test kit, we aim to establish a demographic, clinical, and neuropsychological profile, focusing on the differences between a positive and negative test result using data from the Biomarkers and Cognition Study, Singapore (BIOCIS)⁴. BIOCIS is a 5-year longitudinal study examining data from plasma biomarkers, neuroimaging, neuropsychological assessments, demographic and behavioural questionnaires within a Southeast Asian population. By doing so, it would be able to more reliably assist in evaluating and predicting future onset.

METHODS

The urine test kits were administered and means analysis was conducted based on data gathered from participants (n=46) that were either cognitively unimpaired, have subjective cognitive decline, or have mild cognitive impairment, based on the Petersen's criteria⁵. Participants were divided based on test kit positivity, and compared across the full range of data available, some of which is displayed in Table 1.

RESULTS

There was a significant difference in A β -42/40 ratio between the two groups. Other risk factors, like age, vascular risk factors, and sleep quality were also trending in the correct direction. A test from the working memory cognitive domain was significantly different ($\alpha=0.05$) between the two groups. Other tests from the domains of episodic memory, visuospatial ability, and attention were approaching significance ($p<0.1$), with the remainder trending in the correct direction.

CONCLUSION

There seems a non-insignificant difference in profile between individuals that test positive and negative on the test kits that is worthy of further exploration. To build on this, we plan to conduct a longitudinal study assessing the validity of the test kit as a predictor for AD onset, and to cement a factor profile indicative of higher risk to supplement the test.

Characteristic	Overall (n=46)	Test Negative (n=17)	Test Positive (n=29)	p-value
Age	58.92 ± 9.33	55.99 ± 10.48	60.64 ± 8.30	0.128
Sex (Males)	15/46 (33%)	5/17 (29%)	10/29 (34%)	0.723
Education Years	13.89 ± 3.43	14.18 ± 2.40	13.72 ± 3.94	0.614
Aβ 42/40 ratio	0.059 ± 0.01	0.065 ± 0.01	0.056 ± 0.01	0.015**
NFL	14.95 ± 5.82	13.89 ± 4.56	15.57 ± 6.44	0.460
MCI (%)	16 (35%)	6 (35%)	10 (34%)	
HTN	6 (13%)	1 (5.9%)	5 (17%)	0.390
HLD	16 (35%)	4 (24%)	12 (41%)	0.376
DM	8 (17%)	2 (12%)	6 (21%)	0.807
MOCA	26.26 ± 2.38	26.82 ± 2.24	25.93 ± 2.43	0.206
VCAT	27.26 ± 2.33	27.24 ± 2.46	27.28 ± 2.30	>0.999
Semantic Fluency	18.26 ± 3.82	18.00 ± 2.87	18.41 ± 4.32	0.672
FCSRT delayed	12.65 ± 2.09	11.88 ± 2.32	13.10 ± 1.84	0.051*
Logical Memory delayed	18.98 ± 3.36	19.65 ± 3.18	18.59 ± 3.46	0.318
Block Design	40.35 ± 12.27	40.24 ± 12.25	40.41 ± 12.50	0.855
RCFT copy	33.54 ± 2.85	34.59 ± 1.46	32.93 ± 3.29	0.087*
CT 1 ⁺	45.61 ± 15.38	40.85 ± 16.02	48.40 ± 14.54	0.068*
CT 2 ⁺	89.19 ± 31.04	80.55 ± 23.73	94.26 ± 33.99	0.123
Digit Span Backward	9.35 ± 2.17	9.47 ± 2.65	9.28 ± 1.89	0.782
Number Symbol Coding Test	72.65 ± 15.08	79.71 ± 12.11	68.52 ± 15.29	0.011**

⁺ - reverse-coded tests

Table 1 – Comparing means differences between individuals with test negative and positive results on urine test kit.



KEYWORDS

Dementia, Amyloid, Early Detection, Urine Analysis

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EFFECTIVENESS MEMANTINE IN ELDERLY WHO DIAGNOSED VASCULAR DEMENTIA: A CASE REPORT

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INTRODUCTION

Vascular Dementia (VaD) is a progressive neurodegenerative syndrome that causes memory impairment and cognitive decline due to cerebrovascular disease.^{1,2} VaD is recognized as the second most common cause of cognitive impairment after Alzheimer's disease.³ Dementia impacts 10% of individuals aged 65 and above, and the prevalence increases to 35% among those aged 90 and above, leading to significant cognitive, behavioral, and functional implications.^{4,5} Although the prevalence of VaD is relatively high, evidence regarding the clinical effectiveness of treatment remains limited. Memantine is a moderate-affinity uncompetitive antagonist of NMDA glutamate receptors permitted for use in moderate to severe Alzheimer's disease.^{1,4}

CASE REPORT

A 67-year-old woman was admitted to our hospital with complaints of gradual memory decline, frequent repetition of the same questions, misplacing items, engaging in repetitive tasks, and often recognizing someone but forgetting their names, which had started for eight years since 2015. The patient also frequently experiences excessive worrying, such as repeatedly checking if the house gate is locked. To help herself remember, the patient repeatedly states the location of her belongings. She is a retired civil servant and now a housewife caring for her grandchild. The patient withdraws from social activities and only engages in activities at home. She doesn't want to attend religious gatherings regularly. There is no history of being easily irritated. Occasionally, she had difficulty falling asleep. The patient has a history of Parkinson's disease and has been taking donepezil since 2021. She only takes memantine 2x10mg, citicoline 2x500mg, and mecobalamin 2x500mg regularly.

General and neurological statuses were normal. Upon medical evaluation, a CT scan revealed signs of brain atrophy. ADS-INA yielded a score of 4, indicating cognitive disturbance; the token test score was 44, indicating a high average. The patient scored 19/30 on the Mini-Mental State Examination (MMSE), indicating probable cognitive impairment, and the Montreal Cognitive Assessment (MoCA) score was 14/30, indicating cognitive impairment. In a month, the patient scored 21/30 on the Mini-Mental State Examination (MMSE) and scored 14/30 on the Montreal Cognitive Assessment (MoCA). The third examination on March 25th 2024 showed a 23/30 score for MMSE and a 18/30 score for MoCA-INA.

Figure 1: MMSE and MoCA first test on June, 17th 2023, 19/30 scored on the MMSE and 14/30 scored on the MoCA

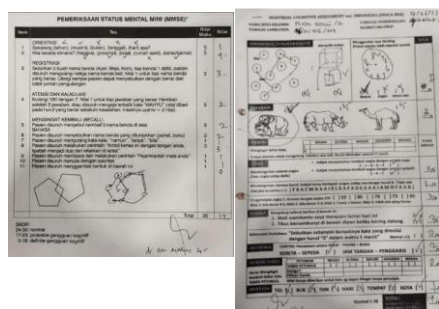


Figure 2: MMSE and MoCA second test on July, 13th 2023, 21/30 scored on the MMSE and 14/30 scored on the MoCA-INA

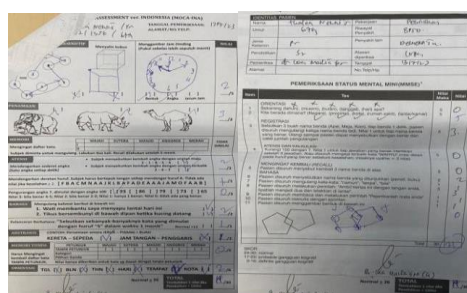
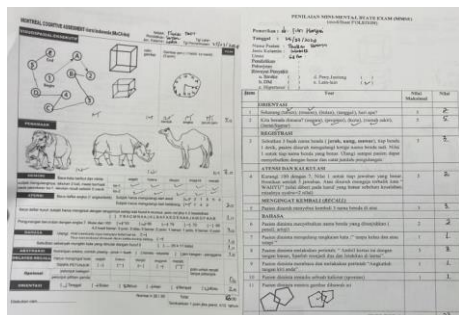


Figure 3: MMSE and MoCA third test on March, 25th 2024, 23/30 scored on the MMSE and 18/30 scored on the MoCA-INA



CONCLUSION

In this case study, we reported a case of a 67- year-old woman with Vascular Dementia (VaD) who consumed memantine for a month, which showed a statistically significant improvement in MMSE. Memantine can be administered in moderate to severe dementia and improve cognition consistently across cognitive scales, with at least no deterioration in global functioning and behavior. Memantine can also be used as a first-line treatment, for example, in patients with moderate dementia who present for the first evaluation but are not using any medication for cognition. Another use is for patients who cannot tolerate acetylcholinesterase inhibitors. Memantine could also reduce cognitive impairment following electroconvulsive therapy.

KEYWORDS

Memantine, Vascular Dementia, Loss memory

RETINAL NERVE FIBER THICKNESS AND BLOOD FLOW AS BIOMARKERS FOR EARLY DETECTION OF COGNITIVE IMPAIRMENT IN A MULTI-ETHNIC ASIAN COHORT: PRELIMINARY INSIGHTS FROM BIOCIS

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BACKGROUND

The transition towards preventive healthcare emphasizes the necessity of early detection and intervention in cognitive disorders such as dementia and mild cognitive impairment (MCI). However, there remains a significant gap in accessible and early predictive markers particularly within Asian populations. Eye scans such as Optical Coherence Tomography (OCT) can be a cost-effective and efficient method for early dementia detection due to their non-invasive nature, rapid assessment capabilities, and the availability of existing OCT devices in clinical settings.

METHOD

This cross-sectional analysis is part of the longitudinal community-based study - Biomarkers and Cognition Study, Singapore (BIOCIS). Currently, 38 multi-ethnic subjects have been recruited in this study; recruitment efforts are ongoing. Neuropsychological assessments (NPAs) measuring cognitive functions were utilized to categorize participants into cognitively normal (CN) and mild cognitive impairment (MCI) groups. 6x6 mm optic disc-centered OCT scans were employed to evaluate the circumpapillary retinal nerve fiber layer (RNFL) thickness and RNFL blood flow density in all participants, enabling an analysis of retinal OCTA thickness and blood flow parameters in both MCI and control individuals.

RESULTS

Variance analysis revealed a thinner of the RNFL, with the most significant reduction observed in MCI patients compared to healthy controls. This reduction was particularly notable in the temporal region, where a statistically significant difference was identified ($P=0.031$, Table 1). In addition, the trend of lower blood flow density is shown in MCI group, although the difference is not significant due to current small sample size.

CONCLUSION

The findings from this study highlight the potential of OCT in the early detection of MCI within a diverse Singaporean cohort. The observed thinning of the RNFL and diminished blood flow in MCI patients relative to controls indicates that retinal changes could serve as early biomarkers of neurodegeneration. These results support incorporating OCT into screening

protocols to boost preventive cognitive health strategies. This aligns with the global move towards preventative healthcare, highlighting the need for accessible, reliable, and cost-effective diagnostic tools, especially in Asian populations.

KEYWORDS

Mild Cognitive Impairment, Retinal Nerve Fiber Layer, Optical Coherence Tomography, Retinal Blood Flow, Oculomics.

Table 1: RNFL thickness and blood flow density				
Variable	MCI: Mean $\pm$ std (n=9)	CN: Mean $\pm$ std (n=29)	T-test value	P-value
Age	62.33 $\pm$ 5.70	55.97 $\pm$ 11.61	0.124	
Temporal(μ m)	73.56 $\pm$ 9.76	82.00 $\pm$ 9.90	0.031	
Superior(μ m)	117.11 $\pm$ 30.95	120.31 $\pm$ 20.31	0.719	
Nasal(μ m)	73.78 $\pm$ 14.61	76.38 $\pm$ 10.85	0.567	
Inferior(μ m)	120.22 $\pm$ 18.02	124.14 $\pm$ 19.50	0.596	
Thickness_Avg (μ m)	94.11 $\pm$ 14.22	98.55 $\pm$ 10.97	0.329	
Temporal_flow (%)	44.22 $\pm$ 3.80	44.72 $\pm$ 6.55	0.829	
Superior_flow (%)	44.11 $\pm$ 5.33	46.10 $\pm$ 4.40	0.266	
Nasal_flow (%)	43.89 $\pm$ 3.48	43.69 $\pm$ 4.05	0.895	
Inferior_flow (%)	46.22 $\pm$ 4.63	47.66 $\pm$ 2.74	0.257	
Flow_RNFL_AVG (%)	45.10 $\pm$ 2.62	45.91 $\pm$ 3.27	0.504	

COGNITIVE PROFILES OF AT-RISK MIXED DEMENTIA, ALZHEIMER'S DEMENTIA AND VASCULAR DEMENTIA IN THE BIOMARKER AND COGNITION STUDY, SINGAPORE (BIOCIS) COHORT

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BACKGROUND

Early detection of cognitive decline is crucial for preventing Alzheimer's Disease (AD) and Vascular Dementia (VaD), the primary causes of dementia (Anstey KJ et al., 2010; Vipin A. et al., 2021). AD, marked by amyloid β plaques and phosphorylated tau, initially affects episodic memory (Scheltens P. et al., 2021), while VaD, stemming from cerebrovascular pathology, induces cognitive deficits through vascular injury (Iadecola C, 2013). As the population ages, the prevalence of Mixed Dementia (Mixed), characterized by both AD biomarkers and vascular pathology, increases (Bruce R. R. et al., 2007; Eckerström C et al., 2020), necessitating a deeper understanding of cognitive profiles, particularly in Eastern populations. Our aim is to delineate cognitive profiles among at-risk Mixed, AD, VaD, and Normal participants in the BIOCIS cohort.

METHOD

460 participants from the Biomarker and Cognition Study, Singapore (BIOCIS) who underwent a series of Neuropsychological Assessments (NPA) tests, including Montreal Cognitive Assessment (MoCA), Visual Cognitive Assessment Test (VCAT), blood collection and neuroimaging were recruited (Leow, 2024). Participants were categorized into AD ($A\beta_{42}:A\beta_{40}$ ratio <0.05 , Total Fazekas <5), VaD (Total Fazekas ≥ 5 , $A\beta_{42}:A\beta_{40}$ ratio ≥ 0.05), Mixed ($A\beta_{42}:A\beta_{40}$ ratio <0.05 , Total Fazekas ≥ 5), and Normal groups. Each group was further stratified based on the presence (N+) or absence (N-) of neurodegeneration based on Average MTA score ≥ 2 . Demographic and cognitive test scores were analyzed by Chi-squared test, ANCOVA and Post-Hoc Tukey-HSD test.

RESULTS

Mixed (N+) participants (Mean age = 72.06 years $\pm$ 6.90, Mean education = 12.88 years $\pm$ 4.56) are significantly older and have fewer years of education compared to other N+ groups (Table 1). After adjusting for age and education, Mixed (N+) participants consistently performed worse in MoCA and VCAT than all other groups except for AD (N+) in MoCA. The N+ groups performed significantly worse than the N- groups for AD and VaD ($p < 0.05$).

CONCLUSION

Mixed Dementia participants with neurodegeneration have worse cognitive profiles than those with pure AD pathophysiology or VaD pathophysiology. This is also seen in AD and VaD

participants with and without neurodegeneration. Presence of neurodegeneration could be driving these cognitive differences. Future research should delve into subdomains of VCAT, MoCA and other neuropsychological tests to further delineate the cognitive profiles of individuals with Alzheimer's, Vascular or Mixed Dementia.

KEYWORDS

Cognitive Profiles, Mixed Dementia, Neurodegeneration

Table 1. Demographics and Neuropsychological test scores for At-Risk Mixed, AD, VaD and Normal

	AD (n=48)		VaD (n=140)		Mixed (n=45)		Normal (n=227)		P-Values **	Tukey- HSD
	N+ (n=12)	N- (n=36)	N+ (n=48)	N- (n=92)	N+ (n=26)	N- (n=19)	N+ (n=36)	N- (n=191)		
Age*	60.16 ± 11.67	62.79 ± 9.78	68.12 ± 6.90	62.51 ± 7.36	72.06 ± 6.68	72.06 ± 6.69	58.45 ± 12.32	55.67 ± 10.53	< 0.001	
Female (n, %)	7 (58.33)	24 (68.57)	26 (54.17)	55 (59.78)	15 (57.69)	13 (68.42)	14 (38.89)	112 (59.26)	0.29	
Years of Education*	13.19 ± 3.39	13.26 ± 3.40	14.08 ± 3.63	13.51 ± 4.33	12.88 ± 4.56	13.62 ± 3.26	14.94 ± 3.03	14.80 ± 3.21	0.003	
MoCA*	23.92 ± 4.42	26.94 ± 2.25	24.00 ± 3.82	25.84 ± 2.57	23.96 ± 3.46	25.21 ± 2.78	26.19 ± 2.52	26.43 ± 2.38	0.005	0.03* 0.005◇
VCAT*	25.58 ± 5.00	25.53 ± 3.44	24.42 ± 4.40	26.97 ± 2.53	24.15 ± 4.10	26.00 ± 3.11	27.64 ± 2.34	27.15 ± 2.35	0.007	<0.001 ◇

Abbreviations. AD = Alzheimer's Disease, VaD = Vascular Dementia, Mixed = Mixed Dementia, Normal = Normal Biomarker profile, N+ = Neurodegeneration positive, N- = Neurodegeneration negative, MoCA = Montreal Cognitive Assessment, VCAT = Visual Cognitive Assessment Test

* Mean ± SD

** MoCA and VCAT P-values adjusted for Age and Education Years

▪ Pairwise Tukey-HSD between AD (N+) and AD (N-)

◇ Pairwise Tukey-HSD between VaD (N+) and VaD (N-)

FAVORABLE CELLULAR ALTERATIONS IN THE FRONTAL CORTEX AND HIPPOCAMPAL REGIONS OF THE MICE BRAIN BY QUERCETIN AND NARINGENIN: A PROMISING ROLE IN ALZHEIMER'S DISEASE

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BACKGROUND

Alzheimer disease is an age-related brain disorder that causes neurodegeneration and is linked with insulin resistance at molecular, clinical, and demographic levels. With the aging of the population, the number of patients with dementia is expected to almost double every 20 years to reach 78 million by 2030 and 139 million by 2050, as estimated by WHO. Insulin possesses neuroprotective and memory-enhancing effects indicating the role of insulin in cognition. The cerebral uptake of glucose decreases with aging due to the reduction of the expression of glucose transporters in the brain. Defective insulin signaling promotes A β aggregation and accelerates A β formation in the brain leading to Type III diabetes. Prolonged exposure to hyperglycemia and hyperinsulinemia increases A β accumulation on brain lesions, exacerbates oxidative stress, neuroinflammation, cholinergic loss, and mitochondrial dysfunction, impairs neuronal integrity, and causes neurodegeneration resulting in poor cognitive performance. Objective: The objective of this research project is to demonstrate a linkage if any between the risk of developing Alzheimer's disease and insulin resistance.

METHODS

Diabetes was induced in mice by injecting Alloxan (100mg/kg i.p.) and orally administering sucrose 35% solution. Glucose level was monitored, quercetin (100 mg/kg and 200 mg/kg) was suspended in CMC and administered orally and naringenin (100 mg/kg and 200mg/kg) was suspended in tween 80 and administered orally. Behavioral models employed in the present study were the Morris water maze (MWM), actophotometer, and novel object recognition (NOR) test. Biochemical estimations were carried out by measuring mitochondrial, glutathione, catalase, SOD, lipid peroxidase activity, and acetylcholinesterase activity in the brain tissue. Histopathological evaluation of the hippocampal region was carried out under a bright field microscope.

RESULTS

Alloxan (100mg/kg i.p.) and sucrose 35% solution (p.o.) administration produced significant hyperglycemia in mice as compared to the control group. Alloxan selectively inhibits glucose-induced insulin secretion through specific inhibition of glucokinase, the glucose sensor of the beta cell, and the ability to destroy the insulin-producing β cells of the pancreas. It causes a state of hyperglycemia which is one of the main characteristics of insulin resistance. Alloxan administration did not produce any significant effect on weight change and locomotor activity. During the acquisition test (learning), alloxan-treated mice significantly delayed the escape latency period recorded to reach the submerged platform as compared to the control group in the MWM test. However, Quercetin and Naringenin administration decreased the escape latency time indicating a significant improvement in memory performance. In the NOR test,



alloxan- treated mice spent more time near the familiar object, and the quercetin-treated group spent more time near the novel object. Alloxan treatment also disrupted the mitochondrial levels and lowered the catalase, glutathione, and SOD levels, and increased the lipid peroxidase and acetylcholinesterase levels.

CONCLUSION

Administration of Quercetin and Naringenin significantly reversed alloxan-induced behavioral, biochemical, and cellular alterations in both the frontal cortex as well as in hippocampus. These findings suggest that they may be looked upon as a promising memory-enhancing agent in preclinical studies. Therefore, clinical trials may be undertaken to establish the memory-enhancing property of quercetin and naringenin.

KEYWORDS

Cognition, Insulin, Type III Diabetes

A COGNITIVE STRESS TEST APP FOR EARLY DETECTION OF MILD COGNITIVE IMPAIRMENT IN THE COMMUNITY

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BACKGROUND

Mild Cognitive Impairment (MCI) represents the stage between expected cognitive decline of normal aging and onset of dementia. Early detection is crucial for mitigating progression to Alzheimer's disease (Petersen et al., 1999). The ability to identify MCI within community settings using accessible technology could significantly enhance early intervention strategies. The objectives are to create an app to assess associations between app-based cognitive performance and blood oxygenation level-dependent responses measured by functional Near-Infrared Spectroscopy (fNIRS) and detect MCI early in a community-based sample.

METHOD

The study utilised a novel app comprising four cognitive games designed to test attention, working memory, executive function, and visuospatial cognition. Participants were allowed retries upon failing a level, enabling the analysis of cognitive stress points and resilience patterns. Each game ends when a level is failed twice successively. The next game begins after a 30-second rest. Aurora fNIRS data was collected using an 8x8 grid optode placement on the prefrontal cortex to measure neural activity and its association with game performance (Metzger et al., 2016). This study included 15 participants with MCI, 14 with Subjective Cognitive Decline (SCD), and 13 Cognitively Normal (CN), taken from the Biomarker and Cognition Study (BIOCIS) at Dementia Research Centre (Singapore). Data analysis was conducted using linear mixed-effect models (LMEMs) to determine the relationship between game performance and diagnosis. Between-subjects t-tests were used to determine differences between oxygenation levels at success and failure points. Success values were determined by the difference in mean oxygenation from the last successful level to baseline, while failure values measured the change between mean oxygenation across consecutive failed levels and baseline.

RESULTS

LMEMs showed that SCD has a significant effect on failure value($p < 0.05$).

Diagnosis	Mean (SD)		p-value	
	Success	Failure	Success	Failure
CN	0.19 (0.59)	0.23 (0.42)	0.73	0.80
SCD	-0.06 (0.63)	-0.02 (0.49)	0.06	0.04*
MCI	0.31 (0.74)	0.17 (0.45)	0.70	0.46

Table 1. Linear mixed effects models p-values

Between-subjects t-test showed significant difference between success and failure values for MCI group($t(59) = -2.27$, $p < 0.05$).

CONCLUSION

Results show that success and failure values may be predictive of an SCD diagnosis, indicating the app's potential to identify individuals at MCI-risk. T-test comparisons of oxygenation levels during peak success and successive failures show significant differences only within MCI, potentially distinguishing MCI and non-MCI individuals. Future app iterations will be designed to expand its predictive capability and accurately detect early-stage MCI.

KEYWORDS

fNIRS, Dementia, Mild Cognitive Impairment, App, Games

ASSESSING SERUM MBDNF AND PRO-BDNF LEVELS IN MILD COGNITIVE IMPAIRMENT AND EARLY DEMENTIA: A SYSTEMATIC REVIEW

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BACKGROUND

Mild cognitive impairment (MCI) and early Dementia (ED) are recognized as significant public health problems as Dementia and Alzheimer's risk with annual conversion rates often ranging from 10% to 15%.. Brain-derived neurotrophic factor (BDNF) and its precursor, pro-BDNF, have emerged as potential biomarkers for neurodegenerative diseases due to their roles in neuronal survival, growth, neurotransmitter modulator and neuronal plasticity. The present study investigated changes in plasma concentrations of mature brain-derived neurotrophic factor (mBDNF), and its precursor protein (pro-BDNF) levels in the patients with MCI and ED.

METHODS

A comprehensive literature search for studies published between 2014 and 2024 was conducted in major databases, including PubMed, Embase, Medline, Cochrane, and Web of Science for studies reporting plasma levels of mature BDNF and Pro-BDNF in MCI and ED Patients. Keywords and Medical Subject Headings (MeSH) terms related to "brain-derived neurotrophic factor", "pro-BDNF", "mature BDNF", "mild cognitive impairment", and "early dementia" were used in various combinations to ensure the retrieval of relevant studies.

RESULTS

Several studies reported alterations in serum mBDNF and pro-BDNF levels in individuals with MCI and early dementia compared to healthy controls, although findings are inconsistent across studies. A decreased level of serum mBDNF is expected.

CONCLUSION

This meta-analysis may suggest that mBDNF and Pro-BDNF may be potential MCI or ED biomarkers.

KEYWORDS

pro-BDNF, mature BDNF, Mild cognitive impairment, Early dementia, Systemic review

UTILITY OF PLASMA P-TAU181 / A β 42 AND A BRIEF COGNITIVE TEST AS A SCREENING TOOL FOR ELEVATED BRAIN AMYLOID

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BACKGROUND

Brain amyloid burden is an important marker of Alzheimer's disease pathology and is correlated with concurrent or subsequent cognitive impairment and dementia. However, brain amyloid is currently measurable by positronic emission tomographic imaging, an expensive platform not wide available. Here, we assess whether a combination of plasma P-tau181/A β 42 and routine clinical assessments provides adequate utility as a screen for brain amyloid deposition (A β +).

METHODS

This study included cognitive intact (n=42), cognitive impairment, no dementia (n=88), Alzheimer's disease (n=40) and vascular dementia (n=21) participants. Brain amyloid status (A β - vs A β +) based on visual read of amyloid PET scans was assessed alongside clinical measures (age, gender, clinical diagnoses, MMSE and medial temporal lobe atrophy scores).

RESULTS

Four combinations of clinical measures showed moderate performance in detecting A β (area under the receiver-operator curve, AUC ranging from 0.752 to 0.798). The addition of plasma P-tau181 / A β 42 ratio significantly improved diagnostic performance for all combinations (AUC = 0.906 to 0.915; all p < 0.001). Using a 3-range reference for stratification of participants into low, intermediate or high risk of being A β +, addition of plasma P-tau181/A β 42 ratio to a basic clinical model of age, gender and MMSE reduced the needed confirmatory PET from 48% to 8%, while achieving an accuracy of 90%.

CONCLUSION

A combination of routine clinical measures and plasma P-tau181 / A β 42 shows potential as an optimized biomarker panel in screening for presence of brain amyloid pathology.

KEYWORDS

Alzheimer's disease, Biomarkers, Dementia, Screening

COMBINATION OF PLASMA ALZHEIMER'S DISEASE BIOMARKERS WITH ROUTINE CLINICAL ASSESSMENT FOR THE IDENTIFICATION OF ELDERLY AT RISK OF COGNITIVE DECLINE

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BACKGROUND

Given the multifactorial nature of dementia, the incorporation of plasma Alzheimer's disease (AD)-related biomarkers and neuroimaging markers of cerebrovascular disease (CeVD) and brain atrophy may improve the accuracy of basic, routine clinical assessment in identifying elderly at risk of future cognitive decline. In this study, we aimed to determine which of these plasma and neuroimaging measures should be combined with a basic clinical model to produce an optimal model for predicting cognitive decline.

METHODS

Cognitive decline was defined as an increase in clinical dementia rating (CDR) global of ≥ 0.5 points at any annual follow-up visit. Of the 357 participants included in this study, 176 (49%) developed cognitive decline within the time period of 4 years. The basic clinical model consisted of age, sex, years of education, mini-mental state examination (MMSE) and vascular risk factors status. Plasma AD-related biomarkers included P-tau181, P-tau181/A β 42 ratio, neurofilament light (NfL) and glial fibrillary acidic protein (GFAP). Neuroimaging markers of CeVD included white matter hyperintensities (Fazekas score < 2 vs ≥ 2), lacune (count 0 vs ≥ 1), cortical infarct (count 0 vs ≥ 1) and cerebral microbleed (CMB; count 0 vs ≥ 1). Markers of brain atrophy included medial temporal lobe atrophy score (< 2 vs ≥ 2), global cortical atrophy score (< 2 vs ≥ 2) and central atrophy score (< 2 vs ≥ 2).

RESULTS

The model selection process is shown in Figure. The basic clinical model performed moderately well in predicting cognitive decline within 4 years (area under the curve [AUC]=0.744). The best model fit (lowest Akaike information criterion [AIC]) was obtained by incorporating plasma NfL and P-tau181/A β 42 ratio, as well as CMB and lacune status, into the clinical model. This model (AUC=0.792) outperformed the clinical model ($P=0.005$). Next, the parsimonious model was derived ($\Delta AIC < 2$ as compared with best model fit, and with as few predictors as possible). The parsimonious model (AUC=0.785), which excluded CMB status, continued to outperform the clinical model ($P=0.013$). Finally, the addition of plasma NfL and P-tau181/A β 42 ratio alone (AUC=0.779) was sufficient to improve the performance of the clinical model ($P=0.024$).

CONCLUSION

Combining plasma AD biomarkers with routine clinical assessment may improve the prediction of cognitive decline.

KEYWORDS

Biomarkers, Prognosis, Prediction

Figure. Logistic regression model selection process and performance for predicting cognitive decline within 4 years

Model selection	Basic clinical measures	Plasma biomarkers	MRI markers	MoCA	AIC	AUC (95%)
Basic clinical model	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status				448.03	0.744 (0.693, 0.796)
Best model fit	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status	Plasma NFL, Plasma P-tau181/Aβ42 ratio	CMB status, Lacune status		424.11	0.792 (0.745, 0.840)*
Parsimonious model	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status	Plasma NFL, Plasma P-tau181/Aβ42 ratio	Lacune status		426.07	0.785 (0.737, 0.833)*
Parsimonious model without MRI markers	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status	Plasma NFL, Plasma P-tau181/Aβ42 ratio			427.49	0.779 (0.731, 0.827)*
Parsimonious model without MRI markers and plasma P-tau181/Aβ42 ratio	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status	Plasma NFL			440.66	0.758 (0.708, 0.808)
Parsimonious model without MRI markers and plasma NFL	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status	Plasma P-tau181/Aβ42 ratio			434.13	0.767 (0.718, 0.816)
Parsimonious model without plasma biomarkers	Age, sex, education, MMSE, hypertension status, hyperlipidemia status, diabetes status, cardiovascular disease status		Lacune status		447.31	0.750 (0.699, 0.801)

*p<0.05 vs basic clinical model

The basic clinical measures are included as fixed terms (that is, to be included in all models) in the logistic regression model selection process. Best model fit shows the model with the lowest AIC. The parsimonious model shows the model that had a similar model performance ($\Delta AIC < 2$ as compared with best model fit) with as few predictors as possible. In subsequent models, variables were removed in a stepwise procedure from the parsimonious model. ROC curve analyses of the different models for distinguishing those who developed cognitive decline (defined by an increase in CDR global of ≥ 0.5 points at any annual follow-up visit, compared to the baseline) versus those who remained cognitively stable. Comparisons between AUCs were performed using DeLong test.

AIC, Akaike information criterion; AUC, area under the ROC Curve, CDR, clinical dementia rating; CMB, cerebral microbleed; MMSE, mini-mental state examination; MRI, magnetic resonance imaging; ROC, receiver operating characteristic.

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CHARACTERISTICS OF COGNITIVE FUNCTION AND SLEEP QUALITY IN POST COVID HEALTHCARE WORKER AT DR. ZAINOEL ABIDIN REGIONAL HOSPITAL IN BANDA ACEH

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BACKGROUND

COVID-19 infection can lead to neurological symptoms, structural and functional changes in the brain. Cognitive problem are one of the most commonly reported symptoms in people experienced long COVID (the chronic illness that follows COVID-19 infection), which affects between 10% and 25% of patients. The symptoms may include diminished memory and attention, language impairment, severe psychomotor slowing (53,5%), and sleep disturbances. Healthcare workers had greater occupational risk of exposure and infection Covid-19 than the general population. The aim of this study is to show the characteristics of cognitive function and sleep quality in post-COVID healthcare worker at dr. Zainoel Abidin Regional Hospital in Banda Aceh.

METHODS

A Cross-sectional study conducted at dr. Zainoel Abidin Regional Hospital, Banda Aceh in 2023. The subjects are 54 health workers infected with COVID-19. The sample was selected using the consecutive sampling techniques, and participants completed the questionnaires. Measurement was done using the Indonesian version of the Montreal Cognitive Assessment (MoCA) and The Pittsburgh Sleep Quality Index (PSQI). Data were tabulated and analyzed using bivariate analysis to present frequencies, mean and percentages.

RESULTS

The mean age of samples in this study was 35.5 ± 4.9 years. This study were dominated by women (79.6%), graduate/professional (64.8%), MOCA-Ina score >26 (74.1%), and PSQI >5 (57.4%). The highest mean MOCA-INA domain score is in orientation and the lowest is in memory (executive function: 4.2 ± 0.8 ; naming: 2.9 ± 0.1 ; memory: 3.8 ± 1.2 ; attention: 5.5 ± 0.5 ; language: 2.8 ± 0.2 ; abstraction: 1.7 ± 0.3 ; and orientation: 5.9 ± 0.1). The highest mean PSQI domain score was in daytime sleep dysfunction and the lowest is in sleep medication (subjective: 0.6 ± 0.5 ; latency: 1.2 ± 0.9 ; duration: 1.0 ± 0.8 ; efficiency: 1.3 ± 1.4 ; sleep disorder: 0.8 ± 0.4 ; sleep medication: 0.0 ± 0.0 ; and daytime sleep dysfunction: 1.56 ± 0.8).

CONCLUSION

Healthcare worker who had infected COVID-19 in this study generally had good cognitive function but poor in sleep quality.

KEYWORDS

Cognitive Function, Long Covid, Sleep Quality.

DELAYED DEVELOPMENT IN LANGUAGE AND ISOLATED SEIZURE IN A YOUNG CHILD DUE TO SCHIZENCEPHALY – A RARE CASE

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INTRODUCTION

Schizencephaly, is a rare, congenital cerebral malformation. In literature, only few cases have been reported. Schizencephaly is an uncommon, congenital disorder showing developmental cerebral malformation characterized by clefts in the cerebral cortex, which extends from the ependymal surface of the ventricle through the white matter to the pial surface. Symptomatic patients present as hemiparesis, developmental deficits to seizures. This condition is usually found at birth and presents during early years. Appropriate diagnosis of the disease is necessary to avoid incorrect treatment. Here, we present a rare case of right unilateral cleft, open lips schizencephaly in a child presenting with seizures.

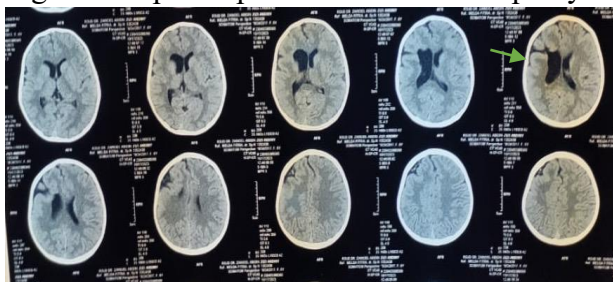
REPORT

A 6 years-old girl was referred to the Neurology Outpatient Clinic of dr. Zainoel Abidin Hospital with focal seizure. There was no history of seizure 6 months before admission. When she was 2 years old, she had mild language delay and left limb weakness until atrophy but not progressive.

Vital signs were normal. In detail, blood and other laboratory investigations were done to rule out metabolic and other causes of seizure. Family history and birth history were insignificant. The patient family then was asked about his birth history which was found normal. His mother had no complications during pregnancy. There were no postnatal complications.

On Examination Found: Motorik 5/4+ 5/4+, left superior atrofi. A non contrast brain computed tomography (CT) was performed showing findings that are in relation to open lip schizencephaly (right frontal brain cleft lined by gray matter which is connecting subarachnoid space to the right ventrikular system). One the diagnosis of the Open-lip Schizencephaly was established, the patient received neuro-rehabilitation and antiseizure treatment with Valproat Acid, presenting adequate control of the seizure.

Figure 1: Open-Lip Unilateral Schizencephaly



CONCLUSION

Our results showed that the majority of patients with neurological deficits were detected. The most common initial presentation of the patients with unilateral open-lip schizencephaly was hemiparesis, language deficits, various type of epileptic seizure with partial seizure being the most common, also found with generalized tonic clonic seizure. Computerized Tomography Scan (CT-Scan) and Magnetic Resonance Imaging (MRI) is the diagnostic method of choice.

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CENTELLA ASIATICA L. EXTRACT ATTENUATES CHRONIC STRESS INDUCED CHANGES IN HIPPOCAMPUS AND CATALASE LEVELS IN BRAIN OF MALE WISTAR RATS

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Background

When an external stimulus is applied to an organism it reacts physiologically and psychologically and when the stimuli is prolonged it produces chronic stress which results in depression. The pathology of chronic stress includes alteration to neuro-endocrine axis leading to hypersecretion of glucocorticoids which causes damage of the neurons in the hippocampus of brain through changes in the oxidative stress. The body responds to this oxidative stress by producing enzymatic and non-enzymatic antioxidants to counter the effects. Catalase (CAT) an antioxidant which is in the peroxisomes, splits the hydrogen peroxide which is produced during the oxidative stress to water and oxygen which are non-toxic, thus offering a protective effect. The treatment of depression with the available anti-depressants have been limited by their late onset of action and toxicity. *Centella asiatica* (CA) an herb which is known for its neuroprotective properties and has been used since ancient times as neuro-tonic has an added advantage of having less toxicity.

The aim of the study is to examine the neuroprotective effects of crude extract of CA on hippocampal neurons using Nissls stain and level of expression of mRNA CAT in brain tissues of chronic mild stress (CMS) induced male Wistar rats.

Method

Thirty-six Male Wistar rats aged 8–10 weeks were held in six groups. One group was assigned as control. The other groups were administered CMS by various stressors viz. restrain, forced swimming in cold water, overnight food and water deprivation, wet bedding, cage tilt at 45°, tail pinching, overcrowding the cages and change of cage mates randomly for a period of 64 days. One of the stress induced groups was retained as model group while others were administered with crude extracts of CA at the doses of 200, 400, 800 and fluoxetine (Flx) 10 mg/kg body weight. At the end of 64 days, the rats were euthanised and the brain tissue was collected for Nissls staining of the hippocampus and expression of mRNA CAT levels using RT-PCR.



Results

The rats of the model group exhibited reduced number of viable neurons in the hippocampus as observed in Nissls stain and reduced levels of expression of mRNA CAT in the brain tissue while the rat groups receiving CA showed increase in number of viable neurons and increase expression of mRNA CAT in the brain tissues. The results were comparable to that of fluoxetine.

Conclusion

CA effectively attenuates CMS induced neuronal loss in the hippocampus of the rats brain and also the expression of mRNA CAT anti-oxidant levels. CA could prove to be a useful agent in the long-term prevention of chronic stress induced neurologic damage and depression.

Keywords

Chronic stress, *Centella asiatica*, Hippocampus, Catalase, Fluoxetine.

BLOOD BIOMARKERS AND NEUROPSYCHIATRIC SYMPTOMS, PATHWAYS TO EARLY DETECTION OF COGNITIVE IMPAIRMENT IN A SOUTHEAST ASIAN POPULATION - BIOMARKERS AND COGNITION STUDY, SINGAPORE (BIOCIS)

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BACKGROUND

Behavioural changes and Blood-based biomarkers could potentially be a less invasive and easily detectable biomarker for early identification of Alzheimer's disease and dementia. However, the contributions and pathobiology of behavioural and blood biomarkers to disease trajectory and prevalence in Asians requires further definition. We examined the association between blood-based markers (BBM) of Alzheimer's disease and neuropsychiatric symptoms (NPS) in a multi-ethnic Southeast Asian (SEA) population.

METHODS

475 participants were recruited from the Singaporean community. 288 were cognitively unimpaired (CU), 187 with mild cognitive impairment (MCI), and mean age=61.27 years, mean education=14.46 years with 42.1% males. Participants underwent blood biomarker tests of Apolipoprotein (APOE) ε4, Neurofilament Light Chain (NfL), Amyloid Peptides (Aβ)42, Aβ40, Glial fibrillary acidic protein (GFAP) and Phosphorylated Tau at position 181 (P-Tau181) as well as self-reported questionnaires using the Depression Anxiety Stress Scales (DASS) and Mild Behavioural Impairment-Checklist (MBI-C). Linear and Logistic Regression Analyses was conducted.

RESULTS

In the MCI group, pTau181 were significantly associated with overall MBI-C (estimate -0.484; 95% CI [-0.93, -0.04]; p=0.03), MBI-C-Social (estimate -0.177; 95% CI [-0.311, -0.043]; p=0.01) and MBI-C-Beliefs (estimate -0.12; 95% CI [-0.217, -0.024]; p=0.014), and pTau181/Aβ42 (estimate 0.2; 95% CI [-0.01, 0.39]; p=0.038) were significantly associated with MBI-C-Interest. None of the blood biomarkers was significantly associated with cognitive diagnoses in the CU group.

Interestingly, a higher pTau181 concentration is significantly associated with lower odds of depression in the CU (B = -1.661, 95% CI: -3.251 to -0.071, p=0.041), MCI (B = -1.734, 95% CI: -3.280 to -0.188, p=0.028) and overall sample (B = -1.638, 95% CI: -2.717 to -0.559, p=0.003). Across the total sample, pTau181 concentration significantly predicts a reduction in stress (B = -1.629, 95% CI: -3.181 to -0.078, p=0.04).

In predicting cognitive diagnoses, increased GFAP significantly raises the odds by 2.495 times (95% CI: 1.452–4.285, p=0.001), whereas higher pTau181 reduces the odds to 0.433 (95% CI: 0.222–0.844, p=0.014); and MBI-C-interest increases the odds by 1.876 times (95% CI: 1.227–2.87, p=0.004).

CONCLUSION

This study highlights the significance of BBM in detecting NPS and cognitive impairment in a SEA cohort. Elevated pTau181 was associated with reduced depression and stress, possibly due to its involvement in maintaining neuronal stability and protecting mood-regulating brain regions from early neurodegenerative changes. Higher GFAP levels increased the likelihood of cognitive impairment, likely through increased astrocytic activation, which is often associated with neuroinflammation and neurodegeneration. MBI-C dimensions were influenced by biomarker profiles, underscoring a complex relationship between neurodegeneration markers and behavioural symptoms. Findings emphasize potential of developing non-invasive diagnostic strategies that are culturally and regionally tailored for Asian populations.

KEYWORDS

Blood biomarkers, Mild Behavioural Impairment, Mild Cognitive Impairment

Table 1. Participant demographics, blood-based biomarker levels, and behavioural phenotype characteristics by cognitive function

	Cognitively Unimpaired	Mild Cognitive Impairment	Total sample	p
N	288 (60.63%)	187 (39.37%)	475	-
Age †	58.43 ± 10.10	64.29 ± 9.58	61.27 ± 10.47	0.000
Sex (Male) ‡	111 (38.95%)	89 (47.59%)	200 (42.1%)	0.033
Education †	15.238 ± 3.36	13.66 ± 3.75	14.46 ± 3.71	0.000
Presence of APOE ε4 gene ‡				0.043
‡	41 (14.29%)	39 (21.31%)	140 (16.84%)	
Aβ42 †	1.61 ± 0.34	1.7 ± 0.35	1.645 ± 0.348	0.005
Aβ40 †	4.18 ± 0.45	4.4 ± 0.41	4.272 ± 0.444	p<0.000
Aβ42/40 †	0.06 ± 0.01	0.055 ± 0.01	0.58 ± 0.01	p<0.000
GFAP †	4.18 ± 0.46	4.47 ± 0.46	4.301 ± 0.485	p<0.000
P-Tau (181) †	2.92 ± 0.34	2.97 ± 0.35	2.942 ± 0.346	0.005
P-Tau (181) / Aβ42 †	5.14 ± 3.4	5 ± 3.49	5.07 ± 3.44	0.293
Depression Anxiety Stress Scales				
Clinical depression ‡§	20 (6.94%)	19 (10.16%)	39 (8.2%)	0.233
Clinical anxiety ‡§	35 (12.2%)	21 (11.2%)	56 (11.8%)	0.732
Clinical stress ‡§	9 (3.13%)	10 (5.35%)	19 (4%)	0.239
Mild Behavioural Impairment-Checklist				
Total †	0.66 ± 0.88	0.87 ± 1.02	0.76 ± 0.95	0.007
Interest †	0.22 ± 0.50	0.31 ± 0.63	0.26 ± 0.57	0.02
Mood †	0.3 ± 0.57	0.43 ± 0.69	0.36 ± 0.63	0.039
Control †	0.38 ± 0.59	0.5 ± 0.69	0.44 ± 0.64	0.022
Social †	0.06 ± 0.23	0.13 ± 0.35	0.09 ± 0.28	0.029
Beliefs †	0.04 ± 0.21	0.09 ± 0.31	0.07 ± 0.28	0.113

Note. † = mean ± Standard Deviation, ‡ = Frequency (percentages), § = based on established clinical cut-offs

Abbreviations: CU = Cognitively Unimpaired, MCI = Mild Cognitive Impairment, APOE = Apolipoprotein E, Aβ = Amyloid Peptides, GFAP = Glial fibrillary acidic protein, P-Tau (181) = Phosphorylated Tau at position 181

ISCHEMIC STROKE PATIENTS UNDERGOING DSA: A CLINICAL PROFILE

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INTRODUCTION

Stroke is the second leading cause of death and the third leading cause of disability worldwide, which can be caused by a wide range of risk factors, disease processes, and mechanisms. Several modifiable risk factors, such as hypertension, diabetes mellitus, atrial fibrillation, and high cholesterol, can cause ischemic stroke. Digital Subtraction Angiography has become the gold standard for diagnosing cerebrovascular abnormalities, such as aneurysms, and arterial and venous malformations.

METHODS

The design used in this study is retrospective, utilizing the medical records of ischemic stroke patients who underwent Digital Subtraction Angiography at dr. Zainoel Abidin Regional Hospital from January 2023 to December 2023. The sampling technique used in this study was total sampling, which encompasses all populations determined by the researcher as research samples. A total of eighty-four patients were included as research samples according to the inclusion criteria.

RESULTS

It was found that the most patients undergoing Digital Subtraction Angiography were in the age group of 41-59 years (50.0%), with 53.5% of them being male patients. Regarding education, the majority were bachelor's degree graduates (64.2%), and in terms of occupation, civil servants accounted for 54.7%. The most common risk factors accompanying Digital Subtraction Angiography procedures were hypertension (45.2%), the most clinical symptoms were cranial nerve deficits and hemiparesis (38.0%), and the common stenosis and occlusions are located in left anterior cerebral artery (21.4%) and right anterior cerebral artery (17.8%).

CONCLUSION

Hypertension stands out as the most important modifiable risk factor for stroke, and males were predominantly affected by ischemic stroke in this study. Bachelor's degree graduates and civil servants play a significant role in stroke development. Cranial nerve deficits and hemiparesis were common clinical symptoms observed. Knowledge of vascular and cerebral anatomy is crucial for localizing strokes and understanding their mechanisms.

KEYWORDS

Digital Subtraction Angiography, Ischemic stroke, Risk factor

CENTELLA ASIATICA ATTENUATES ALUMINIUM CHLORIDE AND D-GALACTOSE INDUCED ALZHEIMER'S DISEASE VIA TNF- α INHIBITION BY MICROGLIA IN THE HIPPOCAMPUS OF MALE ALBINO WISTAR RATS

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BACKGROUND

Alzheimer's disease (AD) is a neurodegenerative disease characterised by cognitive, memory, and behavioural changes in the affected people. AD affects an estimated 50 million individuals worldwide adding heavy burden on the existing healthcare system. The existing pharmaceutical molecules bring about symptomatic relief, yet no treatment is available to stop the progression of AD. The microglia present in the central nervous system plays a vital role in the pathogenesis of AD by acting on various degenerative pathways. *Centella asiatica* (CA) is a medicinal herb that has been used in traditional medicine as a memory enhancer. An aqueous extract of CA was used in this experiment to study the neuroprotective properties on rat model of Alzheimer's disease.

METHOD

Male albino Wistar rats were randomly divided into six groups of six rats each. The groups include the control group, the model group, the positive control group, and three doses of treatment groups. The control group was administered distilled water; all the other groups were administered $AlCl_3$ (200 mg/kg/oral) and D-galactose (60 mg/kg/i.p.). In addition, the positive control group was also administered donepezil 1 mg/kg orally, while the CA was administered in dosages of 100, 200, and 300 mg/kg orally daily for a duration of 10 weeks. The rats were euthanized after 10 weeks, and immunohistochemical analyses were performed to determine microglial activity using the Iba-1 marker and Tumor Necrosis Factor Alpha (TNF- α) level using the ELISA method.

RESULTS

The results showed that the model group rats had a significant loss of microglia expression and increased levels of TNF- α (p 0.05). Nonetheless, CA at a dose of 300 mg/kg attenuated these changes in rats by improving microglial expression and decreasing TNF- α .

CONCLUSION

These findings provide scientific evidence to support the use of CA as a safe and effective medicinal plant to consider in the fight against inflammation in AD.

KEYWORDS

Alzheimer's disease, *Centella asiatica*, microglia, TNF- α , Hippocampus

EFFECTS OF TRASTUZUMAB ON COGNITIVE FUNCTION IN BREAST CANCER PATIENTS: A PROSPECTIVE COHORT

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BACKGROUND

Chemobrain is an emerging long-term consequence in cancer survivors. Whether trastuzumab, a monoclonal antibody against human epidermal growth factor receptor 2 (HER2), could impair cognitive function during the short-term exposure is still uncertain. This study aimed to evaluate the cognitive function in breast cancer patients during their 1-year trastuzumab treatment.

METHODS

Ninety women with newly-diagnosed breast cancer were consecutively recruited between January 2020 to August 2022. All patients received doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²) every 3 weeks for 4 cycles as neoadjuvant or adjuvant therapy and breast surgery. Paclitaxel (175 mg/m²) every 3 weeks for 4 cycles in patients with positive lymph node(s), as well as trastuzumab (8 mg/kg loading then 6 mg/kg) every 3 weeks for 18 cycles in patients with HER2-positive breast cancer, was post-operatively administrated. Cognitive function was evaluated using Montreal Cognitive Assessment (MoCA) with an additional 1 point for patients who had 12 years or less of formal education. In patients receiving trastuzumab (DOX + TRZ), MoCA was assessed at baseline (before chemotherapy), after doxorubicin chemotherapy and prior to trastuzumab treatment (as month 0), then every 3 months until complete treatment, while comparable schedule was set in those without trastuzumab treatment (DOX). Linear regression (with 95% confident interval) was used to analyze the changes of MoCA score during trastuzumab treatment.

RESULTS

The mean age was 50.5±11.7 years in DOX (n=65) and 49.1±10.1 years in DOX + TRZ (n=25) (p=0.604). About one third of patients in both groups had 12 years or less of formal education. MoCA score at baseline was not different between groups (24.1±3.7 vs. 23.3±4.3, p=0.393). Repetitive MoCA assessment could lead to the significant increase in the score in DOX.

However, the score remained unchanged in DOX + TRZ. Interestingly, in patients with baseline cognitive impairment (MoCA score <26), the improvement of MoCA score over time was significantly different between groups, while MoCA score was constantly normal in those without cognitive impairment. (Figure)

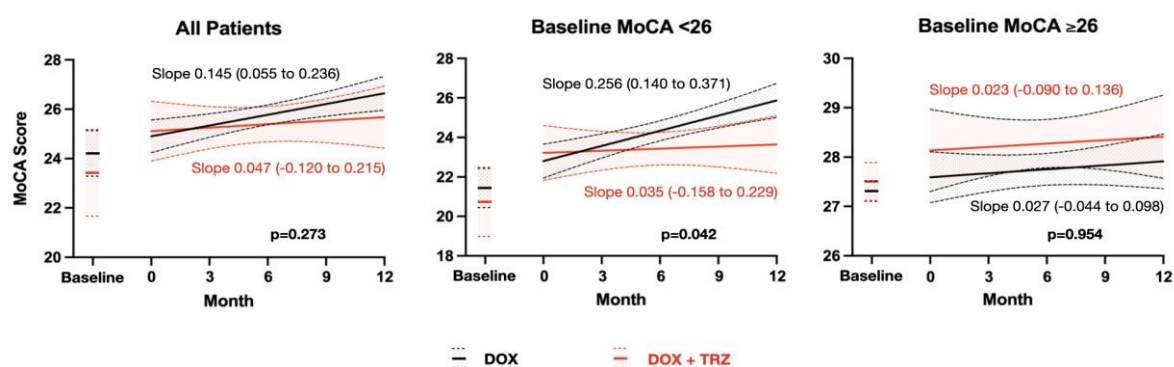
CONCLUSION

Trastuzumab impaired cognitive function during the treatment, especially in patients with baseline cognitive impairment.

KEYWORDS

Chemobrain, cognitive impairment, trastuzumab

Figure. MoCA score during trastuzumab treatment



THE ROLE OF METHIOPROPAMINE IN REGULATING SPATIAL COGNITION IN MICE

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BACKGROUND

Methiopropamine (MPA), an analogue of methamphetamine (METH), has been associated with non-spatial cognitive deficits in animal models. It would be insightful to investigate the effects of MPA on different types of memory, such as spatial memory, to gain a more comprehensive understanding of its cognitive impacts. This study was carried out to determine the subacute effects of MPA on spatial cognitive function, using the 8-radial arm maze (8-RAM) test in mice. Additionally, microarray analysis was performed to identify potential neuropathological pathways involved.

METHODS

A total of 40 male Swiss Albino mice were randomly divided into four groups (n=10). Each group received daily intraperitoneal injections of either normal saline, METH at a dosage of 1 mg/kg, or MPA at dosages of 1 mg/kg or 3 mg/kg for seven days. The 8-RAM test was carried out in three phases; habituation, training, and testing. In the testing phase, re-entries into previously visited arms were recorded as working memory errors which indicate short-term memory impairment, and entries into unbaited arms were recorded as reference memory errors, which indicate long-term memory impairment. Prefrontal cortex (PFC) samples (n=5 for each group) were selected for microarray analysis, and bioinformatic evaluation performed using Gene Set Enrichment Analysis (GSEA).

RESULTS

Administration of MPA at a dosage of 3 mg/kg resulted in a significant deterioration of both working and reference memory, compared to the control groups. Conversely, METH administration only led to an impairment in reference memory, with no observable effect on working memory. GSEA results indicated a significant upregulation of the monoaminergic pathway in the METH-treated group.

CONCLUSION

These findings indicate that repeated treatment with MPA induced impairments in both short-term and long-term spatial memory. These neurotoxic effects may be attributed to alterations in monoaminergic activities, particularly within the PFC region.

KEYWORDS

Methiopropamine; NPS; cognitive impairment; methamphetamine; neurotoxicity

CASE REPORT: HYPOACTIVE DELIRIUM IN REFRACTORY CHRONIC HYPONATREMIA AND LATE-STAGE ALZHEIMER'S DISEASE WITH BPSD ELDERLY PATIENT

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INTRODUCTION

The primary challenges of delirium treatment associate with two conditions, those are encephalopathy and acute nonspecific psychosis. The risk of delirium may be due to the interaction of predisposing and precipitating factors, include dementia, infectious complications, and hyponatremia.(1) Hyponatremia is multifactorial with special attention in elderly population, especially in diagnostic approach and treatment.(2)(3) Dementia is the seventh leading cause of death and a leading contributor to disability worldwide with Alzheimer disease as the most common form.(4) Behavioral and psychological symptoms of dementia (BPSD) affects up to 97% of community-dwelling patients with dementia. BPSD includes a range of neuropsychiatric disturbances such as depression and apathy.(5) All these conditions are particularly vulnerable to hospital re-presentation, making a good discharge planning, not only helping the patients, but also the patient's family and health care providers.(6)

REPORT

A 78-year-old diabetic and hypertensive man admitted to Ciptomangunkusomo Hospital with fatigue and transferred to geriatric department for evaluation and treatment for management hypoactive delirium with diarrhea and hyponatremia. This patient had already diagnosed as Alzheimer's dementia with BPSD (depression and apathy) and repeated hyponatremia. There was history of levothyroxine therapy, coronary artery disease, repeated falls, benign prostatic hyperplasia, and repeated pneumonia. Vital sign was normal after resuscitation from dehydration state, but still with time, place, and person disorientation. There was increase of peristalsis. From the comprehensive geriatric assessment, we found total dependent, malnutrition, instability, polypharmacy, high risk of decubitus, frailty, and predictive sarcopenia. The sodium level was from 122 mEq/L to 132 mEq/L with normal potassium. Colonoscopy was normal with microscopic colitis as the differential diagnose. Biopsy revealed a chronic ileitis and non-specific colitis. Cognitive and depression were observed by Neurologist and Psychiatrist. Diarrhea was resolved without antibiotic used. Sodium was corrected carefully. There was difficulty when we had to diagnose a lucid state with considering dementia with BPSD. After 18 days hospital care, patient went back home with a better orientation. The big homework for us after this admission was the discharge planning, transition from hospital to home and prevent subsequent re-presentations to hospital. We did a family meeting to ensure not only the goal of this treatment but also the discharge planning. Further evaluation was done in outpatient clinic.

CONCLUSION

This case illustrates the complexity of assessment and treatment in Alzheimer's dementia elderly patient with hypoactive delirium. Geriatric patients need an interdisciplinary team for a better outcome.

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PREDICTORS OF COGNITIVE IMPAIRMENT FOLLOWING INTRACEREBRAL HAEMORRHAGE: AN OBSERVATIONAL STUDY

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BACKGROUND

Spontaneous intracerebral haemorrhage (ICH) is the most common form of haemorrhagic stroke, representing 10-20% of all strokes. It occurs due to rupture of small vessels afflicted with microangiopathies and carries significant morbidity and mortality when compared to ischaemic stroke. Post-stroke cognitive impairment (PSCI) among patients with ICH is understudied despite its significance in overall function and quality of life of patients and carers. This observational study examines the prevalence of PSCI, its association with quality of life among patients with ICH and outcomes in patients post-ICH.

METHODS

We conducted a cohort study, recruiting patients aged 18 years and above admitted with spontaneous non-traumatic ICH. We excluded patients with traumatic ICH, haemorrhagic transformation in ischaemic stroke, subarachnoid or subdural haemorrhage, known neurodegenerative or psychiatric disorders, and stroke mimics. The participant's sociodemographic and clinical data were collected with a data collection sheet. Subsequently, we contacted the participants three months from onset via telephone and assess their Modified Rankin Score(mRS), EuroQol 5 Dimension 5 Level (EQ-5D-5L) assessment to measure quality of life, and Ascertain Dementia or "Eight-item Interview to Differentiate Aging and Dementia" (AD8). The AD8 contains eight items that test for memory, orientation, judgment, and function. Cut-off points are: normal cognition 0-1; impairment in cognition 2 or greater.

RESULTS

Eighty-five participants were recruited, with a mean age of 60.04 years (SD $\pm$ 14.9). The median GCS score within our cohort was 13 [6.5, 15] and hematoma volume was 14.63[3.73, 32.64] mL. Thirty-four of the participants died within three months. Factors associated with mortality were a prior history of stroke, chronic kidney disease, smoking, age, GCS on arrival, location of ICH, presence of intraventricular haemorrhage, and hydrocephalus ($p < 0.05$). Binary logistic regression revealed a significant association between infratentorial ICH, GCS on arrival, hematoma volume, and presence of hydrocephalus with mortality ($p < 0.05$). We further

analyzed the fifty-one surviving participants with the AD8 score, demonstrating 41.2% with a score of 2 or greater. Factors significantly associated with PSCI were age, GCS on arrival, hematoma volume, ICH score, mRS, EQ-VaS and three dimensions in EQ-5D-5L assessment: D1 – Mobility, D2 – Self-care, and D3 – Usual activities. A moderate correlation was observed between D1, D2, D3, EQ-VAS and mRS score with PSCI (r .590, r .513, r .562, r -.574 and r .632, $p < 0.01$), while a weak correlation was observed between the ICH score (r .276, $p < 0.05$) and PSCI.

CONCLUSION

ICH is a condition associated with high mortality. A significant proportion of ICH patients who survive experience PSCI. The prevalence of PSCI is underestimated and its negative impact on patients' functional outcome is often neglected. Regular screening with questionnaires such as AD-8 should be carried out to identify patients with PSCI who may benefit from therapies and treatment that would improve their outcome and quality of life.

KEYWORDS

Intracranial haemorrhage (ICH), cognition, post-stroke.

ASSOCIATIONS BETWEEN POTENTIAL RISK FACTORS AND BLOOD-BRAIN BARRIER WATER PERMEABILITY IN MIDDLE-AGED AND OLDER ADULTS

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BACKGROUND

Blood-brain barrier (BBB) dysfunction is suggested to be a potential mediator between vascular risk factors and cognitive impairment. To measure BBB permeability, a novel arterial spin labelling MRI technique (BBB-ASL) can be used to derive the time of exchange (Tex), arterial time transit (ATT), and cerebral blood flow (CBF). While ASL has been used extensively, no study has employed BBB-ASL to assess the relationship between vascular risk factors and BBB permeability. In this study, we investigated the relationships between age, sex, and vascular risk factors and BBB water permeability as well as their relationship with cognition.

METHODS

Two studies with community-dwelling participants aged 55-80 years were used in this analysis (n=144, median age 59 years, 57% females). Participants with history of any physical disability, prevalent dementia or significant neurological disease or contraindications to MRI were excluded. Multi-echo-ASL acquisition technique (BBB-ASL), were acquired and processed to obtain Tex, ATT and CBF. The association of potential risk factors, such as age, sex, body mass index (BMI), blood pressure (BP), and medical history, with these BBB parameters were assessed. The relationship between BBB permeability and cognitive performance measured by MoCA was also assessed.

RESULTS

Males had higher BBB permeability, reduced CBF and prolonged ATT. Older age was associated with longer ATT and a lower CBF. Participants with hypertension were observed to have associations with higher BBB permeability, reduced CBF and prolonged ATT. We found that increased BMI was associated with decreased CBF. Systolic BP and Diastolic BP showed associations with all ASL parameters; Systolic and diastolic BP were negatively associated with Tex and CBF but positively with ATT. With regards to cognition, Tex had borderline associations with MoCA, and only CBF was significantly associated with MoCA.

Table 1. Multivariate linear regression adjusting for sex, age, and hypertension with ASL parameters.

Models	GM Tex		GM ATT		GM CBF	
	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value
Age	0.24 (-0.46, 0.95)	0.5	0.01 (-0.01, 0.03)	0.282	0 (-0.02, 0.02)	0.722
Model 1 Sex	-21.56 (-32.47, -10.65)	<0.001	0.5 (0.15, 0.85)	0.005	-0.98 (-1.30, -0.65)	<0.001
Hypertension	-14.57 (-26.50, -2.63)	0.018	0.37 (-0.02, 0.75)	0.063	-0.26 (-0.61, 0.10)	0.158
Model 2 BMI	-0.03 (-0.07, 0.02)	0.256	0.04 (0.00, 0.08)	0.077	-0.06 (-0.10, 0.02)	0.002
Model 3 SBP	-0.02 (-0.03, -0.01)	<0.001	0.02 (0.01, 0.02)	0.002	-0.01 (-0.02, 0.00)	0.039
Model 4 DBP	-0.03 (-0.05, -0.01)	<0.001	0.03 (0.01, 0.04)	0.002	-0.03 (-0.04, 0.01)	0.001

GM – Gray matter; Tex – Time of exchange; ATT – Arterial Transit Time; CBF – Cerebral blood flow; BMI – Body Mass Index; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure. Model 1: Single ASL parameter ~ age + sex + hypertension. Model 2: Model 1 + BMI, Model 3: Model 2 + SBP, Model 4: Model 3 + DBP.

CONCLUSION

This study unveils associations between potential risk factors and BBB-ASL parameters. Our findings indicated that ageing, sex, and risk factors like BMI and blood pressures are associated to BBB permeability. These outcomes underscore the potential of using BBB-ASL, warranting further research to strengthen these findings.

KEYWORDS

Arterial Spin Labelling, Blood-brain Barrier, Risk Factors

MULTI-DOMAIN LIFESTYLE BEHAVIOURAL FACTORS AND COGNITIVE IMPAIRMENT IN AN ASIAN POPULATION

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BACKGROUND

Increase in life expectancy has led to a rise in age-related diseases, particularly cognitive impairment and dementia. There is increasing evidence on the impact of lifestyle factors on cognitive decline. However, more research is needed to identify the important modifiable risk factors for targeted prevention interventions. This study aims to investigate the association between multi-domain lifestyle behavioural factors and cognitive impairment in a multi-ethnic cohort from Singapore.

METHODS

This cross-sectional study utilized data from the Multi-Ethnic Cohort Phase 1 (MEC1) Revisit (n=2,048; ages 40-91 years). Participants were Singaporeans of Indian, Malay, and Chinese ethnicity. Data on lifestyle factors (cigarette smoking and alcohol consumption) were collected through questionnaires. A semi-quantitative food frequency questionnaire [1] and International Physical Activity Questionnaire (IPAQ) [2] validated in Singapore were used to collect diet and physical activity information. Weekly physical activity level (MET-h/week) and modified Dietary Quality Index - International (mDQI) [3] were calculated. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) and analysed as both a continuous score and a binary outcome of cognitive impairment, using education-based cut-offs. Multivariable linear and logistic regression analyses were employed to investigate associations between lifestyle factors and cognitive function, adjusting for sociodemographic factors, body mass index (BMI), and presence of comorbidities.

RESULTS

A total of 632 (30.9%) participants had cognitive impairment. Dietary quality index showed a significantly inverse association with cognitive impairment (OR:0.92; 95% CI: 0.85, 0.99). Compared with lower tertile of mDQI-I, middle (OR 0.77, 95%CI 0.61, 0.98) and higher (OR 0.81, 95%CI 0.64, 1.04) tertiles had higher odds of cognitive impairment. Compared with the lower tertile of physical activity volume, the middle (OR: 1.07, 95% CI 0.84, 1.36) and higher (OR: 1.38, 95% CI 1.07, 1.78) tertiles had higher odds of cognitive impairment. Smoking and alcohol consumption were not significantly associated with cognitive impairment.

CONCLUSION

In an Asian population, a healthier diet was associated with better cognitive function, while physical activity, cigarette smoking, and alcohol consumption showed no significant

association with cognitive impairment. These findings underscore the importance of prioritizing dietary quality as a preventive strategy to reduce the risk of cognitive decline.

KEY WORDS

cognitive impairment, physical activity, diet.

Table 1. Fully adjusted associations between lifestyle factors and cognitive impairment

Lifestyle factors	Cognitive Impairment		MMSE [#] (continuous)	
	OR (95% CI)	p-value	β (95% CI)	p-value
Smoking				
Never smoker	ref		ref	
Ever smoker	1.01 (0.77, 1.34)	0.93	-0.00 (-0.01, 0.01)	0.99
Alcohol consumption				
Rarely or never	ref		Ref	
Occasional	0.99 (0.70, 1.41)	0.97	0.01 (-0.01, 0.02)	0.32
Frequent	0.95 (0.64, 1.41)	0.82	0.002 (-0.01, 0.02)	0.78
Physical activity, per 100 MET-hr/week[#]				
PAL tertiles				
Lower tertile	Ref		Ref	
Middle tertile	1.07 (0.84, 1.36)	0.60	0.00 (-0.01, 0.01)	0.65
Higher tertile	1.38 (1.07, 1.78)	0.01	-0.01 (-0.02, 0.00)	0.04
	p-trend	0.01	p-trend	0.04
mDQI-I[#] per 10-unit score				
mDQI-I tertiles				
Lower tertile	Ref		Ref	
Middle tertile	0.77 (0.61, 0.98)	0.03	0.01 (0.00, 0.02)	0.01
Higher tertile	0.81 (0.64, 1.04)	0.09	0.01 (0.00, 0.02)	0.004
	p-trend	0.09	p-trend	0.004

Full model: adjusted for age, gender, ethnicity, education level, marital status, work status, Body Mass Index (BMI), history of hyperlipidemia, hypertension, diabetes and stroke, smoking, alcohol consumption, physical activity level and modified Diet Quality Index-International (mDQI).

[#] MMSE, Mini-Mental State Examination.



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ASSOCIATION OF COMBINED RISK FACTORS WITH COGNITIVE FUNCTION AMONG SINGAPOREANS

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BACKGROUND

Multiple modifiable factors are associated with a higher risk of dementia and cognitive impairment, but studies on how these factors collectively impact cognitive health are limited. This study aims to examine the association of combined risk factors with cognitive function using a longitudinal Singaporean cohort.

METHOD

A total of 164 subjects from NEURO-BMC, an ongoing multi-ethnic cohort of Singaporeans aged 45-85, were included in this study. At baseline and year-1 follow-up, participants completed questionnaires gathering information, including age, sex, ethnicity, education level, blood pressure, weight, height, marital status, hypertension and diabetes, as well as lifestyle of alcohol consumption, smoking, physical activity and diet. Cognitive function (including domains of executive function, attention, language, verbal memory, visual memory, visuoconstruction, and visuomotor speed) were assessed using the Vascular Dementia Battery and depression level using modified Geriatrics Depression Scale (mGDS).

A combined risk score was calculated based on the number of existing risk factors, including regular alcohol consumption, smoking history, low physical activity, low DASH score, mGDS score above 4, diabetes, hypertension and having obesity (BMI above 29.99). A higher score indicates a greater number of risk factors. Generalized estimation equation was applied to examine the association of the combined risk score with cognitive function, with adjustments of age, sex, ethnicity, education level and marital status.

RESULTS

A higher combined risk score was associated with lower performance across all cognitive domains, although the associations reached significance only for verbal memory (β -0.10, 95%CI -0.18, -0.01) and visuomotor speed (β -0.13, 95%CI -0.23, -0.04). Similarly, a higher combined risk score was associated with lower cognitive performance in all domains except attention and visuoconstruction, with significant associations observed only for executive function (β -0.20, 95CI -0.38, -0.01) and language (β -0.16, 95%CI -0.25, -0.06). Additionally, a higher combined risk score was associated with a faster decline in executive function and language but a slower decline in other domains, although none of the associations reached statistical significance.

CONCLUSION

In this ongoing cohort of Singaporeans, a higher accumulation of dementia risk factors was associated with poorer cognitive function both at baseline and during follow-up assessments.

KEYWORDS

physical activity, diet, cognitive function

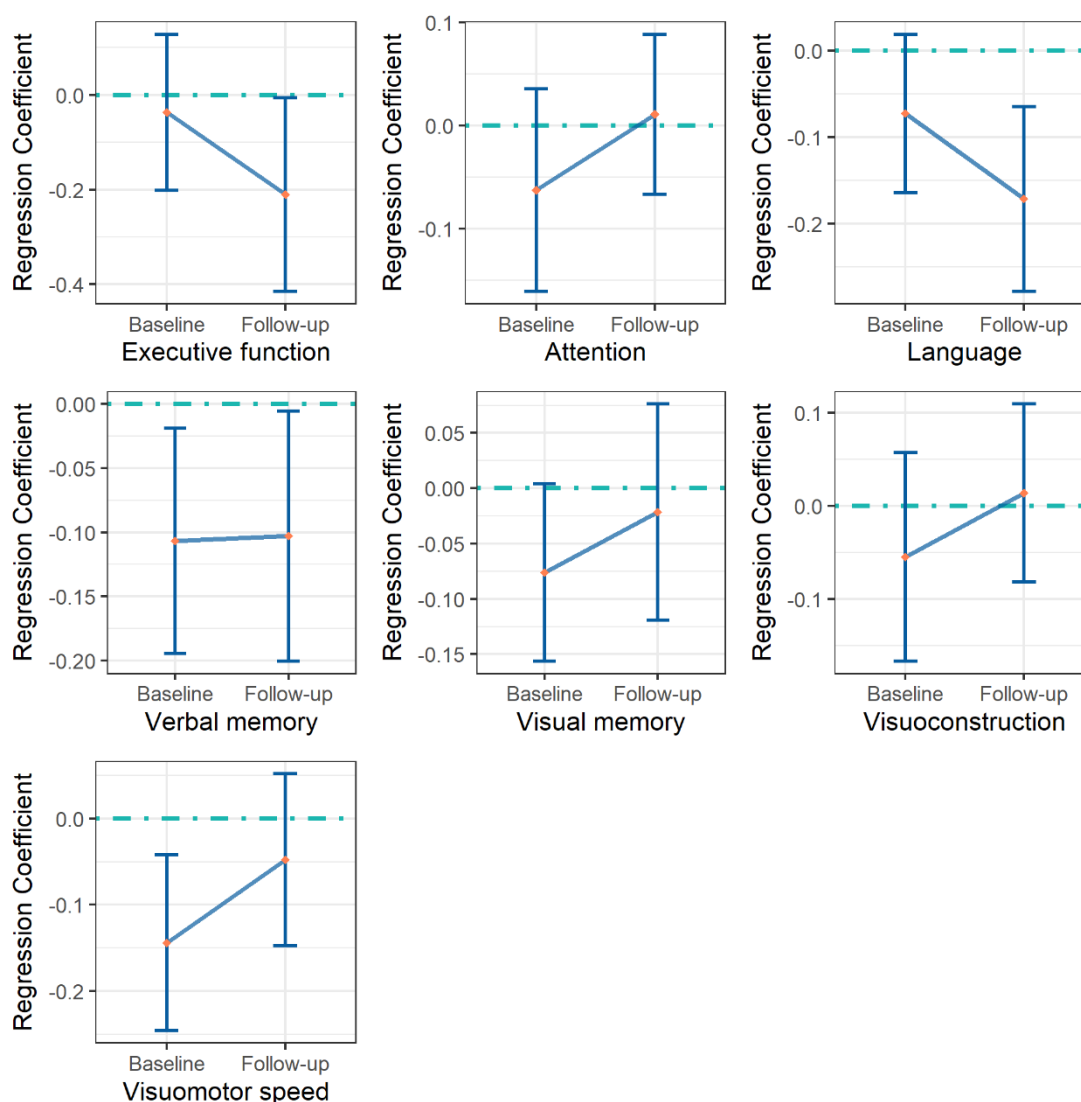


Figure 1. Association between combined risk factors and cognitive function

FICUS DELTOIDEA IMPROVES COGNITIVE IMPAIRMENT AND PREVENTS NEURODEGENERATION IN ALZHEIMER'S DISEASE-LIKED RATS

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INTRODUCTION

Alzheimer's disease (AD) is a common neurodegenerative ailment that primarily affects elderly. It entails loss of normal cognitive functions and a substantial decline in memory. AD imposes a significant global burden and has a substantial financial impact, in addition to the surge of victims. AD cases are expected to exceed over 200 million worldwide by 2050, up from 50 million in 2018. In search of a concrete solution, various alternatives have been thoroughly investigated, including synthetic drugs and natural products, with positive outcomes in both fields. The field of natural products, including medicinal plants are diverse, and numerous plants have compounds that can be potentially applied to treat AD. *Ficus deltoidea* (FD) is a widely cultivated plant in the southeast Asia, popularly known as mas-cotek in Malaysia. FD has a long history of being utilized as a traditional medicine for the treatment of different ailments, but very limited claim have been made in neurodegenerative disease. Therefore, our study was conducted to investigate the effect of FD on behavioral and histology in line with AD on AD-like rats.

METHODS

In this study, male albino Wistar rats were subjected to AD mimic symptoms by administering D- galactose and aluminum chloride for 70 days. Simultaneously, the AD-induced rats received FD extract orally at different doses of 50mg/kg, 100mg/kg and 200mg/kg. Following treatment, a spontaneous alternation T-Maze behavioral test was conducted to access their spatial memory and learning, which was hippocampus-dependent. The histological study was further conducted on the hippocampal CA1 region using Hematoxylin & Eosin (H&E) stain to examine the morphology of the pyramidal neurons.

RESULTS

The T-Maze behavioral test revealed a significant difference in exploratory behavior between FD- administered groups and the AD model group, with the rats from FD group preferred to explore a novel arm over a familiar one. However, the AD model group made the lowest alteration. Furthermore, the histological analysis with H&E stain revealed viable and intact pyramidal neurons in the CA1 region of hippocampus of all the FD groups in contrast to the AD model group, which were degenerated and shirked.

CONCLUSION

The findings of this study indicate that the administration of FD has shown to improve the cognitive function of AD-liked rats after behavioral studies and has prevented neurodegeneration in the CA1 region of the hippocampus indicating a proper memory function because of the critical role CA1 region plays in memory formation. It is important to further explore the effect of FD on other regions of the brain that play role in cognitive functions.

KEYWORDS

Alzheimer's disease, *Ficus deltoidea*, Cognition, Behavioral studies, Hippocampus

CASE REPORT: AN ELDERLY LADY WITH FREQUENT FALLS AND IMPAIRED MEMORY TREATED FOR NORMAL PRESSURE HYDROCEPHALUS

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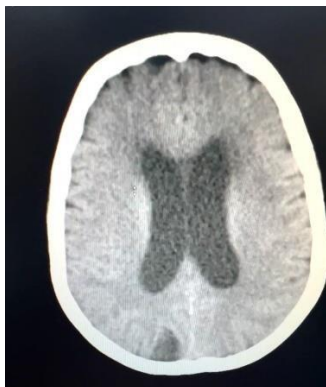
INTRODUCTION

Normal pressure hydrocephalus (NPH) typically presents with a clinical triad of gait disturbance, urinary incontinence, and cognitive deficits. NPH is a potentially reversible syndrome characterized by enlarged cerebral ventricles and shows clinical improvement with shunting.

REPORT

We are presenting a case of elderly lady with comorbidities of DM, HPT, Ischemic Stroke (no residual weakness) initially presented with 3 months history of forgetfulness, frequent falls, urinary incontinence. She had difficulty in walking thus used quadripod to ambulate. Clinically alert but mild dementia, MMSE score 19, having ataxic broad-based gait and intentional tremors, other cerebellar signs were negative. Sensory and motor examination unremarkable, thus urgent CT Brain was arranged to rule out recurrent stroke. CT Brain revealed dilated ventricles. Thus, we proceed diagnostic lumbar puncture (LP), 50cc of CSF was drained, opening pressure 5 cm H₂O, biochemistry and cultures normal and gait showed improvement post LP. Thus, as she showed positive response to tap test, diagnosis of NPH was made and given neurology clinic with MRI Brain & physiotherapy outpatient for gait training and was counselled for future plan for CSF shunting.

Figure 1: CT Brain plain



IMPRESSION

Disproportionate dilatation of the ventricles in relation to cerebral sulci raises the possibility of normotensive hydrocephalus.

DISCUSSION

The usual NPH classification into idiopathic (iNPH) and secondary (sNPH), resulting from subarachnoid hemorrhage, meningitis, intracerebral hemorrhage, brain tumor or head trauma.

Other than ventriculomegaly, there is no definitive pathological or radiological diagnostic finding for NPH. Ventriculomegaly is the central element in the clinical syndrome due to the hydraulic pressure effect. NPH is classically defined as a communicating form of hydrocephalus without a fully effective non-invasive treatment.

CSF shunting and subsequent drainage continues to be the first-line therapy for NPH, with the symptoms usually improving after the intervention. The tap test works by temporarily decreasing intraventricular pressure, mimicking the effect of a shunting procedure, allowing the physician to evaluate the patient's response to a substantial (50 ml) CSF removal.

CONCLUSION

In conclusion, NPH is a relatively prevalent medical condition, especially in the older age group. Gait disturbance is the most common and usually the first to manifest itself. The treatment of NPH can be highly beneficial, both from the viewpoint of prevention of frequent falls, head injury, subdural hematomas, trauma and hip fractures in the elderly, as well as for the improvement of quality of life with disappearance of incontinence, control of the risk of repeated urinary tract infections and sepsis, freedom of ambulation, and in some selected cases, cognitive improvement.

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CASE DESCRIPTION OF FRONTOTEMPORAL DEMENTIA ADMITTED TO DR. CIPTO MANGUNKUSUMO NATIONAL CENTRAL PUBLIC HOSPITAL IN 2023

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BACKGROUND

The main issue in Indonesia is that despite having a relatively high prevalence of dementia, the rate of formal diagnosis in Indonesia is very low, even reaching less than 1% of the actual Indonesian dementia population, which is only 0.2%.¹ It can be said that if using the prevalence in the study by Farina et al.¹, which is 27.9%, and the total population of Indonesia based on the World Bank in 2022² is 275.5 million lives, then there are around 77 million dementia patients, and only about 154 thousand patients have a formal dementia diagnosis. This is especially dire for frontotemporal dementia formal diagnosis rate, as one of the lesser-known types of dementia despite the debilitating effects it has on patients. Frontotemporal dementia (FTD) is a group of brain disorders characterized by progressive degeneration of the frontal and temporal lobes, leading to significant changes in behavior, personality, language, and motor skills, often occurring at a younger age than other forms of dementia.^{3,4} Due to its rarity and lack of understanding, FTD is often misdiagnosed as Alzheimer's or other dementias. Symptoms can be mistaken for intentional misbehavior, causing frustration and conflict.^{5,6} Hence we make this case description to raise awareness of FTD in Indonesia.

METHOD

This is a case description study from an electronic health record database from January 2023 to December 2023. Data were gathered from the executive function clinic in dr Cipto Mangunkusumo National Central Public Hospital utilizing standardized diagnostic criteria such as the DSM-5⁷ or ICD-10⁸.

RESULT

In the year 2023, we found 4 patients diagnosed with frontotemporal diagnosis; 1 female and 3 males, with a mean age of 61.25 years old (youngest was 55 and eldest was 77). All four of them could no longer work. About 25% of patients did not finish elementary school, 50% finished junior secondary school, and 25% finished high school. After adjusting for length of education, all four had very low MoCA-INA scores indicative of cognitive impairment. Interestingly, two patients also had epilepsy occurring after the onset of dementia or behavioral changes. Only half of the patients received cognitive strengthening medication (donepezil), one received anti-epileptic drugs, and one received SSRI. All four were subjected to cognitive therapy. Further analysis of cognitive domains revealed that about half had trouble speaking, memory functions were mostly impaired for all patients, especially for immediate memory and

delayed verbal, executive functions were generally impaired for all sub-domains, and visuoconstruction abilities were impaired for all patients.

CONCLUSION

Frontotemporal case descriptions in Indonesia are crucial for advancing the understanding, diagnosis, treatment, and more importantly, for raising awareness of frontotemporal disorders (FTDs) in Indonesia. Further efforts to improve Indonesia's rate of formal diagnosis of frontotemporal dementia are needed due to the debilitating and early onset nature of this progressive degenerative disease.

KEYWORDS

frontotemporal dementia, dementia, case descriptions

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SUBARACHNOID HAEMORRHAGE: RARE PRESENTATION OF CEREBRAL VENOUS SINUS THROMBOSIS THAT SHOULD NOT BE OVERLOOKED

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INTRODUCTION

Non-accidental subarachnoid haemorrhage (SAH) is most often caused by ruptured cerebral aneurysm and rarely caused by other vascular lesions. Whilst cerebral venous sinus thrombosis (CVST) itself is a rare cerebral vascular disease, it has a wide spectrum of clinical manifestations making it arduous to be diagnosed. Its diagnosis will be further intricate when a patient initially presents with acute SAH. We here in report two cases of dural venous sinus thrombosis with SAH, in which the initial clinical suspicion was to rule out ruptured aneurysm.

CASE REPORT

A 55 year-old lady with underlying ovarian cancer (FIGO 3). She was presented with sudden onset of left sided body weakness, drooling of saliva and facial asymmetry. Physical examination revealed power on the left side was 0/5 for upper and lower limb with hypotonia and hyporeflexia. Plain CT brain showed acute subarachnoid haemorrhage within the right fronto-temporo-parietal lobes and right Sylvian fissures. Adjacent white matter hypodensity was seen. The anterior until distal 3rd part of the superior sagittal sinus (SSS) appeared denser than usual. CT angiography (CTA) excluded any cerebral aneurysm and CT venography (CTV) confirmed presence of thrombosis within the SSS. Similar 2nd case of a 44 year-old lady presented with sudden multiple episodes of fitting within 1 week. She denied any headache, aura, blurring of vision or muscle weakness. Neurological examination was unremarkable. Plain CT brain showed multiple acute SAH at bilateral high parietal and left frontal lobes with punctuate left frontal intraparenchymal haemorrhage. CTA revealed no cerebral aneurysm and thrombosis within the SSS on CTV was initially missed. This finding was detected upon discussion during neuroradiology conference. Both patients improved with anticoagulant therapy.

Figure 1: Plain CT brain showed acute SAH at right fronto-parietal lobes (a) and dense SSS (b). CTV showed corresponding filling defect in keeping with thrombosis.

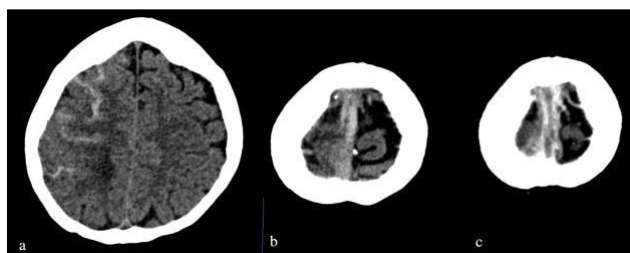
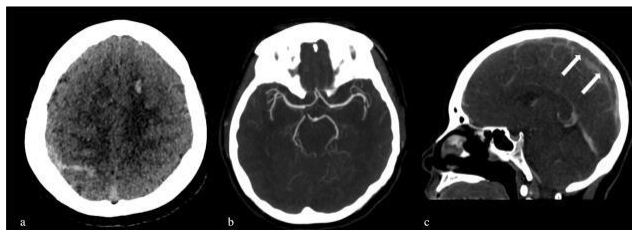


Figure 2: Plain CT brain showed convexity acute SAH within the right parietal sulci with punctuate haemorrhage at left frontal lobe (a). CTA ruled out cerebral aneurysm (b). Sagittal CTV showed long segment SSS thrombosis.



CONCLUSION

Although CVST is rarely presented as acute SAH, this diagnosis should always be suspected when CTA reveals no evidence of cerebral aneurysm. Further study of CTV should be performed if there is suspicious of dense venous sinus on plain CT or location of SAH is at the cerebral convexities that spares the basal cistern. Making a correct diagnosis of venous thrombosis is important as cerebral aneurysm will usually be managed surgically or with endovascular therapy, whilst the mainstay treatment of cerebral thrombosis is by anticoagulant. Wrong diagnosis may lead to a devastating outcome.

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EFFECTIVENESS OF THE INTERVENTIONS IMPLEMENTED TO INCREASE THE COMPLETION RATE OF THE COGNITIVE FUNCTION ASSESSMENTS (CFA) VIA A SMARTPHONE APP

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BACKGROUND

Our previous Digital Phenotyping (DP) study using a smartphone app called Linus Participant (LP) to assess the cognitive functions of our elderly participants, faced a decline in the completion rate among the participants. We are actively investigating the factors contributing to the decline in the completion rate. Our app developers from Davos Alzheimer's Collaborative (DAC), Boston University and Linus Health are still working on solving the technical issues (ie: font size, pause button) and providing the after-test scores to improve the completion rate. Concurrently, various interventions have been implemented as well to increase participant adherence, including Whatsapp and Call reminders, newsletters and webinars. In this study, our aim is to evaluate the effectiveness of the interventions implemented so far to increase the completion rate of the longitudinal app-based CFA.

METHOD

This ongoing study, initiated in December 2022, involves a longitudinal self-assessment of the cognitive functions every 3-month over an 8-cycle period, remotely, spanning approximately 2 years period, via LP app. Participants were recruited from the Transforming Cognitive Frailty into Later-Life Self-Sufficiency (AGELESS) cohort, aged 55 years and above, through electoral rolls and sampling frames. Our targeted sample size is 1000 (currently, n = 816).

Every 3 months, after their registration date, participants will receive a new set of assessments via the app and they are required to complete the assessments within 2 weeks. At the start of every new assessment received by participants, Whatsapp and Call reminders are sent to them as reminders to complete the assessments. Once they reach their fifth assessment (after 1 year), the participants are invited for their second in-clinic visit to compare their results remotely and in-clinic under our supervision. Starting August 2023, we decided to disseminate monthly newsletter discussing in depth about their participation in this DP study. In April 2024, we collaborated with Boston University to do bi-monthly

webinars via Google Meet to increase participants adherence. Last but not least, a feedback form was also distributed to the participants to gather their feedbacks on the study.

CURRENT RESULTS

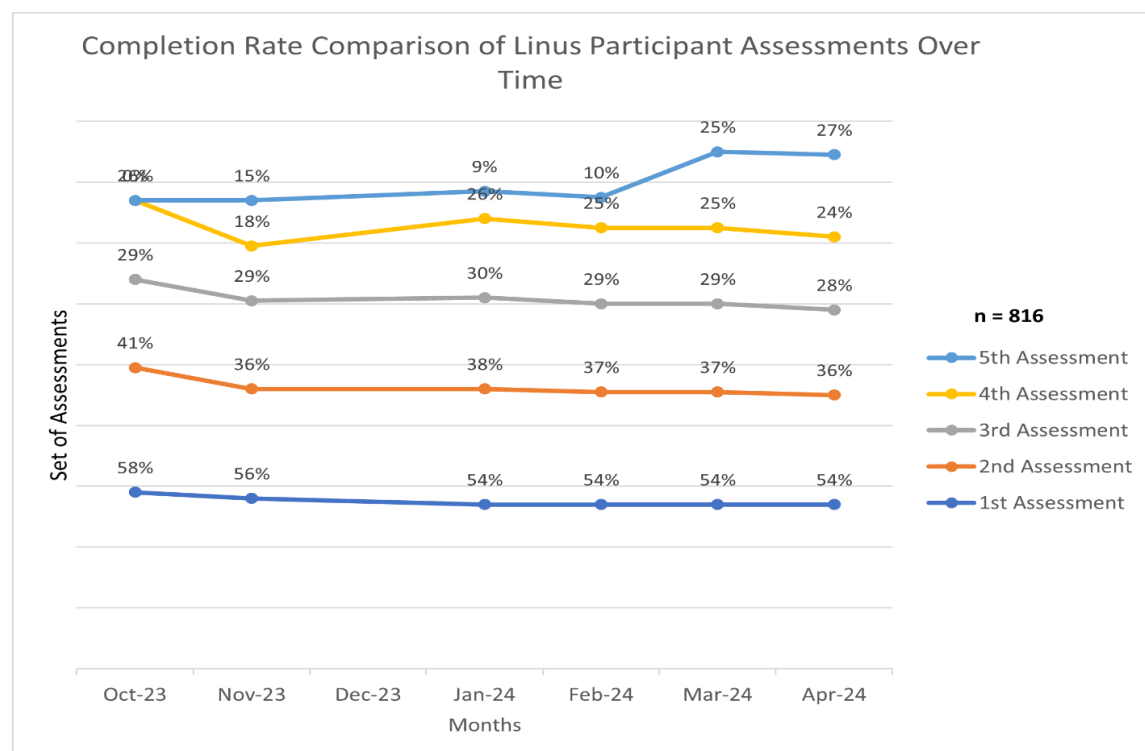
816 participants have been recruited (mean age = 67.92) (43% male, 57% female). Despite the implementation of multiple interventions, the completion rates exhibited minimal improvement and fluctuated over time as depicted in Figure 1. Up to this date, 6 Newsletters have been disseminated and 1 webinar has been conducted. Only 5% (n=38) reverted their feedback forms and 65.7% of them rated the app overall as great or nearly great. Only after we invited some participants for their second in-clinic visit, the completion rate started to increase significantly again by 15%.

CONCLUSION

An unexpected increase in the completion rate observed following the in-clinic visit, suggesting a preference for in-person interventions among participants compared to online interventions. The online interventions need more efforts in term of its accessibility to be more effective in increasing the completion rate since some participants are not tech-savvy and feared of being scammed. A more effective and automated system is also required to send reminders instead of doing them manually.

KEYWORDS

Digital Phenotyping, completion rate, interventions.



THE IMPACT OF GLYCEMIC VARIABILITY ON COGNITIVE DECLINE AND ALZHEIMER DISEASE: A SYSTEMATIC REVIEW

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BACKGROUND

Increasing evidence has established a connection between fluctuations in glucose metabolism and the onset of Alzheimer Disease (AD). Current research supports the notion that this metabolic imbalance significantly affects cognitive health. However, the specific mechanisms through which these fluctuations influence neurodegeneration, eventually leading to AD, require further exploration.

This study aims to determine the association between blood glycemic variability with or without T2DM and the risk of AD, further providing the most recent and comprehensive summary of the evidence in this field.

METHODS

Following the PRISMA 2020 guidelines, a comprehensive search was conducted across PubMed, Elsevier, Research Gate, and Cochrane databases using specific terms: (“glucose variability” or “glycemic variability” or “glucose fluctuation” or “glucose instability” or “glycemic fluctuation”) And (“Alzheimer’s disease” or “Alzheimer disease” or “Alzheimer dementia” or “Alzheimer”). Studies published between 2014 and 2024, written in English, and examining the relationship between glucose variability and AD, were included. The outcomes measured were risk of cognitive impairment and Alzheimer, cognitive performance, and incidence of AD.

RESULTS

The literature search yielded 142 records, with six studies meeting the eligibility criteria. Parameters for glycemic variability included fasting plasma glucose (FPG) variability, glycated hemoglobin (HbA1c) variability, FPG variability independent of the mean (VIM), FPG coefficient of variation (CV), and FPG standard deviation (SD). The studies revealed a positive correlation between glycemic variability and the risk of AD over time, and the findings indicated that maintaining stable glycemic levels might reduce the risk of cognitive decline among individuals with or without T2DM. However, due to the limited number of studies available, despite a calculated relative risk of 2.65 indicating a higher risk of AD among



subjects with glycemic variability, the inclusion of the null value in the confidence interval (0.61 to 11.45) renders these findings statistically insignificant.

CONCLUSION

This systematic review revealed that glycemic variability plays a role in cognitive decline and the risk of AD among individuals with or without diabetes. The studies individually demonstrate a correlation between higher fluctuations in glucose levels and an increased risk of AD, highlighting the importance of managing blood sugar levels to mitigate dementia risks. Despite these strong associations, the actual incidence rates of AD in the studied populations remain relatively low. Overall, the results were not significant. Thus, further research is recommended to explore the risk of AD among individuals with fluctuations in blood glucose levels.

KEYWORDS

glycemic variability, cognitive decline, cognitive impairment, dementia, Alzheimer disease

MSSA BACTEREMIA ASSOCIATED ACUTE HEMORRHAGIC LEUKOENCEPHALOPATHY

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INTRODUCTION

Acute hemorrhagic leukoencephalitis (AHLE), also known as Hurst disease, is a severe variant of acute disseminated encephalomyelitis (ADEM) which is an uncommon inflammatory disease predominantly affecting the white matter of the CNS. AHLE is characterized by acute onset and rapid progression, having higher rate of morbidity and mortality.

REPORT

A 59-years-old woman with underlying hypertension and autosomal dominant polycystic kidney disease (ADPKD) on weekly dialysis presented with fever, headache, chills and rigors for five days. On examination, there was pus discharge seen from the right internal jugular vein catheter. Patient also had GCS drop and was subsequently treated as MSSA bacteraemia. Her total white count and CRP on admission was raised, $24.8 \times 10^3/\mu\text{L}$ and 307mg/L respectively. Her urea was also raised, 26.6 mmol/L. Initial CT Brain (Figure 1) showed symmetrical bilateral bifrontoparietal white matter hypodensities with no significant mass effect and sparing the basal ganglia. MRI Brain (Figure 2) showed extensive, fairly symmetrical T2 FLAIR white matter changes in bilateral corona radiata with extension into the centrum semiovale, sparing the subcortical U-fibres and cortices. These changes also show peripheral diffusion restriction, surrounding the necrotic-appearing white matter. There are foci of microhaemorrhages within these signal change. In view of symmetrical involvement of the supratentorial brain, this raises the suspicion of systemic pathology. Since the patient presented with symptoms and signs of infection, haemorrhagic leukoencephalitis is a more likely diagnosis. Other consideration would be toxic leukoencephalopathy secondary to uraemia or drugs.

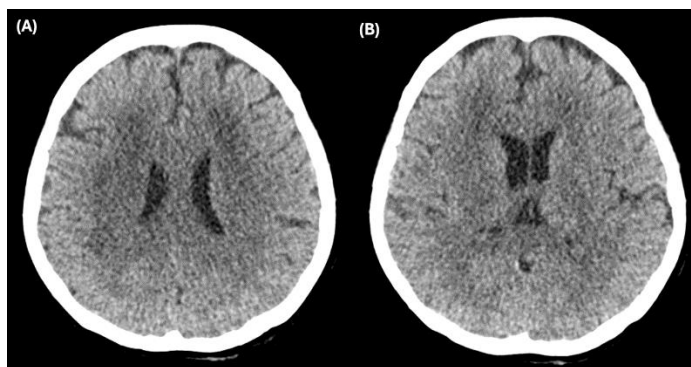


Figure 1: Axial non-contrasted CT brain shows relatively symmetrical white matter hypodensity at the level of (A) corona radiata and (B) third ventricle

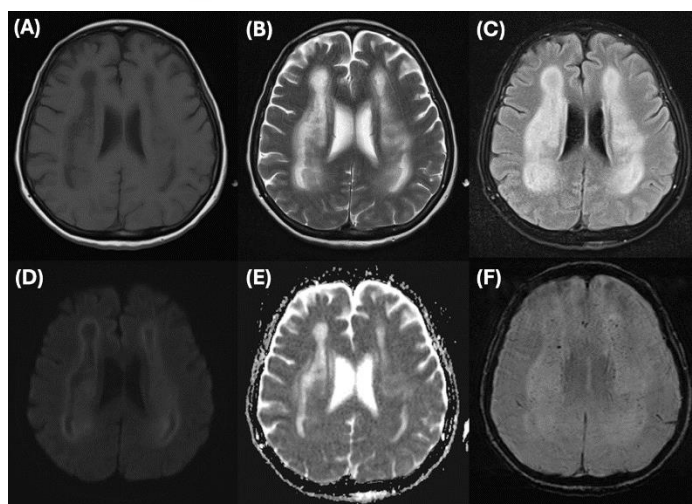


Figure 2. Axial MRI Brain in (A) T1-weighted, (B) T2-weighted, (C) FLAIR, (D) DWI, (E) ADC, and (F) SWI sequences showing extensive, fairly symmetrical T2 FLAIR white matter changes in bilateral corona radiata sparing the subcortical U-fibres and cortices. These changes also show peripheral diffusion restriction, surrounding the necrotic-appearing white matter with foci of microhaemorrhages within these signal change.

CONCLUSION

AHLE should be considered in cases of acute loss of consciousness or neurological deficits with MRI findings of white matter lesions with hemorrhagic foci and neutrophilic leukocytosis in CSF. Timely diagnosis and early aggressive treatment with high-dose corticosteroids, plasmapheresis, or intravenous immunoglobulins can be lifesaving.

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3D GENOMIC PROFILING OF ALZHEIMER'S DISEASE (AD) PATIENTS FOR THE DEVELOPMENT OF BLOOD-BASED EPISWITCH® BIOMARKERS

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BACKGROUND

Clinically, Alzheimer's Disease (AD) diagnosis is based on measurements of memory impairment, brain imaging as well as neurological and physical examination. Ultimately, AD diagnosis could be supported using biomarkers derived from biofluids and brain imaging. There is significant global variation in the use of auxiliary means of diagnosis, due to the invasiveness, such as cerebrospinal fluid, or availability of advanced imaging, from magnetic resonance imaging to positron emission tomography.

In Oxford Biodynamics (OBD)(1), we have successfully demonstrated the power of its EpiSwitch® biomarker platform to deliver clinical biomarker tests of high accuracy, with utility spanning everything from early detection (2), to treatment prediction (3), to prognosis (4, 5), in indications ranging from oncology and autoimmune to neurodegenerative. The EpiSwitch® Amyotrophic Lateral Sclerosis (ALS) prognostic test has been utilized in a Phase IV clinical trial with Mitsubishi Tanabe for Radicava (Edaravone, 5), a drug that slows progression of the disease in fast ALS patient sub-group.

METHODS

3D genomic chromosomal conformation libraries were prepared from frozen whole blood samples. Fifty microliter of whole blood sample was diluted and fixed with formaldehyde containing EpiSwitch® buffer. Density cushion centrifugation was used to purify intact nuclei. Following a short detergent-based step to permeabilise the nuclei, restriction enzyme digestion and proximity ligation were used to generate the 3D libraries of each blood sample. Quant-iT Picogreen dsDNA Assay kit (Invitrogen) was used to quantify the 3D libraries before interrogation using EpiSwitch® array platform.

RESULTS

In this study 16 patients (8 AD, clinically diagnosed with ^{18}F -PET versus 8 cognitively impaired (CI), where screened on EpiSwitch® array platform to isolate 199 statistically significant 3D genomic markers that differentiate between AD v CI. The biomarkers were then mapped to their 3 closest protein coding regions. For biological interpretation of the data we used EpiSwitch® knowledge environment tools. Further investigations and comparison of these results were performed with OBD knowledge graph base, comprised of more than 30M abstracts and prior knowledge (STRING, Pathways etc). This allows the user to mine and predict relationships from the known biology. We identified a network formed around APP (Amyloid Precursor Protein), BAN2401 (Lecanemab), as directly linked with a network generated from the EpiSwitch® discovery data. The processing of APP results into accumulation of Amyloid-b, which is implicated in pathogenesis of AD. It also showed that

how BAN2401 is unique in its selectivity related to inhibition of neurodegenerative process in AD by binding to protofibrils of soluble Amyloid- β over plaques.

CONCLUSION

This study has provided an improved insight and delivered better understanding of the disease, all through the EpiSwitch® 3D genomic biomarker modality. It offers the potential to more accurately predict the risk of an individual AD development, provides opportunities for earlier diagnoses, improves participant selection for clinical trials and appropriate use of emerging therapies.

KEYWORDS

3D genomic, Early Diagnoses, Blood test, EpiSwitch®

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EFFECT OF CHEWING GUM ON COGNITIVE FUNCTION

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BACKGROUND & OBJECTIVE

As the global population ages, the prevalence of dementia is increasing. The resulting increase in treatment costs is emerging as a serious social problem. Therefore, early intervention in preclinical stage is more critical to delay progression and reduce the prevalence and severity of dementia.

Chewing is an important function not only for eating food but also for maintaining general health conditions. In particular, chewing exercise using gum has been found to increase the secretion of saliva and increase brain blood flow through exercise of muscles around the mouth. It is also known that it can be expected to improve cognitive function including attention, reduce chronic stress and pain, and exercise effects in the brain by helping brain activity.

With the support of the Lotte Central Research Institute, we investigated the effect of chewing gum on cognitive function in normal and mild cognitive impairment. In addition, we analyzed the brain volume and cortical thickness changes shown in brain magnetic resonance imaging. Through these results, we suggest the necessity of chewing gum exercise to prevent dementia.

METHOD

Among patients who visited Inha University Hospital, Ewha University Hospital, Ajou University Hospital, Bobath Memorial Hospital, and Seongnam Senior Center for health, a total of 94 patients selected who classified as subjective cognitive impairment or mild cognitive impairment in clinical diagnosis. Each institution registers the subjects through competitive registration, and allocates 1:1 to the control group and the intervention group through random allocation by the SAS macro program using the Permitted Block Randomization technique. The gum intervention group is required to chew a non-flavored gum once daily. The gums for the elderly are provided for 12 weeks. The primary end point is evaluated as the change in the total scale index score of the Repetitive Battery for the Assessment of Neurological Status (RBANS). Secondary end point is assessed by changes in brain volume and cortical thickness using Neurophet shown in brain magnetic resonance imaging.

RESULT

In demographics, no significant differences were observed between age, education, gender, and clinical evaluation variables between the two randomized groups. The retention rate at the end

of the study was 91.5% (43/47) in the chewing group and 78.7% (37/47) in the control group. In ANCOVA analysis adjusting the baseline score of RBANS as a covariate, no significant difference was observed in the change in RBANS total scale index score between the chewing group and the control group. When comparing the index scores for each cognitive domain, the scores of language function in the chewing group significantly improved compared to the control group. In the results of changes in brain volume and cortical thickness analyzed using Neurophet, the volume of insula in control group generally decreases with age while volume differences in intervention group increases with time. Also, positive correlation of cortical thickness was observed in the bilateral caudal middle frontal, rostralmiddel frontal, superior frontal, left parstriangularis, and right parsorbitalis regions.

CONCLUSION

The group that chewed gum for 12 weeks showed improvement in language function of RBANS, an increase in the insular volume and cortical thickness of several areas mainly involved in the frontal lobe compared to the control group. This suggests that chewing gum may be an easily applicable dementia prevention method. The limitations of this study are the small number of participants and short intervention period. If this limitation is overcome, it is expected to reveal that chewing gum helps improve cognitive function and prevent dementia.

KEYWORD

chewing, gum, dementia, cognition

CHARLES BONNET SYNDROME (CBS) FOLLOWING TREATMENT OF NIVOLUMAB AND IPILIMUMAB, IN THE SETTING OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES): A FIRST CASE REPORT IN MALAYSIA

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Introduction

Charles Bonnet Syndrome is a neurological syndrome where the patients observe visual hallucinations following vision loss. It has been documented to occur after PRES. PRES is a well-known, but rare complication of immunotherapy.

A literature search found one documented case of CBS following immunotherapy in the U.S, but no documentation of such cases in Malaysia (1).

Report

A 59-year-old Malaysian-Chinese lady presented to a tertiary hospital in Kuala Lumpur, Malaysia following vision loss occurring 24 hours ago. On examination, she had zero visual acuity and relative afferent pupillary defect (RAPD) was present. No long tract signs nor cerebellar signs were present.

She was diagnosed with oesophageal carcinoma in 2022 and was treated in Thailand with nivolumab for 12 months. Following stomach metastasis, she was subsequently commenced on combination nivolumab and ipilimumab for 6 months.

An MRI brain showed diffuse bilateral symmetrical T2 white matter hyperintensities in the parieto-occipital lobes and inferior cerebellar hemispheres, which is consistent with PRES.

She was normotensive and was treated with intravenous methylprednisolone for 5 days. Her immunotherapy remained unchanged. She developed visual hallucinations on days 3 (green patchy images), 4 and 5 (red images and vivid numbers 2 and 3) of treatment. Hence, she has evidence of CBS.

She was reassured that CBS is self-limiting. Her visual acuity gradually improved over the next 2 weeks to 6/9, with persistence of her visual hallucinations. After 6 weeks, her symptoms have completely resolved.

Conclusion

This case report describes the first documented case of CBS following immunotherapy in the setting of PRES in Malaysia. Her symptoms resolved after treatment with intravenous methylprednisolone. Therefore, this highlights that visual hallucinations in the setting of PRES may not always stem from psychiatric causes, but rather, can arise from organic pathology. Hence, this raises awareness about CBS, an underreported condition.

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ELECTROCONVULSIVE THERAPY IN REFRACTORY AND SUPER-REFRACTORY STATUS EPILEPTICUS IN ADULTS: A SCOPING REVIEW

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INTRODUCTION

Electroconvulsive therapy (ECT) has been suggested as a treatment option for refractory status epilepticus (RSE) and super-refractory status epilepticus (SRSE). We aim to conduct a scoping review on the role of electroconvulsive therapy (ECT) as a treatment option for refractory status epilepticus (RSE) and super-refractory status epilepticus (SRSE).

METHODS

We searched Ovid MEDLINE and Scopus for journal articles from database inception until February 2024. Articles were then selected based on predetermined inclusion and exclusion criteria.

RESULTS

We identified 5 retrospective case series with a total of 28 adult patients receiving ECT for RSE or SRSE. ECT was administered within 3 to 70 days (mean, 20 days) after development of status; and the mean number of ECT courses ranged between 1 to 12 sessions for each patient. There was no difference in outcomes between fixed dose and titrated ECT regimes. A total of 20 out of 28 patients (71%) showed clinical improvement, with two (10%) having complete cessation of seizures. However, it is important to note that given lack of control, there could be over-reporting of clinical improvement in these studies. There were 11 (39%) patients who were deceased due to causes that were not directly related to ECT treatment. Four (14%) patients reported adverse effects of ECT included memory, concentration, and/or cognitive impairment.

CONCLUSION

There are OCEBM level 4 and low GRADE level of evidence to suggest ECT as a treatment option for RSE and SRSE. Routine use of ECT for RSE and SRSE is not recommended for all cases of RSE and SRSE. Across all studied regimes, stimulations were given until a seizure activity was observed. More prospective studies are required to determine the efficacy of ECT in aborting status, and its associated adverse effects.

INSIGHTS INTO ABNORMAL ELECTROENCEPHALOGRAPH PATTERNS IN ACUTE ISCHAEMIC STROKE: AN OBSERVATIONAL STUDY

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INTRODUCTION

Electroencephalogram (EEG) allows non-invasive, continuous assessment of brain activity, providing insights into cortical activity and connectivity following an acute episode of stroke. In the absence of clinical seizure, its utility is understudied. This observational study examines the prevalence and factors associated with EEG abnormalities in post-stroke patients.

METHODS

We conducted a single-centre, cross-sectional study recruiting patients aged 18 years and above admitted with acute ischaemic stroke. We excluded those presenting with stroke mimics, delirium, traumatic brain injury, seizures, known neurodegenerative or psychiatric disorders, history of neurosurgery, brain tumour, or diagnosed epilepsy. Each participant's clinico-demographic details were collected with a data collection sheet, where sociodemographic information, clinical history, type of stroke, risk factors, imaging studies and stroke severity based on the National Institute of Health Stroke Scale (NIHSS) were documented. An EEG was recorded inpatient within 48 hours of presentation for each participant via the Nicolet One Extension (V32 Amplifier) according to the international 10-20 system. Each recording is performed for a minimum of 30 minutes before it is interpreted by two neurologists blinded to the clinical details of the participant.

RESULTS

We recruited 97 post-stroke patients, with a mean age of 65.26 years (SD±12.10). The median NIHSS score of our study population was 6 (IQR 12). Over half of EEG recordings show abnormality (58.76%), with focal slowing as the predominant pattern observed. Mann-Whitney U test demonstrated a significant relationship between EEG abnormalities and comorbid history of atrial fibrillation ($p=0.011$) with weak correlation ($r=0.234$, $p<0.05$). An independent t-test was performed on NIHSS and EEG abnormalities show statistical significance ($p=0.013$).

CONCLUSION

EEG abnormalities are prevalent post-stroke despite the absence of seizure. Background history of atrial fibrillation and stroke severity are associated with abnormal EEG post-stroke.

RITUXIMAB DOSES AND HEALTH-RELATED OUTCOMES IN MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW

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INTRODUCTION

Rituximab, a commonly used off-label treatment for multiple sclerosis (MS), is administered in various doses, with the standard 1000 milligram dosing on Day 1 and Day 15 being the most prevalent. A comprehensive systematic review was undertaken to synthesise available evidence on variations in dosing and administration and impact on health-related outcomes in MS patients.

METHODS

The systematic review was registered with PROSPERO (CRD42024520844) and conducted as per PRISMA guidelines. The search strategy was : rituximab AND (multiple sclerosis OR relapsing remitting OR secondary progressive). Articles published in the English language were retrieved from electronic databases (PUBMED, Ovid MEDLINE and SCOPUS) along with grey literature up to March 2024. Critical appraisal of the included studies was conducted using the Newcastle-Ottawa quality assessment scale (NOS) for observational studies, Cochrane RoB-2 for Randomised Control Trials, and Risk of Bias in Non-randomised Studies of Interventions (ROBINS) for non-randomized intervention study.

RESULTS

Among 2940 articles, 84 were screened, with 34 studies recruiting a total of 4331 patients analysed. Rituximab induction varied: 2 doses of 1000mg (n=14), 1000mg then 500mg/1000mg (n=3), 375mg/m² weekly for 4 weeks (n=3), and intrathecal doses of 20mg or 25mg (n=2). Maintenance dosing (500mg-1000mg every 6 months) was common. Another 3 studies adjusted the maintenance dose based on the findings of CD19+ or CD27+, such as CD19+ exceeding 1% of peripheral mononuclear cells and the percentage of total CD19 + cells being 2% or more. Outcomes measured included EDSS, MRI, relapse rate, CWD, CD19, CD20, and B cell count.

CONCLUSION

Rituximab dosing for multiple sclerosis has evolved from the initial phase of using oncological dose for neurological indication till the development of dosing guided by CD 19 suppression along with observation of health-related outcomes.

TENECTEPLASE VERSUS ALTEPLASE FOR HYPERACUTE ISCHAEMIC STROKE: A RETROSPECTIVE ANALYSIS ON EFFICACY AND SAFETY OUTCOMES

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INTRODUCTION

Acute ischemic stroke is the third leading cause of mortality in Malaysia and often contributes to permanent disabilities. Reperfusion therapy is strongly associated with better outcomes. Currently, Alteplase is the only thrombolytic agent approved by the local drug agency. Tenecteplase emerged as a potential alternative, known to have longer free plasma half-life, allowing single IV bolus administration.

The primary objective of this study is to compare the efficacy of Alteplase with Tenecteplase in eligible hyperacute ischemic stroke patients by assessing functional outcome using Modified Rankin Score (mRS) score at 90 days. Secondary objectives include drug efficacy and safety outcomes in terms of symptomatic intracerebral hemorrhage and all-cause mortality rate.

METHODS

This is single-center retrospective analysis to assess non-inferiority of Tenecteplase as compared to alteplase among hyperacute ischemic stroke patients treated within 4.5 hours after stroke. Data were analyzed from Hospital Sultan Abdul Aziz Shah (HSAAS) stroke registry that include all thrombolysed stroke patients from the year of 2020 to 2023.

RESULTS

Sample size is calculated based on referred study and would require 122 subjects for Alteplase and 61 subjects for Tenecteplase (2:1 ratio) to achieve a power of 80% for detecting a difference in proportions of -0.20 between the two groups at a two-sided p-value of 0.05. Generalized Estimating Equations (GEE) was used to test if there is any difference of the mRS across the timepoint (pre, discharge and 90 days). The result shows that the mRS was nominally higher in the Tenecteplase group compared to the Alteplase group, however the GEE analysis indicates that the difference is not statistically significant.

CONCLUSION

In this retrospective 3-year analysis of ischemic stroke patients receiving thrombolytic agents at HSAAS, the efficacy and safety profile of Tenecteplase is non inferior to alteplase. Larger trials are needed to validate this single retrospective study.

EXPLORING THERAPEUTIC EFFECTS OF QUR'ANIC RECITATION AND CLASSICAL MUSIC THERAPY IN COGNITIVE IMPAIRMENT: A COMPARATIVE CASE SERIES

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INTRODUCTION

The escalating incidence of cognitive impairment globally caused high demand for innovative therapeutic strategies beyond conventional pharmacological approaches.¹ This retrospective case series aimed to assess the efficacy of classical music therapy,² Qur'anic recitation,³ and their combination on cognitive function and religious engagement in patients with cognitive impairment. Additionally, this case series highlighted the unique cases of vasculitis related to systemic lupus erythematosus and Balint syndrome within the series, underlining the prevalence of vascular cognitive impairment across all cases. This study provided valuable insights into diverse manifestations of neurological disorders causing cognitive impairment and potential of non- pharmacological interventions in managing these complex conditions.

REPORT

Seven patients diagnosed with cognitive impairment caused by various vascular disorders, including vasculitis related to systemic lupus erythematosus, cerebral small vessel disease, and Balint syndrome, were categorized into three treatment groups: classical music therapy, Qur'anic recitation, and combination of both. Each patient underwent MRI brain, cognitive assessment using Montreal Cognitive Assessment-Indonesian version (MOCA-INA), evaluation of religious engagement using the Dementia Solat Score (DSS), also lipid profile and C-reactive protein (CRP) examination. Statistical analysis using the Friedman test was conducted to compare outcomes across the treatment groups.

CONCLUSION

Notably, patients treated exclusively with Qur'anic recitation showed the most significant improvement in cognitive function and religious engagement compared to the other groups ($p < 0.05$). Despite potential conflicting effects of sound waves from Qur'anic recitation and classical music, Qur'anic recitation therapy had superior results. Future studies with bigger sample sizes are warranted to validate these findings and explore additional avenues for non-pharmacological interventions in vascular cognitive impairment.

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SAFETY AND EFFICACY OF FREXALIMAB IN RELAPSING MULTIPLE SCLEROSIS: 48-WEEK RESULTS FROM THE PHASE 2 OPEN-LABEL EXTENSION

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INTRODUCTION

Frexalimab is a second-generation anti-CD40L monoclonal antibody that blocks the costimulatory CD40/CD40L pathway, which is important for activation and function of adaptive and innate immunity. In the 12-week double-blind period (DBP), frexalimab demonstrated safety and efficacy with the high-dose treatment showing an 89% reduction (vs placebo) in new gadolinium-enhancing (Gd+) T1-lesions. Over 24 weeks in the open-label extension (OLE), frexalimab was well-tolerated, and the number of lesions further decreased.

METHODS

In the DBP, participants were randomized to frexalimab (N=52), frexalimab (N=51), or matching placebo arms (placebo, N=12; placebo, N=14). At W12, participants receiving placebos switched to respective frexalimab arms and entered the OLE. Key assessments during the OLE included safety and efficacy (number of Gd+ T1-lesions and new/enlarging T2-lesions).

RESULTS

125/129 (97%) participants completed the DBP and entered the OLE; 112 (87%) remained in the study at W48 cut-off. At W48, the number of Gd+ T1-lesions (mean [SD]) remained low in participants who continued receiving frexalimab and in those who switched from placebo to frexalimab at W12 (frexalimab: 0.0 [0.2]; frexalimab: 0.2 [0.5]; placebo/frexalimab: 0.2 [0.6]; placebo/frexalimab: 0.1 [0.3]). Furthermore, 96% participants in frexalimab, 87% in frexalimab, 90% in placebo/frexalimab, and 92% in placebo/frexalimab arms were free of Gd+ T1-lesions at W48. New/enlarging T2-lesion counts and T2-lesion volume change remained low with frexalimab through W48, and lymphocyte counts were stable over 48 weeks. Overall, frexalimab treatment was well-tolerated through W48; the most common adverse events included nasopharyngitis, headache, and COVID-19.

CONCLUSION

Frexalimab continued to show favorable safety and efficacy in RMS participants through W48. These data support its further development as a potential high-efficacy, non-lymphocyte-depleting treatment option in MS.

FREXALIMAB IN RELAPSING MULTIPLE SCLEROSIS AND NON-RELAPSING SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS: DESIGN OF PHASE 3 FREXALT AND FREVIVA TRIALS

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INTRODUCTION

Frexalimab is a second-generation anti-CD40L monoclonal antibody that blocks the costimulatory CD40/CD40L pathway, which is important for activation and function of adaptive and innate immunity. In the phase 2 trial (NCT04879628) in participants with relapsing MS (RMS), frexalimab was well-tolerated and showed an 89% reduction in new gadolinium-enhancing (Gd+) T1 lesions in the high-dose arm vs placebo at week 12. In the ongoing open-label extension, 96% of participants in the high-dose arm were free of Gd+ T1 lesions at week 48.

METHODS

FREXALT (comprising two trials, FREXALT-1 and FREXALT-2) is a double-dummy, active-controlled, event-driven (6-month composite confirmed disability worsening [cCDW] pooled across studies) trial with variable treatment duration of approximately 20–40 months in RMS participants. Planned enrollment is 1400 participants randomly assigned 1:1 to frexalimab or teriflunomide. Key eligibility criteria include RMS diagnosis, Expanded Disability Status Scale (EDSS) ≤ 5.5 , and ≥ 1 relapse within 1 year or ≥ 2 relapses within 2 years or ≥ 1 Gd+ lesion within 1 year. Primary endpoint is adjudicated annualized relapse rate, and key secondary endpoint is time to onset of 6-month cCDW (as assessed by the composite of EDSS, timed 25-foot walk and 9-hole peg tests). FREVIVA is a placebo-controlled, event-driven (6-month composite confirmed disability progression [cCDP]) trial with variable treatment duration of



approximately 27–51 months in nrSPMS participants. Planned enrollment is 858 participants randomly assigned 2:1 to frexalimab or placebo. Key eligibility criteria include previous diagnosis of relapsing-remitting MS, current SPMS diagnosis, CDP within 1 year, EDSS 3–6.5, and no relapse within 2 years. Primary endpoint is time to onset of 6-month cCDP, and secondary endpoints include time to onset of 3-month cCDP and time to onset of 3-month/6-month CDP. Other secondary endpoints in both trials include clinical/MRI assessments, patient-reported outcomes, and safety evaluation.

RESULTS

Enrollment has started in December 2023.

CONCLUSION

These phase 3 trials will assess the efficacy and safety of frexalimab in RMS and nrSPMS, which is a population with no approved therapeutic options.

CEREBRAL SINUS VENOUS THROMBOSIS IN MIDDLE-AGED MALES: A SERIAL CASE REPORT

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INTRODUCTION

The cases of cerebral sinus venous thrombosis (CSVT) are getting more frequently reported. They were reported not only in young females, but also frequently in males with various risk factors. This serial case report describes two cases of CSVT in middle-aged males with different risk factors and clinical manifestations.

REPORT

Case 1, a 48-year-old male came with headache, vomiting, hypertension, right facial nerve palsy, and papilledema. The venography showed partial thrombosis in the left transverse sinus. Case 2, a 55-year-old male presented with sudden weakness of four limbs, slurred speech, and a history of nasopharyngeal carcinoma. The venography showed thrombosis in the left transverse and sigmoid sinus. Both of them received low molecular weight heparin (LMWH) continued by oral anticoagulant and gained clinical improvement.

CONCLUSION

The incident of CSVT on male may be higher than has been reported. Risk factors for CSVT are inflammatory disease (e.g., Behcet's disease) in younger male and carcinoma in older male. The clinical manifestations of CSVT differ according to the place of the obstructed vein(s). A diagnosis can be made by starting with the suspicion toward CSVT based on the clinical pictures and risk factors; it is then confirmed by imaging study of venography. Administering anticoagulant of heparin or LMWH in the acute phase continued by oral anticoagulant is the cornerstone of CSVT management. There has been evidence that showed non vitamin K antagonist oral anticoagulants are as equally effective as warfarin. Prevention is done by modifying identified risk factors.

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FOCAL SEIZURE? INTRACEREBRAL HEMORRHAGE? A CASE OF SUDDEN ONSET MOVEMENT DISORDER

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INTRODUCTION

Diabetic striatopathy is an extremely rare hyperglycemic complication of diabetes with a prevalence reported as 1 in 100,000 which could be underestimated as most physicians are not aware of this condition¹.

OBJECTIVE

To report a rare case of diabetic striatopathy to raise awareness.

METHODS: Case Report

REPORT

A 56-year-old Iban man presented with sudden onset violent involuntary movements over right upper limb and lower limb. He was known to have hypertension and poorly controlled type 2 diabetes mellitus, his HbA1c ranged from 8-15.2 in the past 5 years and had 5 admissions for uncontrolled diabetes mellitus.

On examination, he was alert and oriented. His blood pressure was 176/84, heart rate 107, capillary blood sugar 13.3mmol/L(239.4mg/dL). Neurological examination revealed hemiballismus of right upper limb and lower limb, otherwise his power was 5/5, sensation intact, cranial nerves intact.

A CT Scan was performed which revealed a hyperdense lesion over left basal ganglia, concordant to his right sided hemiballismus.

The diagnosis of diabetic striatopathy was made, he was admitted to ward for insulin adjustment. The next day, his involuntary movements became less violent, he was started on haloperidol.

After 3 weeks, his symptoms did not fully resolved, hence we switched to tetrabenazine, eventually he achieved near complete recovery with tetrabenazine and strict sugar control.

A repeated CT scan 23 days after his admission was performed, the hyperdense lesion had shrunken more than half in size.

CONCLUSION

Diabetic striatopathy is a known complication of poorly controlled diabetes mellitus, unfortunately it is less well recognised and may easily be misdiagnosed as acute stroke with luxury reperfusion or basal ganglia hemorrhage. Clinicians must be aware of this entity and initiate intensive sugar control. The prognosis is good, the clinical and radiology findings are reversible if the condition is diagnosed early and treated promptly.

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PARADOXICAL TREATMENT IN SUBARACHNOID HEMORRHAGE WITH ANTICOAGULANT

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INTRODUCTION

This was a 51-year-old lady, presented with first onset of seizure (generalized tonic clonic) early October 2023. She had no known epilepsy history and denied fever, altered mental status prior to presentation.

She was a known case of T2DM, hypertension, Left breast cancer stage 2, done left mastectomy in 2014 and completed chemotherapy, radiotherapy, and hormonal therapy, currently in complete remission. This admission, she suffered recurrent seizures and required intubation for impending status epilepticus. Initially non contrasted computed tomography (CT) of brain showed subarachnoid hemorrhage; thus, another CT angiography of brain was performed to rule out any aneurysm bleed or arteriovenous malformation.

REPORT

Despite loaded with intravenous phenytoin and on standard sedation regime, failed to control the seizures. CTA was then reported as dural sinus thrombosis. Taking the moderate SAH into consideration and weighing the risk of further bleeding, anticoagulant was started at a reduced dose (s/c Enoxaparin 80mg daily), without delay.

Fortunately, she responded well to anticoagulant and remained fit free. CT brain was repeated in 1 week to reassess the SAH before increment to full dose of enoxaparin. Patient was extubated with no obvious neurological deficit.

Malignancy work up done to look for recurrence or metastasis. Her corrected calcium was on high at 2.6-2.8mmol/L and was given IV pamidronate in ward.

She was otherwise denied constitutional symptoms. CECT thorax, abdomen and pelvis was unremarkable with no evidence of local or distance metastasis.

Available tumor markers and multiple myeloma were negative.

CONCLUSION

This is a challenging case because of the presence subarachnoid hemorrhage. Initiation of anticoagulant despite at a lower dose, showed marked improvement. She responded well to this regime, remained seizure free and SAH not worsening in size. Etiology of SAH is salient to the treatment of this patient.

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INTUBATION PRIOR TO THROMBOLYSIS: A CASE SERIES

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INTRODUCTION

Since the introduction of thrombolysis service in Sarawak General Hospital, cases where patients were intubated prior to thrombolysis are few. Intubation prior to thrombolysis makes it challenging

for the thrombolysis team to assess the NIHSS score and improvement post thrombolysis. This poster aims to highlight these cases and the challenges associated with it as well as their outcomes.

METHODS

We analyse data from our thrombolysis registry from January 2021 up until January 2024. From the data, patients who are intubated on arrival or shortly prior to onset of thrombolysis were shortlisted. Patients that underwent thrombectomy after thrombolysis were excluded.

RESULT

A total of 6 patients were shortlisted. These patients were intubated <1H after presentation prior to onset of thrombolysis. All of them had GCS of <8 during presentation, with the highest GCS of 7 documented. In all cases except 2, thrombolysis was initiated after 4 hours with many factors contributing to the delay. Interestingly, all patients were later diagnosed to have posterior circulation infarct with repeated CT scans. There were more males than females affected. All had comorbid of hypertension, with 2 of them eventually were diagnosed with AF. Half of the cases were complicated with obstructive hydrocephalus. Only 2 out of 6 patients were able to regain consciousness and return home well. These 2 were also the ones with the shortest onset-to-needle time. There were no scoring used to assess improvement, with GCS recovery being the surrogate to determine thrombolysis success.

CONCLUSION

Intubation prior thrombolysis poses special challenges to the thrombolysis team as there are no established measures to assess improvement. The clinical outcome is affected by the onset-to-needle time, with the 2 patients with shortest onset-to-needle time fared the best. More studies should be done to come up with scoring systems for thrombolysis in intubated patients.

ANGIOGRAPHICALLY NEGATIVE SUBARACHNOID HEMORRHAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by involvement of multiple organs. Subarachnoid hemorrhage (SAH) is rare in SLE patients. The typical causes of SAH in this population include distal fusiform aneurysms, multiple saccular aneurysms, and angiographically negative SAH.¹ The underlying mechanisms may involve atherosclerosis, hypertension, coagulopathy, and vasculitis disorders.^{2,3} However, the cause of angiographically negative SAH remains elusive. Here, we present a case of a newly diagnosed SLE patient with angiographically negative SAH.

REPORT

A 55-year-old woman with a history of medullary thyroid cancer was admitted to our hospital due to acute psychosis. She exhibited symptoms of talking to herself, shouting, and speaking incoherently. Upon physical examination, she appeared confused and displayed orolingual dyskinesia. Full blood count revealed mild thrombocytopenia with normal results for renal, liver, and coagulation profiles. Viral screening tests were negative, and CSF analysis showed normal findings. Imaging studies initially appeared normal, but an MRI later revealed SAH involving specific brain regions. Despite being normotensive and negative antineutrophil cytoplasmic antibodies (ANCA), further investigation revealed significantly positive antinuclear antibody results and a diagnosis of SLE with neuropsychiatric involvement. Treatment resulted in improvement, but she was readmitted later due to altered behavior and seizure. Non-contrast head computed tomography showed SAH. Digital subtraction angiography revealed no intracranial vascular abnormalities but stenosis involving bilateral superficial temporal arteries were observed. Treatment comprised intravenous methylprednisolone, followed by prednisolone, intravenous immunoglobulin, and anti-seizure medications, leading to gradual recovery.

CONCLUSION

SAH is uncommon in SLE patients but warrants extensive investigation for potential causes, including vasculitis, coagulopathy, and structural abnormalities. Negative angiography and ANCA tests may complicate diagnosis, emphasizing the need for prompt treatment to prevent severe outcomes. Management of cerebral arteritis associated with SLE may require proactive immunomodulatory therapy.

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CEREBRAL VENOUS SINUS THROMBOSIS: UNUSUAL CLOT-FORMING PHENOMENON POST HEAD TRAUMA

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is commonly seen in daily practice, especially in those with predisposing factors. Clinicians might miss the diagnosis if there is a low index of suspicion during clinical assessment of head injury cases, particularly in those without the risk factor.

REPORT

We report a case of a post-traumatic head injury with skull fracture and subarachnoid haemorrhage complicated with delayed, countercoup cerebral venous sinus thrombosis in the context of no predisposing factor for thrombosis. He was started on anticoagulant and achieved clinical improvement within a week. CVST is seen in post head trauma patients regardless of severity of the injury. Presence of neurological deficit post head injury like altered mental status, headache, vomiting or focal neurological signs like hemiparesis raised the suspicion of CVST. Occurrence of CVST can be delayed up to more than 10 days post trauma and it can happen at the opposite site of the trauma.

CONCLUSION

High suspicion index is needed to diagnose CVST early and subsequently early intervention or treatment could improve clinical outcome and prognosis of the patients.

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PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN AIDS PATIENT; A NEUROIMAGING DIAGNOSTIC CHALLENGE

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INTRODUCTION

Human Immunodeficiency Virus (HIV)- associated primary central nervous system (CNS) lymphomas (PCNSL) are well recognized with poor clinical prognosis.

REPORT

We report a case of PCNSL in a newly diagnosed Acquired Immunodeficiency Syndrome (AIDS) gentleman who presented to us with non-specific throbbing headache for 3 weeks which later he developed altered sensorium and had status epilepticus. His HIV viral load was 247000 copies/ml. CD4 count was 16. Serial CT Brain with contrast showed solitary rim enhancing lesion at left frontal periventricular region with associated hypothalamic lesion, new intralesional haemorrhage and surrounding white matter edema. MRI brain constellated findings in keeping with CNS infection with formation of left frontal periventricular abscess (3.1 x 1.7 x 1.9cm) which demonstrated hypointense on T1WI/ T2WI, heterogenous hyperintense on FLAIR and peripheral thick nodular rim enhancement on post contrast sequence). There was also diffuse nodular leptomeningeal enhancement involving basal cistern, cranial nerves, hypothalamus, and hippocampi. The cerebrospinal fluid (CSF) analysis showed high protein with normal glucose value. It was negative for opportunistic bacterial infection; Tuberculosis, *Hemophilus Influenza B*, Group B Streptococcus, *Streptococcus pneumoniae*, *Escherichia coli*, *Neisseria meningitidis* and cryptococcus. Toxoplasma serology was negative. He was started empirically on Anti-Tuberculosis and broad spectrum antibiotic. However, his condition showed no improvement with evidence of worsening brain oedema. Therefore, craniectomy, evacuation of clots & lobectomy was done. Unfortunately, he succumbed to death 3 days post-surgery and biopsy of brain result came back retrospectively as diffuse large B-cell lymphoma.

CONCLUSION

The clinical presentation and neuroimaging features of PCNSL in AIDS patients may mimic those of other progressive neurologic disorders, including primary brain tumour, demyelinating disease, autoimmune or paraneoplastic syndromes, or other opportunistic CNS infection. In instances of brain lesions that are not amenable to biopsy or whilst alternative diagnoses are being considered, a comprehensive diagnostic evaluation before biopsy is important.

THE EARLY UTILIZATION OF ELECTROENCEPHALOGRAM IN FIRST ONSET SEIZURES

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INTRODUCTION

A first onset seizure can occur because of a disturbance in the brain activity which can be due to a wide range of etiology. However, it is important to differentiate epileptic seizure from other seizure mimics. The use of EEG in patients with first onset seizure is not widely applied. The majority of first onset seizures were managed by expectant management. The objective of this study is to evaluate the value of early EEG utilization in patients presented with first onset seizures.

METHODS

A retrospective study of patients presenting with first onset of seizure was performed to determine the EEG characteristics. The EEG was done within 72 hours from the onset of seizures. The basic demographic data, EEG findings which classified as normal, focal (includes focal slowing and/or epileptiform discharges) or generalized slowing, and the diagnosis were analyzed.

RESULTS

There were 37 patients recruited in this study. 19 (51.4%) were male and 18 (48.6%) were female. Majority of the patients comprise of Malay (25, 67.6%), followed by Chinese (9, 24.3%), Indian (1, 2.7%) and others (2, 5.4%). 24 (64.9%) had normal EEG, while 13 (35.1%) had abnormal EEG. Out of the abnormal EEG, 7 (18.9%) have focal abnormality, and 6 (16.2%) have generalized abnormality. 22 (59.5%) of the patients were diagnosed with neurological conditions, which include epilepsy (6, 16.2%), meningitis (7, 18.9%), stroke (4, 10.8%), and structural brain lesions (5, 13.5%). There was no significant difference between the patient's age and gender with the EEG findings and the diagnosis of neurological diseases.

CONCLUSION

It is imperative to perform EEG after the first onset of seizure as it can help with the diagnosis and further management of the condition. Therefore, clinicians should be aware of the importance of EEG as part of the initial investigation of first onset of seizures.

AN EPIDEMIOLOGY STUDY ON SEIZURE DISORDER IN NEUROLOGY CLINIC, HOSPITAL SULTANAH BAHYIAH (HSB): LOCAL DATA

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INTRODUCTION

Epilepsy is ranked as the second most burdensome neurological disorder by WHO 2010. However, there is limited data about distribution of epilepsy by seizure types as defined by the new 2017 ILAE Seizure Classification. Epidemiologic studies and surveillance of epilepsy is useful in assessing the burden of epilepsy in a population and the need for healthcare services. This study aimed to determine the distribution of epilepsy and other seizure disorder among adult population in HSB.

METHODS

A retrospective cohort study involving all adult patients with epilepsy and other seizure types in Neurology Clinic HSB was conducted between April 2019 to June 2019 using convenience sampling. Statistical analysis of One-way ANOVA, Kruskal-Wallis ANOVA, and Chi-square or Fisher's exact test were used depending on the data distribution.

RESULTS

Retrieving data from local database in Neurology Medication Therapy Adherence Clinic, there were 163 patients (4.4%) with seizure disorder visiting Neurology Clinic in 2019. 8 subjects were excluded in analysis due to insufficient data from the electronic hospital information system (E-HIS). Out of 155 subjects analysed, 62.6% were male. It was found that age of onset was 16-year-old (IQR= 15) in our study population. Majority of our subjects having seizure disorder for a duration of up to 20 years at the time of observation (74.2%). For type of seizure, 81.9% were diagnosed with generalized seizure while focal seizure contribute 14.2%. We have 6 (3.9%) subjects suffered from seizure disorder with normal EEG results were categorised as unknown onset.

CONCLUSION

Percentage of patient with seizure disorder visiting Neurology Clinic on 2019 was 4.4%. The distribution of patient with seizure disorder should be reviewed every 5 years in order to provide data used in budget allocation.

LONGITUDINAL EXTENSIVE TRANSVERSE MYELITIS WITH MENINGITIS SECONDARY TO MYCOBACTERIUM TUBERCULOSIS

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INTRODUCTION

Longitudinally extensive transverse myelitis (LETM) secondary to tuberculosis has very rare incidence ^[1].

REPORT

A 34-year-old gentleman with newly diagnosed HIV presented with fever and altered conscious level for 2 days and was diagnosed with tuberculous (TB) meningitis, based on CSF results and CNS imaging. Opening pressure of lumbar puncture was more than 50mmH²O. CSF cell count was 951cells/uL, predominantly lymphocyte. CSF protein was raised, 680mg/L and the CSF sugar was 3.9mmol/L (serum sugar was 6.1mmol/L). The CSF Indian ink, cryptococcal and gram stain were negative. He had bilateral lower limb flaccid paralysis with areflexia during his long stay in ICU. Sensation to pain was impaired from T4 level down to lower limbs. He received IV immunoglobulin for 5 days as treatment for Guillain Barre Syndrome. The nerve conduction study showed evidence of motor axonal neuropathy of bilateral lower limbs with preserved sensory responses of upper and lower limbs. MRI spine showed long segment transverse myelitis from T2 until L1 level, complicated with intradural extramedullary abscess from T1 until T6 level, and arachnoiditis. His condition deteriorated, and he succumbed due to severe pneumonia before drainage can be made.

The detection of mycobacterium by usual standard such as acid-fast smear and mycobacterium culture have poor sensitivity^[2]. The CSF PCR in detecting mycobacterium tuberculosis is widely used and the sensitivity is only 50%, but the specificity is 98%^[3]. CSF adenosine deaminase reported to have poor specificity in HIV patients with concurrent infections or lymphoma^[4].

MRI is most sensitive in evaluating spinal cord^[5]. Cervical and thoracic level become the most common level involved with hyperintensity of T2 weight images in transverse myelitis^[6]. Cord edema may present with nodular enhancements along the surface of cord^[5].

CONCLUSION

It is necessary to perform MRI spine in patient with active tuberculosis with paraplegia to determine co-existing TB myelitis.

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HEADACHE THAT SHOULD NOT BE MISSED IN PREGNANCY

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INTRODUCTION

Tuberculosis (TB) in women is associated with six-fold increase in perinatal death and half a million women died from TB in 2018^[1]. The true incidence of TB meningitis in pregnant women is unclear but reproductive age women account for 10-50% of participant in published TB meningitis cohorts^[2].

REPORT

25 years old lady at 25 weeks of pregnancy presented with sudden onset of frontal head for 1 week. She had epigastric pain, vomiting and fever for 3 days. Previously, she had intermittent mild headache. Her clinical examination and MRI brain were normal. Migraine was the initial diagnosis. Regular oral sumatriptan and propranolol were given. Left sphenopalatine ganglion block via left nasal approach was done. IV dexamethasone 8mg was given for status migrainous but the headache remained the same.

After 3 days, she developed fever and was intubated as CGS dropped to 7/15. CT brain showed acute hydrocephalus with generalized cerebral edema. Lumbar puncture showed raised CSF protein, 1616mg/dL with ratio CSF serum glucose ratio 0.48. The CSF cell count showed white blood cell 103.3 with lymphocyte predominant. Repeated MRI brain shows multiple abnormal signal intensities at bilateral cerebral hemisphere involving white matter region and basal ganglia which represent tuberculous meningoencephalitis with tuberculoma and cerebral infarctions.

The CSF gene expert result was positive. Tuberculous therapy commenced. She subsequently underwent tracheostomy for poor GCS recovery. Her neurological recovery has been positive despite slow.

Diagnosing TB in pregnancy is difficult as the symptoms are nonspecific^[3]. Headache, dizziness, and vomiting can occur in normal pregnancy^[4]

The non contrast MRI can show normal findings or subtle changes seen in meningitis^[5]. MRI brain with contrast is more helpful as it may show abnormal meningeal enhancement in basal cisterns and sylvian fissures^[5].

CONCLUSION

High suspicion of TBM is very important in pregnant women that come with intractable headache even when the initial imaging was normal.

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MOTOR NEURON DISEASE COEXISTENCE WITH SJOGREN'S SYNDROME: AN UNDERREPORTED ENTITY

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INTRODUCTION

Nervous system involvement is described in up to 20% of Sjogren's syndrome patients. However, the association between motor neuron disease and Sjogren's syndrome remains rare.

REPORT

A 61-year-old woman with underlying alopecia areata, presented with progressive left lower limb weakness for a month, followed by right lower limb weakness for eight months. A neurological exam revealed bilateral thenar and hypothenar muscle wasting, with tongue fasciculation. Both upper and lower extremities were hypertonia. Diffuse hyperreflexia with a positive Hoffman sign was noted. The muscle power was MRC grade 2/5 in the distal hand muscles and grade 4/5 in the lower limbs. Sensory examination was normal. Electromyography (EMG) demonstrated acute denervation and chronic neurogenic changes in the cervical, thoracic, and lumbar regions. Given the rapid clinical progression, further workup was carried out to exclude autoimmune and paraneoplastic causes. Immunological testing showed antinuclear antibodies positive at the titer of 1:640 (speckled), with extractable nuclear antigen panel showing anti-Ro/SSA positive. The Schirmer test indicated right severe dry eye. MRI of the whole spine was normal. Otherwise, cerebrospinal fluid testing, creatinine kinase, complement levels, tumor markers, and anti-neuronal antibodies were normal. Computed tomography of the thorax, abdomen, and pelvis did not reveal occult malignancy.

Considering the possible Sjogren's syndrome-related neurological involvement, she received intravenous methylprednisolone 500mg daily for five days followed by oral prednisolone tapering over six weeks. However, her limb weakness was not improved. Repeated EMG showed persistent neurogenic changes. Based on the clinical and electrodiagnostic findings, she was diagnosed with motor neuron disease. She was started on Oral Riluzole 50 mg twice daily and co-managed with the respiratory team and rehabilitation unit.

CONCLUSION

Autoimmunity may play a role in the coexistence of MND and Sjogren's syndrome in this patient. Further studies are required to understand the pathogenesis and correlation.

THE RARE MIMICKER: MILIARY TUBERCULOSIS OF THE BRAIN

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INTRODUCTION

The number of tuberculosis is on a rising trend in every part of the world.¹ Miliary TB of brain is a rare yet benign form of CNS TB. There is limited literature regarding this. They often present as multiple, small, round lesions distributed widely at the supra- and infra-tentorial region. It is almost always diagnosed as neurocysticercosis, metastasis and vasculitis.²

REPORT

A 41-year-old, Malay woman presented with progressively worsening dizziness and headache for 2 months, associated with episodes of vomiting. She had a background of SLE in remission and previous history of pulmonary TB. Upon examination, she was hemodynamically stable. The chest and neurological examination were unremarkable. Fundoscopy was normal and there was no other evidence of peripheral causes of dizziness. Routine blood tests including infective markers were normal. CECT Thorax showed collapsed right middle lobe consistent with previous TB changes. Bronchoalveolar lavage analysis was negative for TB. MRI Brain showed multiple, widespread, well defined, solid, and round enhancing lesions seen over the bilateral cerebral cortex, cerebellar hemispheres, and brainstem. Cerebrospinal fluid analysis was normal except for the slightly elevated protein level. She was initially managed as a case of cerebral vasculitis with concomitant meningoencephalitis. Despite one week treatment of intravenous methylprednisolone, Ceftriaxone, and Acyclovir, her symptoms persisted. Hence, we decided to treat her with anti-TB and Dexamethasone as per regime, for disseminated miliary TB of the brain. Post intensive phase of treatment, her symptoms improved. A repeated MRI Brain revealed significant reduction in the numbers and sizes of the miliary nodules.

CONCLUSION

Miliary TB of brain is a rare manifestation of CNS TB that responds well to the standard anti-TB medications with good neurological recovery. A high index of suspicion is needed especially in cases with classical MRI features.

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EXTRAPONTINE MYELINOLYSIS DUE TO ALCOHOL WITHDRAWAL WITH MEASLES CO-INFECTION: A CASE REPORT AND REVIEW ON ALCOHOLISM RELATED NEUROLOGICAL COMPLICATIONS

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INTRODUCTION

Osmotic demyelination syndrome (ODS) constitutes both central pontine myelinolysis (CPM) and extra-pontine myelinolysis (EPM). Isolated EPM is generally rare.

CASE PRESENTATION

A 20-year-old gentleman chronic alcoholic presented seizure and one week of slowing of movement, withdrawn affect, confusion, and reduced oral intake. Prior to onset of symptoms, he developed rash and fever and had contact with his roommate who contracted measles. His last alcohol intake was four days before his first symptoms appeared. Examination revealed Glasgow Coma Scale of E4V4M6 with stable vital signs. He had diaphoresis and orofacial dyskinesia with extrapyramidal signs (bilateral hand tremor - right > left, bradykinesia, right upper limb rigidity). Lumbar puncture showed normal opening pressure and biochemistry and was negative for tuberculosis, viral panel, Japanese encephalitis and bacterial culture. Serum measles IgM was detected, however, electroencephalogram did not show classical findings of Subacute Sclerosing Panencephalitis. His first MRI done one week after admission was unremarkable. His conscious level deteriorated and was treated with intravenous acyclovir, methylprednisolone, and vitamin A with little improvement. A repeated MRI brain one month later revealed bilateral putamen and basal ganglia T2 hyperintensities with restricted diffusion without contrast enhancement.

DISCUSSION

In this patient, the delayed changes in MRI were more in keeping with EPM. Vasogenic oedema is believed to be a significant contributor to EPM; alcohol withdrawal is thought to involve changes in the permeability of the blood-brain-barrier and accumulation of toxic substances in the brain. Alcohol withdrawal can last for up to one week after alcohol cessation. In addition to autoimmune and infective causes, differential diagnosis for encephalopathy in alcoholics include: Wernicke's encephalopathy, Marchiafava Bignami disease, Delirium tremens, ODS (in the context of refeeding syndrome, alcohol withdrawal, over-correction of hyponatremia).

CONCLUSION

Prompt recognition of EPM as a complication of alcohol withdrawal is paramount in guiding subsequent imaging and management decisions.

AN UNUSUAL CASE OF ACUTE TETRAPARESIS IN SPINAL CORD INJURY: A CASE REPORT

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INTRODUCTION

Spinal cord injury (SCI) is a condition resulted from various forms of insult to the spinal cord, including trauma, vascular disorders, and infections. Among the aforementioned, trauma is the most common cause of SCI [1,3]. There are many different mechanisms underlying SCI due to trauma. The most common mechanism is spinal cord compression resulted from damage to the surrounding structures in the form of fractures, dislocations, or disc protrusion [1].

Spinal cord injury is considered to be a serious condition as it can cause severe morbidity and permanent disability [3]. Patients with SCI usually present with neurologic deficits, such as complete or partial loss of motor and/or sensory functions. Furthermore, patients may present with impaired control of autonomic function which can lead to hypotension and bradycardia [1,3].

REPORT

A 29-year-old female presented with chief complaints of weakness in all four limbs, numbness from neck to toes, and difficulty in urination and defecation. She had a history of decreased consciousness for <5 minutes on acute onset after being crushed by a falling coconut tree with her neck bent and head bumped. She also had an open fracture on her left ankle.

The Glasgow coma scale findings were normal at 15/15, but the patient manifested unusual anxiety and agitation. Her neurological examination showed remarkable muscle weakness of all four limbs in which the upper limbs were able to move against gravity while the lower limbs had no muscle contractions. She also showed sensory deficits such as segmental hypoesthesia at cervical level 2 and below and segmental anesthesia at thoracic level 6 and below. However, Hoffman and Tromner's reflexes were positive, and physiological reflexes increased in all four limbs.

A CT scan showed diffuse cerebral edema which narrowed lateral ventricles bilaterally, complete oblique fracture on the anteroinferior aspect of the corpus of the 2nd cervical vertebra (teardrop fracture), burst fractures of the 6th, 7th, and 8th thoracic vertebrae and 4th lumbar vertebra accompanied by retropulsion which compressed the spinal cord at the level of the 7th-8th thoracic vertebrae.

After a week of external immobilization of the cervical spine area with a neck collar along with laminectomy, decompression and stabilization in the thoracal spine, her motor and sensory deficits from neck to chest and upper extremities gradually improved. Tingling and numb sensation also recovered sufficiently although the feeling of numbness from the chest and below was still felt.

CONCLUSION

As yet, patients with spinal cord injury generally have very poor prognoses. Unfortunately, there is no definite treatment leading to recovery for spinal cord injury.

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A GREAT MASQUERADER NOT TO BE MISSED: A SINGLE CENTRE TREATMENT EXPERIENCE FROM THE NORTHERN SARAWAK

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INTRODUCTION

Anti-NMDA receptor (NMDAR) encephalitis is a subtype of autoimmune limbic encephalitis (ALE), being described as one of the most common nonviral encephalitis worldwide. 60% of cases are associated with a neoplasm, mainly ovarian teratoma. The potential symptoms overlap with psychiatric disorder and infectious encephalitis often make the diagnosis very challenging especially in district setting, where neuronal autoantibodies testing is not readily accessible on top of high prevalence of tuberculosis and rabies infection especially in Sarawak.

METHODS

We identified 4 patients with clinically definite anti-NMDAR encephalitis (as per Graus criteria) diagnosed between 2021 and 2023.

RESULTS

The median age is 20 ± 7 years old with M:F ratio of 3:1. Clinical manifestations were seizure, altered behaviour, orofacial dyskinesia and dysautonomia. At presentation, one patient acquired COVID-19 infection category 2 whereas two patients have treatment-naïve hepatitis C infection. CSF analysis revealed median cell count of 30 ± 190 cells/ μ L with median protein level of 0.35 ± 0.15 g/L. Tuberculosis and viral encephalitis workups were negative. Anti-NMDAR antibody detected in all CSFs. MRI brain findings were normal. All patients received intravenous methylprednisolone and intravenous immunoglobulin as first line therapies at a median duration of 18.0 ± 4.5 days from symptoms onset. One patient additionally required IV rituximab 500mg weekly for 4 cycles. After a median follow-up of 20.5 ± 10.3 months, all attained disease remission with no recurrent seizure. Three patients were steroids-free for a median duration of 11.0 ± 2.5 months (mRS 0) whereas one patient is still on tapering dose of prednisolone (mRS 1). No neoplasms were detected.

CONCLUSION

High clinical suspicion especially in the absence of usual infective agent should raise the possibility of ALE. ALE such as anti-NMDAR encephalitis is treatable condition and should be considered as part of working diagnosis in patient presenting with matching neurology manifestation.

A CHALLENGING DIAGNOSIS OF NEUROLOGICAL MANIFESTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by diverse manifestations affecting multiple organ systems. Neurological involvement presents a diagnostic challenge, highlighting the importance of thorough evaluation and differential diagnosis. This case report details the evaluation and management of a young female with SLE, whose neurological manifestations initially suggested a diagnosis of Neuromyelitis Optica (NMO).

REPORT

A 22-year-old female, previously healthy, was diagnosed with SLE following a constellation of multisystemic symptoms. This included serologically positive (ANA, ds-DNA titre >667, anti sm, anti-ro60) hematological abnormalities (pancytopenia), renal dysfunction (acute kidney injury, hypoalbuminemia, and significant proteinuria), and neurological complications. The neurological symptoms, featuring acute urinary retention and progressive lower limb weakness after a dengue fever diagnosis, necessitated further investigation due to their severity and rapid progression. Initial MRI findings were suggestive of Longitudinal Extensive Transverse Myelitis (LETM), a key feature of NMO.

Management of her condition commenced with high-dose corticosteroids and hydroxychloroquine to address the acute symptoms of SLE. Concomitant hypertension was managed with calcium channel blockers and alpha-blockers, while symptomatic management for anemia and low folate levels was implemented.

Upon further examination, testing for anti-aquaporin 4 antibodies resulted negative, and the patient was determined not to fulfill the diagnostic criteria for NMO. This finding necessitated a re-evaluation of the originally suspected NMO diagnosis, redirecting focus towards managing SLE with neurological involvement not attributed to NMO.

CONCLUSION

This case accentuates the diagnostic complexities encountered in patients with SLE presenting with atypical neurological symptoms. Despite initial indications suggesting a diagnosis of NMO, subsequent antibody testing and clinical evaluations disproved this hypothesis. The absence of aquaporin 4 antibodies and failure to meet NMO criteria underscore the necessity for continuous re-assessment and flexibility in management strategies based on evolving diagnostic information. It also highlights the pivotal role of multidisciplinary collaboration in providing comprehensive care to patients with multi-faceted autoimmune diseases like SLE.

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SOCIO-DEMOGRAPHIC AND CLINICAL PROFILE OF PATIENTS WITH PARKINSON'S DISEASE IN A TERTIARY CARE HOSPITAL OF TERENGGANU, MALAYSIA

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INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease with alpha synucleinopathy characterised by bradykinesia, tremor and rigidity. Current data on the pattern of Parkinson's disease in Terengganu, Malaysia is sparse. We aim to provide the demographic and clinical profile of PD patients from state of Terengganu.

METHODS

We conducted a retrospective study at the neurology outpatient clinic of the Hospital Sultanah Nur Zahirah, the tertiary referral hospital of Terengganu, Malaysia that received referrals from whole state of Terengganu- over a period of 17 years from October 2005 to October 2022. The demographic and clinical features of 362 patients were collected and analyzed. Patients that fulfilled the UK PDS Brain Bank Criteria for Parkinson's disease were included while exclusion criteria were patients with Parkinson-plus diseases.

RESULTS

The average age of presentation was 65 years old with a median age of 67 years old. The ratio of male to female was 1.5:1. The racial demographics of our cohort showed majority of patients of Malay ancestry (86%) with Chinese (12%) and Indian (<1%). The number of population over age of 65 years old was 63,254 according to the census of Terengganu in 2020. The official population size of Terengganu was 1,149,440 as according to official census report from Department of Statistics Malaysia. This gives rise of a prevalence rate of 0.03%.

CONCLUSION

Our cohort of PD patients in the state of Terengganu, Malaysia showed a lower prevalence rate compared to regional countries of South East Asia.

PREVALENCE OF PSYCHOTROPICS USED AND OCCURRENCE OF FALLS AMONG OLDER PATIENTS WITH PARKINSON'S DISEASE

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BACKGROUND

Older individuals diagnosed with Parkinson's disease (PD) frequently experience a range of both motor and non-motor symptoms including psychiatric issues. Effective management of these patients requires a combination of multiple medications. We aim to explore the prevalence of psychotropic medication use and the occurrence of falls in PD patients aged 65 years and above in a Quaternary center in Malaysia.

METHODS

This was a retrospective cohort study which included all PD patients aged 65 years and above under follow up in the interdisciplinary geriatric unit in Hospital Kuala Lumpur from 1st January till 31st December 2023. A total of 42 patients were eligible for this study. Baseline demographic data, psychiatric-related information (duration of the psychiatric disorder, management given and types of psychotropic medications prescribed) and the incidence of falls during the study period was collected.

RESULTS

Among 42 patients, the median age was 75 (SD 7) years, and there were slightly more males (52%). The median duration of PD was 5 (SD 5) years. 59% of these patients were in stage 1 to 3 Hoehn and Yahr scale. All patients had polymorbidities and polypharmacy. 62% of these patients were diagnosed to have a psychiatric disorder and 77% were given psychotropic medications. Antidepressants were the most common psychotropic given (75%) followed by anti psychotics (15%), anxiolytics (5%) and hypnotics (5%). None of them had psychotropic polypharmacy. 92% of patients who had been prescribed psychotropic medication had associated falls.

CONCLUSION

A significant proportion of PD patients studied had psychiatric disorders, were on psychotropic medications and experienced at least a fall during the period of the study. Regular review of the ongoing need for these medications and a fall assessment should therefore be central to the comprehensive geriatric assessment in this cohort.

KEYWORDS

Parkinson's disease, Psychotropics, Falls

A CASE OF IMMUNE-MEDIATED NECROTISING MYOPATHY AFTER COVID-19 VACCINATION

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INTRODUCTION

Immune-mediated necrotising myopathy (IMNM) is an uncommon muscle disease characterised by relative paucity of lymphocytic inflammatory infiltrate with muscle necrosis on muscle biopsy, associated with autoantibodies, such as anti-signal recognition particle (anti-SRP), and anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (anti-HMGCR).^{1,2,3} There are reports of IMNM occurring after COVID-19 vaccination.⁴

REPORT

We describe a case of anti-SRP positive IMNM after COVID-19 vaccination.

A 65-year-old Chinese lady presented with proximal lower limbs and axial weakness for 2 months since March 2021 after her third Sinovac vaccination. Her weakness progressively worsened till became wheelchair bound. On examination, there was head drop, camptocormia, predominant proximal limbs weakness, and reduced tendon reflexes. MRC sum score was 42. Needle EMG examination showed irritable myopathic changes, and muscle biopsy showed muscle degeneration, necrosis, and regeneration with MHC-1 upregulation. Her CK level was elevated at 3977IU. Serum SRP antibody test was positive. She had been given 2 courses of IV methylprednisolone and was commenced on oral mycophenolate when she visited another healthcare facility, but her weakness did not improve. We treated her with intravenous immunoglobulin, 1 course of IV rituximab 1g 2 weeks apart and oral steroids. She showed some clinical improvement with MRC sum score improved from 42 to 46.

DISCUSSION

There have been few reports in literature regarding possible IMNM post vaccination, and further studies are needed to evaluate possible causative link.⁴ Patients with IMNM tend to develop debilitating muscle weakness and irreversible muscle wasting early in the disease course.⁵ Early initiation of rituximab and aggressive immunosuppression are important in this condition.^{5,6}

CONCLUSION

Persistent efforts to treat her SRP IMNM with immunotherapy may lead to further clinical improvement despite late therapy.

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CERVICAL SPONDYLOTIC MYELOPATHY WITH PARAVERTEBRAL TUMOUR MIMICKING MOTOR NEURON DISEASE

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INTRODUCTION

Motor neuron disease commonly presents with mixed upper and lower neuron lesions¹. However, cervical myelopathy can present similarly², posing a risk of misdiagnosis in resource-limited setting with restricted MRI slots.

REPORT

A 64-year-old gentleman with poorly controlled diabetes (HbA1C: 8.7%) and hypertension presented with left upper limb weakness for one year, left lower limb weakness for six months, and right upper limb weakness for four months, intermittent muscle twitching and weight loss. Examination revealed wasting of small muscles of the hands, positive Hoffman signs, generalised muscle fasciculations, and hyperreflexia. MRC power examination revealed bilateral upper limb proximal power 4, distal power 3, and lower limb proximal power 4, distal 5, with equivocal Babinski sign. No bulbar or cranial nerve palsy was observed. Patient reported no numbness. A provisional clinical diagnosis of motor neuron disease was made.

Outpatient nerve conduction study showed sensorimotor axonal polyneuropathy with asymmetry. All SNAPs absent and all CMAPs reduced, worse on the left side. EMG revealed spontaneous activity in most tested muscles (right EIP, right biceps brachii, right gastrocnemius, right vastus medialis, thoracic and cervical paraspinal), no reinnervative changes noted.

A delayed outpatient MRI whole spine revealed multilevel prolapsed intervertebral discs at C5/C6 and C6/C7, and a paravertebral mass. The patient developed paraplegia (both lower limbs power 0-1) and underwent surgery for C3-C7 fusion, laminectomy and C4-C5 right-side foraminotomy. Postoperatively, lower limb power improved to 3-4/5. A CECT Thorax revealed a 4cm superior paravertebral enhancing mass. Initial biopsy results suggested atypical spindle cells with neurogenic differentiation, favouring schwannoma. The patient received combined management from the spine and rehabilitation teams.

CONCLUSION

Early MRI of the spine, particularly the cervical region, is essential for patients exhibiting mixed upper and lower motor neuron signs. Identifying treatable spinal cord lesions promptly allows for timely referral for surgical intervention, potentially reversing disability.

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GLUTEN ATAXIA - A CASE REPORT

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INTRODUCTION

Gluten Ataxia is an idiopathic sporadic cerebellar ataxia, with positive antigliadin antibodies or serological evidence of gluten sensitization¹. It may occur with or without enteropathy¹.

REPORT

A 52-year-old with hyperthyroidism on carbimazole, presented with a 6-month history of unsteady gait, dysarthria, giddiness and 10kg weight loss over one year. There were no limb weakness, numbness, urinary or bowel symptoms. Examination revealed slow saccadic eye movement, truncal ataxia, dysmetria and dysidiadochokinesia, worse on the left. Tone, Power, sensory and reflexes were normal, with no signs of parkinsonism. MRI Brain showed brainstem and cerebellum atrophy. Serum paraneoplastic panel, SCA gene including SCA1/2/3/6/7, biohazard screening, ANA, ANCA, serum copper, anti-thyroid peroxidase and anti-thyroglobulin were all normal. Lumbar puncture and nerve conduction study was unremarkable. Blood investigations were normal with no evidence of nutritional deficiency and no other manifestations of celiac disease (CD).

Initial serum anti-deamidated gliadin antibodies (DGP) IgA was elevated at 26 U/ml (normal <7.0) with negative IgG, Anti-Tissue Transglutaminase (TTG) and Anti-Endomysium. He was diagnosed as Gluten Ataxia. OGDS done showed antral gastritis with normal duodenal mucosal. Biopsy taken from duodenum showed no increase in intraepithelial lymphocytes (not supportive of CD), chronic inflammation with focal mild villous blunting. He was advised for strict gluten free diet, which was difficult to adhere. Serum DGP IgA repeated one year later was persistently elevated at 13 U/ml, though reduced compared with baseline. He was comanaged with gastroenterology and rehabilitation team, and was ambulating with walking frame.

CONCLUSION

Gluten ataxia is an important differential for cerebellar ataxia, as it may improve with strict gluten free diet (GFD)², even in cases without enteropathy³. However, this is challenging to adhere in Malaysia. Serial serology marker (IgA TTG or IgA/IgG DGP) can be used as monitoring of adherence to GFD⁴. Long standing cerebellar atrophy in these cases is usually irreversible¹.

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CHALLENGES IN DIAGNOSING AND MANAGING CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP) IN PATIENTS WITH DIABETES MELLITUS (DM) AND END STAGE RENAL FAILURE (ESRF): A CASE REPORT

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INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a symmetric, motor predominant, proximal and distal demyelinating peripheral neuropathy of a progressive or relapsing course. CIDP is caused by inflammatory or immune process against myelin proteins in peripheral nerves. The clinical course of CIDP is usually progressive for more than 8 weeks.^{1,2} Diabetes mellitus (DM) associated with CIDP was present in 9% to 26% of CIDP patients.³

CASE REPORT

A 56-year-old gentleman with underlying poorly controlled diabetes, Hypertension, End Stage Renal Failure (ESRF) for 4 years, on continuous ambulatory peritoneal dialysis (CAPD) at home, assisted by wife presented in January 2024 with bilateral lower limb (LL) weakness for the past 7 weeks. Preceding the LL weakness, he had worsening bilateral LL swelling in November till December 2023. Despite the LL swelling subsided after aggressive hemodialysis (HD), his LL weakness did not improve. Subsequently he was wheelchair bound since discharge. However, after discharge, he complained of bilateral upper limbs (UL) numbness then progressively developed worsening bilateral LL weakness at end of December 2023 leading him bedbound. Otherwise, he denied dysphagia/slurred/soft speech, no urinary/bowel incontinence. He did not have infective symptoms prior to symptoms onset. Physical examination of UL showed generalized UL weakness with MRC scale 3, areflexia but preserved sensation over both UL. Whereas LL examinations showed generalized LL weakness with predominantly proximal muscle weakness of MRC scale 2 and MRC 3 for distal LL, diminished reflex with sensory level of reduced sensation from T12 and below with loss of proprioception over bilateral LL. MRI whole spine done on 15/1/24 showed L4/L5 spondylosis causing spinal canal stenosis, bilateral L5 radiculopathy, L4/L5 annular tear. Case referred to orthopedic team for further management, planned for conservative management as patient not keen for surgical intervention. Blood test done including thyroid function test, serum B12 and folate, all are within normal range. Viral screening (Hep B, Hep C, HIV, VDRL) are non-reactive. Lumbar puncture done shows albuminocytologic dissociation with CSF (total cell count <5, protein slightly raised: 0.47g/l, normal glucose ratio). Nerve conduction study (NCS) done showing electrophysiological evidence to suggest a mix of axonal neuropathy and probable chronic demyelinating polyneuropathy. He was planned for intravenous immunoglobulin (IVIG) total 2g/kg over 5 days. However, IVIG (0.4g/kg/day) was given only for 3 days as patient developed complication of fluid overload requiring high flow nasal cannulation despite slow infusion. Total fluid extraction about 15L was done over 1 week via

HD and cyclical peritoneal dialysis, subsequently he was able to wean off oxygenation. 6 days after the last dose of IVIG, there was slight improvement in his limb power (from MRC 3 improved to 4) but still unable to ambulate. He was advised for continuation of outpatient physiotherapy.

CONCLUSION

Consideration of a range of differential diagnosis is essential when evaluating a patient with symptoms suggestive of CIDP. However, due to progressive motor weakness that developed over a period of <6 months with significant proximal motor involvement and upper limb involvement⁴ plus electrophysiological evidence, a decision has been made to treat for CIDP.

Unraveling CIDP in patients with DM is challenging, as several features of diabetic polyneuropathy may overlap with CIDP. Nevertheless, recognition of CIDP in a diabetic patient is pertinent because CIDP is a treatable disease, and many patients respond to immunosuppressive or immunomodulation therapies.³

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A CASE REPORT: RABIES PRESENTING WITH ACUTE FLACCID PARAPLEGIA MIMICKING GUILLAIN-BARRE SYNDROME

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INTRODUCTION

There are two clinical forms of rabies infection - in affected patients, (i) 2/3rd exhibit furious rabies with hydrophobia/aerophobia and (ii) 1/3rd exhibit paralytic rabies, presenting with acute flaccid paralysis (AFP) without the former prodrome. [1] The latter is more common in those with post-exposure vaccination [2]. This diagnostic challenge often leads to misdiagnosis and disease underreporting. We report a case of rabies in Sarawak presenting with AFP despite receiving post-exposure prophylaxis (PEP).

CASE REPORT

A 55-year-old lady presented to us in February 2024 with rapidly progressive bilateral lower limb weakness with numbness for two days. She was unable to ambulate upon presentation. Two weeks prior, she was bitten unprovoked by an unidentifiable stray dog over her left ankle and dorsum of hand. She received PEP with rabies immunoglobulin (RIG) over the wounds and full rabies vaccination. She had no altered behaviour or hydrophobia/aerophobia. Clinical examination demonstrated bilateral lower limbs areflexia, fasciculations, symmetrical weakness (MRC 2/5) and reduced sensation at L1-2 levels. Proprioception, cranial nerves and upper limbs were intact.

Laboratory investigations were normal. Lumbar puncture was performed with opening pressure measuring at 10cm H₂O. Cerebrospinal fluid and nuchal biopsy for rabies virus RT-PCR were negative. MRI brain showed non-enhancing T2 hyperintense lesions which are not suppressed on FLAIR at the left dorsal medulla, periaqueductal region of dorsal midbrain, and right thalamus with similar multilevel patchy intramedullary lesions scattered along the thoracic spinal cord without cord expansion. Overall features were suggestive of rabies encephalitis and myelitis.

Management was mainly conservative. She became febrile and agitated the following day. She had worsening lower limb power with new bilateral upper limb weakness (MRC 3/5), fasciculations and areflexia. She subsequently developed bulbar involvement, requiring ventilatory support. Despite two doses of intrathecal human RIG (HyperRAB®), she deteriorated further and succumbed on the third day.

CONCLUSION

Rabies infection should still be suspected in patients presenting with AFP after sustaining an animal bite with PEP. For individuals presenting with AFP or acute encephalitis syndrome in endemic areas, a detailed history of animal bite is vital.

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MANIFESTATION OF LG1 AUTOIMMUNE ENCEPHELITIS AND DENGUE ENCEPHALITIS

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INTRODUCTION

This is a case report describing the clinical manifestation of dengue encephalitis following LG1 encephalitis.

METHOD

Case report

RESULTS

A 65 - years - old female with underlying diabetes mellitus, hypertension and normal cognition was presented with one month history of right sided faciobrachial dystonia and rapid progressive dementia. Her MOCA score was 13.

Laboratory testing showed normal full blood count (FBC), CRP, connective tissue and thyroid function. Her malignancy workup were negative. CSF results revealed glucose 3.1, protein 272, cell count 0 and negative culture. LG1 - 1 antibody was detected from CSF and negative anti - NMDAR. EEG showed asymmetrical diffuse moderate to severe cortical dysfunction. MRI brain revealed asymmetrical T2/FLAIR hyperintense signal changes seen at the bilateral temporal lobes with thickened mesial temporal region. She was given methylprednisolone for 5 days followed by PLEX. She showed clinical improvement and discharged with T Prednisolone 60mg OD.

A month later, she was re - admitted for less responsiveness (GCS13) and fever. Due to compensated shock she was admitted to ICU and dengue NS1, IgM and IgG was detected. Dengue encephalitis diagnosis was made. There was no seizure recurrence and MOCA remained same. Repeat MRI and EEG showed resolved encephalitis/encephalopathy changes. However, no lumbar puncture was done during ICU admission. She responded to fluid therapy and discharged well.

DISCUSSION

Encephalitis has many differential diagnosis including infection and inflammation. Imaging of the brain may be non - specific in determining the etiology of the disease. A differential diagnosis of dengue encephalitis is considered for this patient as she was tested positive for dengue infection. Obtaining a CSF sample would aid in achieving the diagnosis.

CONCLUSION

Clinical history and context, aided by specific laboratory markers, imaging and electrophysiology test (EEG) are important in managing complex and critically ill patients.

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A RARE CASE OF PARVIMONAS MICRA ORBITAL CELLULITIS COMPLICATED WITH CEREBROVASCULAR THROMBOSIS AND MYCOTIC ANEURYSM

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INTRODUCTION

Parvimonas micra is a gram-positive anaerobic cocci normally detected in the oral cavity, respiratory and gastrointestinal system. Occasionally, it has been shown to disseminate, causing brain abscesses, spondylodiscitis, endocarditis, intra- abdominal abscesses. Intracranial mycotic aneurysm is a rare complication of this infection and have only been reported twice. We are reporting a case of Parvimonas micra orbital cellulitis, complicated with cerebral venous sinus thrombosis, internal carotid artery mycotic aneurysm which require endovascular intervention.

REPORT

A previously healthy 50-year-old gentleman presented with headache for 10 days followed by bilateral periorbital swelling and fever for 3 days. There was left eye complete ophthalmoplegia with ipsilateral parotitis. CECT brain revealed left periorbital cellulitis with superior orbital vein thrombosis, bilateral cavernous sinus thrombosis, right sigmoid sinus and Torcula herophilli thrombosis. Intravenous ceftriaxone and metronidazole was started upon admission. Blood culture grew Parvimonas micra which was sensitive to the ongoing antibiotics. He improved after a week of treatment with resolution of left ophthalmoplegia. On day 14 of treatment, he developed new right sided partial ptosis and right VI nerve palsy. CT angiogram showed segmental saccular dilatation of the right internal carotid artery extending from lacerum to cavernous segment measuring 1.7x1.4x2.3cm. He deteriorated clinically over the next 2 days with worsening headaches and new right 3rd nerve palsy. A repeated CT angiogram showed a rapidly enlarging right ICA aneurysm now measuring 1.8x1.8x2.6cm. Diagnostic cerebral angiogram showed a right cavernous ICA dissecting aneurysm. Manual compression test on the right ICA showed adequate collateral flow from left ICA to the right via anterior communicating artery. Venous return in both cerebral hemispheres were within less than 2 seconds of each other. In view of high risk of aneurysmal rupture, emergency endovascular aneurysm coil embolization and sacrifice of right ICA was performed successfully. Patient was discharged well after 6 weeks of intravenous ceftriaxone. 6months follow up showed no residual neurological deficit.

CONCLUSION

This is the third Parvimonas micra-related intracranial mycotic aneurysm ever reported. When it comes to treatment of these cavernous mycotic aneurysms, there are no specific treatment pathways, as the disease entity is rare. The variability of aneurysm size and progression of disease make a blanket treatment recommendation a genuine challenge. The decision to



abandon conservative management include persistent/ worsening ophthalmoplegia, or aneurysm, new focal neurological deficits, or aneurysmal rupture. Interventions include surgical ligation/clipping and therapy such as balloon occlusion, coil embolization and stenting.

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OCCIPITAL CONDYLE SYNDROME AS THE FIRST MANIFESTATION OF TRACHEAL CARCINOMA

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INTRODUCTION

Occipital condyle syndrome is a rare condition, manifested as occipital region pain with ipsilateral hypoglossal nerve palsy (1). This underdiagnosed condition is commonly associated with skull-base metastases and primary head and neck tumor (2). Our case demonstrated a patient with occipital condyle syndrome and associated adenoid cystic carcinoma of the trachea.

CASE REPORT

A 53-year-old male with diabetes, presented with a occipital headache for 1 week. An initial plain CT brain revealed a lytic erosive bone lesion involving right occipital condyle and C1 vertebrae. He was being treated for a non-specific headache and discharged. A month later, he presented with a worsening headache. He denied respiratory symptoms or any constitutional symptoms. A thorough examination revealed tongue deviation to the right. Motor-sensory components of all 4 limbs and other cranial nerve examinations were intact.

A diagnosis of occipital condyle syndrome was made. He was worked up to look for a primary source of malignancy. CSF investigations were fairly normal except for raised CSF protein (Protein 0.5g/L; normal range 0.15-0.45).

A contrasted CECT brain/neck showed an enlarged right paratracheal node measuring 4.9x4.6x5.9cm, leading to a referral to the respiratory medicine team for airway assessment. A nodule found at the distal trachea during bronchoscopy procedure, was then biopsied. Histopathological examination of the tracheal nodule revealed adenoid cystic carcinoma. Subsequent staging CT showed evidence of metastases to mediastinal nodes, right adrenal gland, and bone. The patient was referred to the oncology department for palliative radiotherapy in view of metastatic disease. However, his condition deteriorated and he succumbed 1 month after the diagnosis.

CONCLUSION

Occipital condyle syndrome, a rare condition, can be the first manifestation of cancer, and often its unfamiliarity leads to a delayed diagnosis (3). Confirmation of Occipital condyle syndrome usually indicates advanced malignancy (4).

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FOCAL SEIZURE AS THE FIRST PRESENTATION OF SMALL CELL LUNG CARCINOMA

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INTRODUCTION

Hyponatremia secondary to Syndrome of Inappropriate Antidiuretic Hormone (SIADH) is common in Small Cell Lung Carcinoma. We present a case of focal seizure occurred secondary to hyponatremia, subsequently revealing the presence of small cell lung carcinoma.

CASE REPORT

A 65-year-old gentleman, with no known medical illness, presented to the hospital with recurrent episodes of aphasia and mouth twitching, each lasting 5-10 seconds. There was no associated limb weakness. Reduced oral intake was noted along with unintentional 10kg weight loss in one month. Laboratory investigations revealed hyponatremia with a sodium level of 106 mmol/L, raised urine sodium of 77 mmol/L, urine osmolality of 382 mOsm/kg, and serum osmolality of 227 mOsm/kg, consistent with SIADH. Thyroid function test (TFT) was normal. MRI Brain was unremarkable, showing small vessel disease without evidence of intracranial mass lesion. His EEG did not show epileptiform discharges, but displayed abnormal background slowing in delta-theta range, suggestive of moderate cerebral dysfunction.

His symptoms improved with fluid restriction, and sodium levels normalized over two weeks of hospitalization. Lumbar puncture was performed, yielding elevated cerebrospinal fluid (CSF) protein levels of 0.57g/L and CSF glucose levels of 4.26mmol/L. CSF analysis for autoimmune and paraneoplastic panel returned negative.

Worsening transaminitis was noted with elevated AST 216 U/L and ALT 294 U/L. Contrast-enhanced CT of the thorax, abdomen, and pelvis (CECT TAP) showed multiple ill-defined hypodense liver lesions and left hilar and mediastinal lymphadenopathy. Lung Biopsy confirmed small cell lung carcinoma. The patient was transferred to the Oncology Unit. Subsequently, he developed delirium and liver failure due to metastatic infiltration, and the family opted for End-Of-Life care at home.

CONCLUSION

There are numerous potential causes of focal seizures. When considering a seizure in the context of hyponatremia, it is essential to look for a potential cause of paraneoplastic SIADH and underlying malignancy.

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QIASTAT MENINGITIS/ENCEPHALITIS PANEL - AN IMPORTANT TOOL FOR MICROBIOLOGICAL DIAGNOSIS OF CNS INFECTION

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INTRODUCTION

Listeria meningoencephalitis is a commonly overlooked CNS infection in the community. Standard therapy with IV ceftriaxone is inadequate (1), and the QIAstat Meningitis/encephalitis panel is an important diagnostic tool to aid in management. We described a case of Listeria meningoencephalitis in a patient with poorly controlled diabetes mellitus in Sarawak.

CASE REPORT

A 61-year-old lady with diabetes mellitus, presented with fever, headache, and vomiting for 2 days. On examination, she was delirious with GCS of E3V2M2. Initial vital signs showed high grade fever, blood pressure of 80/50mmHg, and pulse rate of 140 bpm. Other than neck stiffness, other systemic examinations were normal. She required intubation and inotropic support. Lab results demonstrated leukocytosis (TWC $18 \times 10^3/\mu\text{L}$), thrombocytopenia (platelet $113 \times 10^3/\mu\text{L}$), and acute kidney injury (creatinine 270 $\mu\text{mol/L}$), with markedly raised CRP of 2877 nmol/L.

The contrast-enhanced CT brain was normal with no leptomeningeal enhancement or brain parenchymal lesion. Lumbar puncture performed showed raised opening pressure at 36cmH₂O, clear CSF fluid, raised CSF protein of 2.75g/L; and cell count of 100 polymorphs. Other CSF investigations including gram stain, culture, AFB, Indian ink, and cryptococcal antigen were all normal.

The CSF QIAstat Meningitis/Encephalitis panel detected Listeria Monocytogenes, negative for other organisms. She was started on IV ampicillin and gentamicin on day 1 of admission. However, due to deteriorating kidney function and gentamicin's nephrotoxicity, she was switched to IV meropenem. Within 5 days of treatment, she was extubated to full consciousness. She was discharged well after completing 4 weeks of antibiotics.

CONCLUSION

Standard CSF investigations for microbial diagnosis with cultures and gram stain are inadequate due to low yield (2). CSF QIAstat hastens microbiological diagnosis, potentially shortens hospitalization, and improves patient outcomes. In a resource-limited setting, empirical IV ampicillin should be considered in cases with high index of suspicion (3).

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TONGUE MYOKYMIA OCCURRING 9 YEARS AFTER RADIOTHERAPY FOR NASOPHARYNGEAL CARCINOMA

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INTRODUCTION

Myokymic discharges are spontaneous bursts of single motor unit potentials firing at 5-150Hz (up to 300Hz) that can appear as doublets, triplets or multiplets. It can be seen in patients with history of radiation therapy such as brachial plexopathy or rarely cranial nerve neuropathies.

REPORT

A 53-year-old lady with underlying history of subtotal thyroidectomy for multinodular goitre 29 years ago, undifferentiated nasopharyngeal carcinoma (Stage T4N1M0) diagnosed 9 years ago and underwent 3 cycles of neoadjuvant chemotherapy with 70Grey and 35 fractions of radiotherapy, presented with slurring of speech for the past 3 months without difficulty in swallowing and chewing. Upon examination, there was right neck radiotherapy mark seen, bilateral lateral tongue border atrophy with fasciculations. Other cranial nerve and extremities examination were normal without any fasciculations seen. Needle electromyography (EMG) on the genioglossus muscle revealed myokymic discharges while other extremities muscles were normal.

DISCUSSION

Tongue EMG can reveal axonal hyperexcitability and myokymic discharges decades later due to delayed effects of radiation therapy. This useful feature distinguishes it from metastatic or nasopharyngeal carcinoma recurrence and other potential mimics such as motor neuron disease. We excluded other mimics such as motor neuron disease via clinical examination and needle electromyography examination in this case.

CONCLUSION

Tongue myokymic discharges can be seen in patients with previous nasopharyngeal carcinoma with radiation therapy and is useful in distinguishing from other conditions.

ATYPICAL PRESENTATION OF POLYNEUROPATHY – AN OMINOUS FOREBODING?

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INTRODUCTION

Atypical Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a challenging diagnosis that may herald a sinister condition.^{1,2}

REPORT

51-year-old gentleman underlying dyslipidaemia, complained of progressive, asymmetric lower limb pain radiating to lower back with paraparesis for 1 month leading to recurrent falls with sudden onset of left oculomotor nerve palsy and bifacial weakness. He denies history of chemical, toxin, drug exposure or familial demyelinating diseases. Examination of lower limbs showed asymmetric weakness (grade 1/5 right hip flexors, knee extensors and ankle dorsiflexors; 3/5 left side) with bilateral areflexia, hypotonia and stocking distribution sensory loss. Nerve conduction study revealed bilateral tibial nerves reduced CMAP and absent SNAP for bilateral sural nerves and superficial peroneal nerves. Magnetic resonance (MR) Brain had leptomeningeal and cranial nerve III, IV, VI, VII enhancement. MR spine showed cauda equina thickening, enhancement and nerve root clumping leading to unsuccessful lumbar puncture. Nerve root biopsy showed chronic inflammatory process without malignant cells. Serum tumour markers, ANA, pANCA, aquaporin antibodies, IgG4, angiotensin-converting enzyme, hepatitis B antigen, hepatitis C, HIV antibodies, vitamin B12, folate was negative. cANCA was positive without symptoms of vasculitis. Contrasted computed tomography of thorax, abdomen and pelvis did not show any malignancy. Positron emission tomography scan 2 months later did not reveal evidence of hypermetabolic uptake and subsequent MR brain findings show enhancement resolution. Patient's weakness improved with intravenous methylprednisolone (5 days) following tapering dose oral prednisolone 2 weekly with maintenance azathioprine. Treating as atypical (focal) CIDP, he responded further to monthly intravenous immunoglobulin (2g/kg over 5 days) for 6 months. However, 6 months later his paraparesis gradually returned with acute dysphasia. Urgent MR brain showed multiple new enhancing lesions at cerebrum and cerebellum, open brain biopsy of lesions showed Diffuse Large B-cell Lymphoma.

CONCLUSION

The delayed emergence of haematologic diagnosis with atypical CIDP underscores the importance of surveillance.

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IDIOPATHIC INTRACRANIAL HYPERTENSION AS THE INITIAL MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) presents with headache and papilledema. It is caused by increased intracranial pressure with normal cerebrospinal fluid (CSF) composition and neuroimaging. It typically occurs in overweight women of child bearing age.

REPORT

A 43-year-old Malay policewoman with underlying hypertension, previous recurrent bilateral uveitis, urticaria vasculitis, microscopic hematuria and bilateral ovarian cysts presented with headache and diplopia for one year. There was no recent weight gain or intake of other medications. Upon examination, there was bilateral papilledema. Her body mass index was 22.5kg/m². Computed tomography with contrast of the brain showed no evidence of cerebral venous thrombosis. Lumbar puncture revealed elevated opening pressure of 35cmH₂O with normal cerebrospinal fluid analysis. Blood investigations showed leukopenia, positive antinuclear antibody, positive double-stranded DNA antibodies, reduced complement levels and elevated erythrocyte sedimentation rate. Brain MRI and MR angiography were normal. She fulfilled 2019 EULAR/ACR criteria for SLE. She was started on corticosteroid and mycophenolate mofetil whereby her symptoms resolved after that.

DISCUSSION

Our patient has fulfilled the criteria for IIH as neuroimaging and CSF results are unremarkable with high lumbar puncture opening pressure. However, she does not have typical risk factors such as obesity and drug use, hence it is important to evaluate for secondary causes. There are a few reports of IIH as an uncommon neuropsychiatric manifestation of SLE. It is important to investigate for secondary cause as the treatment is different. Early treatment with immunosuppressant can prevent visual loss.

CONCLUSION

SLE should be suspected in patients who lack typical association of IIH such as obesity, weight gain and drug use. Early treatment of the underlying SLE is important to prevent permanent visual loss.

DOCTORS VIEWS ON EPILEPSY MANAGEMENT: A QUALITATIVE STUDY ON CARDIAC-BASED SEIZURE PREDICTION DEVICE

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INTRODUCTION

Epilepsy is a chronic neurological disorder affecting approximately 50 million people globally of all ages. Early detection of epileptic seizures can reduce morbidity and mortality, leading to improved quality of life for people with epilepsy. Emerging evidence has described the feasibility of predicting epileptic seizures using cardiac parameters. Although seizure prediction devices have been widely studied in the past decade, a user-centered approach that guides the development of this technology is limited. This study aimed to explore the needs and preferences of doctors managing epilepsy for the design of a seizure prediction tool.

METHODS

One-hour semi-structured interviews were conducted individually among doctors (n=10) of various hospitals who have managed epilepsy for at least two years. An interview guide with open-ended questions was used to explore the needs and preferences of the participants. Think-aloud sessions were used to gather feedback on an early prototype of a web portal that will accompany a seizure prediction device. The interview data were analyzed using a thematic approach to identify relevant themes and subthemes.

RESULTS

The perceived challenges in managing epilepsy among doctors include medication non-adherence and the lack of education and awareness among epilepsy patients. While the think-aloud session revealed interest and acceptability of the prototype web portal, concerns regarding real-time seizure alerts and the importance of an accurate seizure prediction algorithm using heart rate also emerged. Information sharing by integrating the web portal with electronic medical records was also perceived to be crucial to support clinical decisions.

CONCLUSION

The insights gathered from this study will inform the design and development of an online web portal that will accompany a seizure prediction device. Focusing on the viewpoint of doctors who manage epilepsy is valuable to ensure that the functionality and acceptability of the technology align with the user's needs and expectations.

Adult Neurology

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EQ-5D-3L HEALTH STATE UTILITY VALUES IN PEOPLE WITH EPILEPSY IN MALAYSIA

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INTRODUCTION

The lack of access to expensive newer anti-seizure medication (ASMs) is the reality of healthcare disparities in resource-limited countries. As part of a cost-utility analysis to compare benefits in Quality-Adjusted Life Years (QALY) between the epilepsy patients treated with and without newer generations of ASMs, we aimed to define the health states among people with epilepsy (PWE), using EQ-5D-3L.

METHODS

A cross-sectional survey was conducted on PWE using EQ-5D-3L questionnaire, which was designed by EuroQoL group. The survey was self-administered or answered by their caregivers on behalf of patients based on their knowledge of the patient's health status. Scores obtained were converted into individual health profiles and utility scores using the Malaysian EQ-5D-3L value set.

RESULTS

A total of 213 responses were collected. The mean age was 43 ± 17 years and 51.2% were female, mean duration of epilepsy was 21.4 ± 15.3 years. Most patients (53.0%) were on more than one ASMs and had uncontrolled seizures (53.1%). Patients on regimes with newer ASM and uncontrolled seizures reported higher scores for anxiety/depression ($p < 0.05$). Malay ethnicity, higher education, married individuals and controlled seizures were associated with higher EQ-VAS ($p < 0.05$). Higher education and being employed were associated with higher utility scores ($p < 0.05$). Spearman correlation found a significant negative correlation between the number of ASM and EQ-VAS, $r = -0.165$, $p < 0.05$ and utility scores, $r = -0.159$, $p < 0.05$. Multiple linear regression analysis found that Malay ethnicity (OR 0.24) predicts better EQ-VAS and uncontrolled seizure control (OR -0.19) was a significant negative predictor for EQ-VAS. Higher education (OR 0.19) and being employed (OR 0.19) were significant predictors for better utility scores. There were no significant associations between regimes with /without newer ASM and EQ-VAS ($p = 0.554$) or utility scores ($p = 0.305$).

CONCLUSION

Regime with newer ASM did not impact the perceived health state among people with epilepsy in Malaysia.

KEYWORDS

Epilepsy, Utility scores, newer anti-seizure medications

NEUROLOGY TRAINING IN ASEAN COUNTRIES

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INTRODUCTION

The purpose of this study is to describe the variations in neurology training pathways in all ASEAN countries.

METHOD

A cross-sectional survey using questionnaires was conducted among the representatives of ASEAN countries from October 2023 to March 2024.

RESULTS

Neurology training programs are available in nine of the eleven ASEAN countries except for Timor Leste and Cambodia. Most of the countries had less than 10 neurologists (ranges 0.7 to 8.8) per one million population. Thailand, Brunei and Singapore have 11.7, 13.3 and 23.2 neurologists per one million population, respectively. The number of neurology trainees enrolled each year ranges from 2 to 22 per 10 million population, with less than 5 trainees per 10 million in Malaysia, Philippines, Laos, Myanmar and Indonesia. The total duration of training from undergraduate to certified neurologist varies greatly, due to the compulsory internal medicine training and post-internship services. To enroll in the neurology training program, candidates in four countries (Brunei, Singapore, Malaysia, and Myanmar) are required to have completed internal medicine as a prerequisite. Candidates from Thailand and Indonesia need to complete their 2-year compulsory government or general practice services before they can be enrolled in the neurology training program. Overall training duration after a medical degree to be a neurologist ranges from three to 13 years. Malaysia and Myanmar are the two countries in which candidates need to spend more than 10 years to become board-certified neurologists.



CONCLUSION

Certain ASEAN countries face a shortage of neurologists, with low trainee enrollment and long training duration.

KEYWORDS

ASEAN, neurology training



A CASE OF DISSEMINATED CRYPTOCOCCOSIS WITH MULTIPLE RARE COMPLICATIONS IN AN IMMUNOCOMPETENT PATIENT

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INTRODUCTION

Cryptococcal meningitis primarily affects immunocompromised individuals, with estimated 152,000 global cases yearly. Although less common, up to 20-36% of cases occur in the immunocompetent, with variable extent of disease, imposing significant therapeutic challenges.

METHODS

We describe a case of persistent cryptococcal meningitis complicated with pulmonary cryptococcosis, hypercalcaemia, cerebral IRIS and chronic papilloedema in a recently treated, immunocompetent patient.

RESULTS

A 43-year-old gentleman presented with a 2 months history of headache, unstable gait, weight loss, and seizures. Diagnosed with cryptococcal meningitis, he completed 4 weeks of IV amphotericin B and flucytosine in an outside facility, followed by oral fluconazole. A few weeks later, he presented again with features of increased intracranial pressure, papilloedema and hypercalcaemia. CT brain revealed communicating hydrocephalus. A right lung mass was also found on CXR. Despite negative fungal cultures, cryptococcus was detected on Indian ink staining, with high antigen titres. CT guided biopsy of the lung mass confirmed cryptococcal infection with no evidence of malignancy. Biohazard screening and malignancy workups returned negative. Amphotericin B and flucytosine was restarted but later changed to fluconazole and flucytosine due to acute kidney injury. A lumbar drain was inserted for persistently high ICP, but subsequently removed due to ventriculitis. He received a dose of IV pamidronate for hypercalcaemia and also started on a short course of steroids for cerebral immune reconstitution syndrome (IRIS) which he responded well to. He completed another month of induction and 8 weeks of consolidation therapy with fluconazole. Despite permanent visual impairments, his other symptoms resolved and he was able to return to light-duty work on follow up.

CONCLUSION

This case highlights the challenges in managing persistent cryptococcal infection in an immunocompetent patient, emphasizing the importance of early detection and careful management of its complications.

A CASE OF SPINOCEREBELLAR ATAXIA 6 WITH GOOD RESPONSE TO ACETAZOLAMIDE

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INTRODUCTION

The Spinocerebellar ataxias (SCA) are a subset of hereditary cerebellar ataxia that causes progressive cerebellar dysfunction, with or without involvement of other central and peripheral nervous system components. They are usually inherited in an autosomal dominant way (1). To date, more than 40 subtypes have been described which are classified according to the genetic loci in order of identification (2). Spinocerebellar ataxia type 6 (SCA6) is the prototype of a pure cerebellar ataxia, often associated with a severe progressive ataxia and cerebellar dysfunction. It is caused by a CAG repeat expansion in the CACNA1A gene which encodes the alpha-1A subunit of the P/Q type voltage-gated calcium channel (3).

REPORT

A 63-year-old Indian man with underlying hypertension presented with unsteady gait for the past 30 years. He initially found it difficult to walk down the slope. His symptoms gradually deteriorated and he required a walker for the past 4 years. On examination, he has a wide based ataxic gait, horizontal nystagmus, dysidiadochokinesia, past pointing, and heel-shin test were all positive bilaterally. There was no family history of ataxia. There was no family history of episodic ataxias and hemiplegic migraine. Molecular genetic testing revealed pathogenic 13-22 CAG repeats in the CACNA1A gene. Other baseline investigations were normal. Oral acetazolamide was started for this patient. Efforts from the rehabilitation, occupational therapy and physiotherapy teams helped his gait retraining. Currently, he can walk unsupported with residual minimal ataxia.

CONCLUSION

SCA6 can show good response to acetazolamide therapy and should not be missed. A combined multidisciplinary team approach with medical therapy can be helpful in improving the gait ataxia.

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NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) AND ANTI-N-METHYL-D-ASPARTATE RECEPTOR (ANTI-NMDAR) ENCEPHALITIS OVERLAP

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INTRODUCTION

Anti-N-methyl-d-aspartate receptor (anti- NMDAR) encephalitis, is an autoimmune disorder where immunoglobulin G (IgG) antibodies act against the NR1 subunit of the NMDA receptors in the central nervous system (CNS) resulting in complex neuropsychiatric features and encephalopathy. Few studies have reported concurrent or delayed episodes between NMDAR and CNS demyelinating diseases such as acute disseminated encephalomyelitis (ADEM), myelitis and neuromyelitis optica (NMO).

REPORT

A 25-year-old Chinese lady presented with vomiting for 1 week and generalized limb weakness with numbness for 2 weeks. She had generalised body weakness, C5 sensory level and generalized hyperreflexia with bilateral upgoing plantar response. Brain T2 MRI revealed high signal intensity at her medulla. EEG showed moderate diffuse cortical dysfunction. CSF shows high protein 0.65g/dL with normal glucose. Subsequently, she developed seizure till requiring intubation for airway protection. Her neurological deficit deteriorated during intensive care unit stay with power at upper limbs 2/5 and lower limbs 0/5. CSF for NMDAR and aquaporin-4 (AQP4) are positive. Total 9 cycles of plasmapheresis, IV methylprednisolone and 1 cycle of IV rituximab were initiated. MRI whole spine after plasmapheresis shows extensive patchy T2W/STIR hyperintensity from C5 level until conus medullaris. After 2 weeks of rehabilitation, her power at bilateral upper limbs were 4/5, and lower limbs were 2/5. After 1 month, her neurological deficit resolved completely. After her second cycle of IV rituximab 6 months later, she was able to resume work.

DISCUSSION

Anti-NMDAR encephalitis is due to antibody cross linking with NMDARs internalization causing reduced receptor density and synaptic neuronal function. NMOSD causes astrocytic damage via complement dependent cytotoxicity via AQP4 antibodies. Immune complexes can form between AQP4 and NR3A NMDAR subunits, suggesting AQP4 involvement in NMDAR signaling which warrants further future research.

CONCLUSION

Anti-NMDAR encephalitis and NMOSD overlap when treated promptly can lead to excellent outcomes.

A CASE OF GAD ANTIBODY-POSITIVE STIFF PERSON SYNDROME

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INTRODUCTION

Stiff person syndrome is a rare but debilitating condition with progressive muscle stiffness and spasm, which can cause significant disability and impaired mobility. It can be associated with autoimmune or paraneoplastic conditions.

REPORT

We describe a case of a 72-year-old Chinese lady who initially presented with bilateral lower limb stiffness associated with painful spasm after an episode of fall one day prior to onset of symptoms. Examination revealed hyperekplexia, with truncal and bilateral lower limb stiffness, bilateral lower limb equinovarus posturing, with generalized hypertonia. She was initially treated as tetanus which was given intramuscular tetanus immunoglobulin. Her serum Anti GAD was positive with high titer ($>280,000$ IU/ml). EMG showed generalized continuous motor units. She was given 2 cycles of IVIG with tapering dose of steroids which showed mild improvement. She was further treated with two cycles of 1000 mg of intravenous rituximab. Two months post hospitalization, she improved from bed bound to able to walk independently without residual stiffness or hyperekplexia.

DISCUSSION

Diagnosis of stiff person syndrome has been historically difficult to establish and is often underdiagnosed. Our patient fulfilled the diagnostic criteria, as outlined by Baizabal-Carvallo et al. However, she was misdiagnosed initially as tetanus due to similar symptoms to stiff person syndrome and with a history of fall. Early detection and management of stiff person syndrome is crucial which can lead to improved outcomes and quality of life.

CONCLUSION

Stiff person syndrome is a challenging neurological disorder and is often underdiagnosed due to its rarity and variability of presentation, which can mimic other neurological disorders. A high degree of suspicion of stiff person syndrome is required to avoid significant morbidity.

AMPA RECEPTOR ENCEPHALITIS WITH MEMORY LOSS

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INTRODUCTION

Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor autoimmune encephalitis is a rare and common misdiagnosed disorder which lead to seizure, behavioural and cognitive disorder. The AMPAR antibodies target on the cell surface receptor and is express throughout the brain especially the hippocampus and limbic system. AMPA receptor play an important role in memory, learning and brain wave activities. It had been shown that the anti AMPAR encephalitis had various diversity.

REPORT

A 42-years-old man without previous medical illness presented with forgetfulness and behavioural change for 2 months. He had poor short-term memory with Montreal Cognitive Assessment (MOCA) score of 21 out of 30 with scoring zero in the recall segment. Physical examination was unremarkable. His brain Magnetic resonance imaging (MRI) and Electroencephalography (EEG) recorded were normal. Antibodies AMPA receptors were detected in serum and cerebrospinal fluid using indirect fluorescent antibody test. He was treated with IV methylprednisolone 1g daily for five days and subsequently oral prednisolone in tapering fashion. His memory improved and he was able to return to work. Screening for associated malignancy was negative.

DISCUSSION

Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor encephalitis is very rare variant of autoimmune encephalitis. Due to its diverse clinical manifestation, it had been a challenge for many clinicians to diagnose the condition. They can present with memory loss and abnormal behaviour like in our case, confusion, seizures, and motor deficits. Early detection in patients suggestive of autoimmune encephalitis can provide significant impact in patient survival and quality of life.

CONCLUSION

AMPA Receptor encephalitis early recognition can lead to better prognosis and memory improvement when prompt treatment is given.

INCLUSION BODY MYOSITIS PRESENTING LIKE LGMD2G

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INTRODUCTION

Inclusion body myositis (IBM) is an inflammatory myopathy that commonly presents after 50 years old with asymmetrical proximal and distal weakness, typically involving the forearm flexors and quadricep muscles. It is a challenging type of myopathy due to the insidious course, mixed EMG findings and unfavourable response to treatment.

REPORT

A 54-year-old male was referred for progressive proximal limb weakness over 6 years, with dysphagia and dysarthria. The patient had statin consumption for 1 year previously. His nephew with similar symptoms, however the diagnosis is not known.

Neurological examination revealed symmetrical generalised weakness, predominantly involving the limb girdles, quadriceps atrophy, reduced ankle reflexes, normal muscle tone and sensation. Over the next 2 years, he gradually developed distal forearm flexor weakness.

Laboratory test includes CK 1735, LDH 480, ESR 21, negative CTD screen, negative immune myositis antibody profile and negative alpha 1-4 glucosidase enzyme. EMG showed irritative myopathy and MRI showed diffuse fatty infiltrates in proximal and distal lower limb muscles. His right vastus medialis muscle biopsy showed the characteristic rimmed vacuoles, endomysial inflammatory infiltration suggestive of IBM instead of LGMD2G. Genetic studies was not done. His lung function test showed restrictive disease and echocardiogram was normal. Patient was subsequently diagnosed as sporadic IBM and treated conservatively. He is now wheelchair bound and requires non-invasive ventilatory support.

CONCLUSION

Limb girdle muscular dystrophy 2G (LGMD2G) is an autosomal recessive telethioninopathy that typically involve the thigh and anterior leg compartment muscles. Disease onset occurs in childhood or adolescence. Like IBM, they progress slowly, can have bulbar involvement, raised CK and rimmed vacuoles on histopathology.

Proximal weakness is an uncommon IBM presentation mimicking LGMD and histopathology is the gold standard for its diagnosis. Remembering this will help in early recognition of the disease especially in patients with atypical clinical presentation.

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A CASE OF SPINOCEREBELLAR ATAXIA 3

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INTRODUCTION

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease, is a rare hereditary neurodegenerative disorder characterized by progressive cerebellar dysfunction. It manifests with motor impairment, cognitive decline, and psychiatric symptoms, severely impacting the quality of life of affected individuals. The underlying genetic mutation in the ATXN3 gene leads to the accumulation of abnormal proteins, resulting in neuronal dysfunction and degeneration.

REPORT

A 32-year-old right-handed lady, who works as a technician, presented with slowly progressive generalized binocular diplopia, gait imbalance, difficulty in writing, and speech stuttering for the past 11 years. Upon examination, there was nystagmus in all directions, inability of left eye to abduct fully, double vision in all directions except downward gaze, left side past pointing, positive heel-shin test bilaterally and broad-based gait. He was unable to perform tandem gait. Screening for peripheral neuropathy with nerve conduction study (NCS) was negative. Brain MRI showed mild cerebellar atrophy. Genetic testing showed 73 CAG repeats (pathogenic) for ATXN3 gene. Vitamin E level was normal. She had slow deterioration, and since 4 years ago she required a wheelchair for ambulation. She is currently under physiotherapy and rehabilitative medicine care.

CONCLUSION

Early spinocerebellar ataxia recognition with genetic testing is important for patient management.

LAMBERT EATON MYASTHENIC SYNDROME IN SMALL CELL LUNG CANCER

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INTRODUCTION

Lambert Eaton Myasthenic syndrome (LEMS) is disorder of presynaptic neuromuscular junction (NMJ) associated with paraneoplastic syndromes and small cell lung carcinoma (SCLC).

REPORT

A 55-year-old male, chronic smoker for 40 pack years presented with progressive proximal myopathy for 6 months, facial swelling, odynophagia, loss of appetite and reduced effort tolerance for 3 months. He was initially treated as anterior neck cellulitis but did not respond to therapy. Upon examination, he has generalized proximal weakness grade 3/5 with superior vena cava obstruction features such as facial and neck swelling. OGDS revealed esophageal candidiasis. Electrophysiological studies revealed electro-incremental response more than 200% consistent with LEMS. Paraneoplastic panel was positive for Anti SOX1, anti Zic4 and anti- Ampiphysin. CT thorax revealed a right hilar and mediastinal lung spiculated mass with local invasion.

He was treated with pyridostigmine and steroids. Histopathological examination (HPE) from Endobronchial ultrasound-guided Trans bronchial fine needle aspiration (EBUS-TBNA) reveals metastatic high grade small cell lung neuroendocrine carcinoma. Unfortunately, patient passed away due to Klebsiella Pneumoniae septicemia after 1 cycle of chemotherapy.

DISCUSSION

LEMS is an autoimmune disorder against the voltage gated calcium channel (VGCC) in the NMJ and is associated with paraneoplastic syndrome and SCLC. LEMS is a clinical diagnosis and confirmed with antibody testing. His short exercise test showed a typical electro incremental response after 10s exercise which is characteristic of LEMS. Together with presence of anti-SOX-1 antibody, underlying SCLC is very suggestive which was revealed by the lung HPE. Pyridostigmine was started to inhibit acetylcholine degradation. Unfortunately, the patient succumbed to neutropenic sepsis with Klebsiella Pneumonia infection after chemotherapy.

CONCLUSION

A high index of suspicion is needed to diagnose SCLC associated with LEMS and early detection and treatment of the underlying malignancy is important.

ANTI-HMGCR MYOPATHY AND STATINSGoy SM¹, Mohamed Micdhadhu MA¹¹*Department of Medicine, Seberang Jaya Hospital***INTRODUCTION**

Statins are 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors and now commonly used in reducing atherosclerotic vascular disease. With increasing usage of statins, it seems to have higher incidence of anti-HMG-CoA reductase (Anti-HMGCR) myopathy in recent years¹.

REPORT

A 61-year-old Malay woman with underlying hypertension, diabetes mellitus, dyslipidemia on atorvastatin >10 years and vitamin D deficiency with L1 fracture post fall, presented with progressive proximal muscle weakness for 10 months associated with significant loss of appetite and loss of weight of 10kg in this period. She was wheelchair bound prior to admission. Otherwise, she had no dysphagia, rash, muscle ache, traditional medication and supplement ingestion. Clinical examination revealed symmetrical proximal muscle weakness with areflexia over the 4 limbs. Sensory was intact. She was not cushingoid and had no features of dermatomyositis. Creatinine kinase (CK) was 5096U/L on admission. NCS/EMG findings was consistent with irritative myopathy. Anti-HMGCR result came back as strongly positive. CECT TAP showed no malignancy. Skin biopsy was not performed. Statin had been discontinued since admission. Intravenous glucocorticoid was started immediately after NCS/EMG followed by one course of IVIG prior to discharge. Unfortunately, she succumbed for nosocomial infection 2 months later.

CONCLUSION

Anti-HMGCR myopathy is uncommon but let us bear in mind that it could be another differential diagnosis to statin induced rhabdomyolysis. Correct diagnosis leads to correct management and proper prognostification.

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THORACIC CORD LESION PRESENTING WITH LOWER MOTOR NEURON WEAKNESS

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INTRODUCTION

Bilateral lower motor neuron pattern of lower limb weakness is usually associated with demyelinating diseases or peripheral neuropathy. Rarely, central cord pathology does present with lower motor neuron signs and symptom. We present a case of thoracic cord lesion presenting with lower motor neuron symptoms.

REPORT

A 39 years old Malay male presented with chronic back pain, associated with gradual onset bilateral lower limb weakness for 4 months. The weakness worsened for 3 weeks prior presentation, with patient gradually becoming unable to walk. Otherwise, he denied any constitutional symptoms, and there was no sphincter dysfunction. His past medical history is significant for diabetes mellitus and hypertension, which was untreated.

At presentation, he was paralysed from the hips below, with no meaningful movement of the lower limb. On examination, he had symmetrical dense lower motor neurone weakness with mMRC grading of all lower limbs movements 0/5. He was areflexic, and there was generalised wasting of the lower limb muscles. He also had sensory loss which was patchy up till T10 dermatome.

Plain radiograph of the thoracolumbar spine showed diminished height of T8 vertebra. Urgent MRI of the spine was done which revealed T8 vertebra plana with T7-T9 infective spondylodiscitis. There was collection with extradural intraspinal extension causing severe spinal canal narrowing and cord compression with focal cord edema. Image guided biopsy of the T8 paraspinal soft tissue phlegmon revealed positive TB GeneXpert. His sputum TB GeneXpert was also weakly detected. AntiTB was commenced and he underwent physiotherapy and occupational therapy. Unfortunately he did not regain his lower limb power and remained confined to a wheelchair at discharge.

CONCLUSION

A central cord lesion may cause lower motor neuron sign and symptoms. The cause may be structural, as is this case, hence radiological imaging is important for patients presenting with lower motor neuron sign.

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A CASE OF CO-OCCURRENCE OF PROGRESSIVE SUPRANUCLEAR PALSY (PSP) AND IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS (INPH) OR HYDROCEPHALIC MIMIC?

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INTRODUCTION

NPH and PSP are distinct causes of parkinsonism with overlapping clinical features that can mimic each other. This case report demonstrates a typical clinical presentation of the NPH triad with imaging findings suggestive of NPH coexisting with PSP.

CASE REPORT

A 69-year-old retired security guard with a medical history of diabetes, dyslipidemia, hypertension, latent syphilis, and psoriasis presented with frequent falls, an unsteady gait, memory impairment, and urinary incontinence. Physical examination revealed a wobbly and magnetic gait, but no muscle strength deficits. Initial CT imaging and lumbar puncture findings were suggestive of iNPH. However, there was no significant improvement in symptoms despite large amount of CSF drainage. Further imaging with MRI Brain shows midbrain atrophy against a background of NPH which suggestive of coexistence of PSP. The patient also showed signs of PSP, including hypomimia, upward gaze restriction, and difficulty with gait initiation. He was started on Madopar for management subsequently

DISCUSSION

In our case, the presence of early postural impairment and oculomotor abnormalities warrants a re-evaluation of the diagnosis. Research indicates that communicating hydrocephalus may be an under-recognized presentation of PSP. A retrospective study conducted at the Mayo Clinic found that out of 41 suspected NPH patients who underwent shunting, only one-third showed continuous improvement. Interestingly, pathology results from five patients in the ventriculoperitoneal shunt-treated cohort revealed the presence of other neurodegenerative disorders, including PSP.

CONCLUSION

This case highlights the diagnostic challenge of distinguishing between iNPH and PSP, especially when both conditions coexist. Clinicians should maintain a high index of suspicion for alternative diagnoses in patients with overlapping symptoms of neurodegenerative disorders. Further research is needed to elucidate the relationship between iNPH, PSP, and other neurodegenerative disorders, and to optimize diagnostic and treatment strategies for these complex conditions.

NOVEL VARIANTS IN FAMILIAL POLYMICROGYRIA

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INTRODUCTION

Polymicrogyria (PMG) is one of the common cortical developments causing epilepsy. The genetic causes of PMG encompass both contiguous-gene disorders and single-gene mutations, including contiguous gene deletion syndromes and mutations within the tubulin family of genes.

METHOD

Herein, we identified a Malaysian Chinese family with polymicrogyria, featuring childhood and adolescent-onset focal seizures and hemiparesis, potentially attributed to two genes. The proband has been contending with drug-resistant focal motor epilepsy since 13 years old and magnetic resonance imaging of the brain showed unilateral polymicrogyria. Notably, the proband's two siblings, paternal uncle, and grandmother also exhibit either focal seizures or hemiparesis.

RESULT

Whole exome sequencing (WES) analysis of the proband revealed three variants across two candidate genes: *OCNL* p.Tyr122Ter (c.366T>A, rs1199819832) novel variant and *RELN* p.Thr468Pro (c.1402A>C, rs1833136675); p.Asp467Ala (c.1400A>C, rs1833136859) variants that has not been reported in PMG. Polymerase chain reaction amplification and Sanger Sequencing to confirm the variants in the proband's DNA followed by variant segregation analysis are ongoing.

CONCLUSION

WES identified two potential causative genes *OCNL* and *RELN* and their variants in this familial polymicrogyria syndrome with unilateral polymicrogyria, focal seizures, and hemiparesis.

KEYWORDS

Polymicrogyria, Focal seizure, Hemiparesis, *OCNL*, *RELN*

ASCENDING INFECTION FOLLOWING SINUS SURGERY: A CASE REPORT

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INTRODUCTION

Functional endoscopic sinus surgery (FESS) is commonly performed for sinus disease. Skull base or orbital complication following this procedure are relatively low. We report a case of cavernous sinus thrombosis, right orbital apex syndrome and mycotic aneurysm of internal carotid artery post-FESS for right inverted papilloma.

REPORT

A 78-year-old gentleman with underlying diabetes mellitus, hypertension, and allergic rhinitis was admitted to our centre with complaints of right eye pain and drooping of the eyelid with blurring of vision for three days. He also complaint of foul smelling sensation. He has history of FESS done five weeks earlier for right sphenoid inverted papilloma. On examination, there was cranial nerve II, III, IV and VI palsy. CTA with CECT brain and orbit showed two small saccular mycotic aneurysms measuring 3mm and 2mm of right internal carotid artery with right cavernous sinus thrombosis and right optic neuritis. His CSF culture analysis was within normal parameter and negative for culture. His CRP (14 mg/L) and ESR were elevated (>120mm/hour). Nasal endoscopy done by the ENT team showed slough and crusting tissue over sphenoid cavity. Tissue culture taken grew *Pseudomonas Aeruginosa*. He was started on IV Cefepime for two weeks and discharged with anticoagulant.

CONCLUSION

The definitive treatment for inverted papilloma, a benign sinonasal tumor, is surgical resection. Despite having an overall low major complication rate, the anatomic proximity of the cavernous segment, internal carotid artery, and the orbit with sphenoid sinus predisposes these structures to injury and infection. It is suggested that focal infection and inflammation lead to the weakening of vessel wall, hence the formation of aneurysm. This rare complication of FESS requires multidisciplinary team approach and warrants immediate treatment to prevent permanent loss of cranial nerve function.

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ANTI-RI PARANEOPLASTIC SYNDROME – A CASE REPORT

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INTRODUCTION

Anti-Ri Paraneoplastic syndrome (PNS) phenotypically presents as subacute to chronic cerebellar syndrome, brainstem encephalitis, or opsoclonus-myoclonus syndrome.¹ It is associated with breast, lung and medullary thyroid cancer². Cerebellar syndrome is reported to occur in 39% of patients with Anti-Ri PNS at onset and 67% at disease plateau¹.

REPORT

A 65-year-old lady with diabetes and hypertension, presented with unsteady gait for two weeks, dysarthria, right hand clumsiness, and intermittent diplopia. On examination, she had right gaze evoked nystagmus, right sided past-pointing and ataxia. MRI Brain showed non-enhancing bilateral hyperintense T2/FLAIR signal involving 3rd and 4th ventricles periaqueductal region, mamillary bodies, central pontine, hypothalamus, hippocampus and lateral ventricles subependymal region and corpus callosum, with incidental bilateral enhancing optic neuritis. The radiologist reported as Neuromyelitis Optica. Lumbar puncture was unremarkable. Given MRI changes overlapping with Wernicke encephalopathy, a trial of IV Thiamine was concurrently given with IV methylprednisolone 1g OD for 3 days, and continued with oral prednisolone at 1mg/kg OD.

Further investigations showed strong positive CSF Anti-Ri Antibody, negative for other paraneoplastic/autoimmune antibodies, serum Aquaporin-4, and serum MOG. CT TAP revealed right centrilobular lung nodule with cavitation, tiny non-enhancing bilateral breast nodules and bilateral indistinct hypodense thyroid nodules. She was diagnosed with smear-positive Pulmonary Tuberculosis (PTB) and commenced on anti-tuberculous treatment for six months, while also referred to a surgeon for breast and thyroid lesions workup. Given the active PTB, worsening glycaemic control and little neurological improvement, prednisolone was tapered off. She had progressive neuropsychiatric cognitive decline and delirium. Repeated LP was unremarkable and negative for CSF TB-GeneXpert. IV immunoglobulin therapy was considered; however, she defaulted subsequent appointments.

CONCLUSION

Anti-Ri PNS should be considered in patients with sporadic subacute cerebellar ataxia. Managing PNS in elderly with comorbidities is challenging. In cases with occult malignancy, a trial of immunosuppression may be beneficial¹.

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MANAGING MELAS CRISIS IN RESOURCE-LIMITED SETTING

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INTRODUCTION

Mitochondrial encephalomyopathy, lactic acidosis with stroke-like episodes (MELAS) is a rare genetic disorder with multisystem involvement^{1,2}. We report a known case of MELAS presented acutely with lactate acidosis, intestinal pseudo-obstruction and new infarcts on brain imaging.

REPORT

Our patient is a 31-year-old lady with MELAS (positive m.3243A>G mutation in MT-TL1 gene), under yearly neurology clinic follow-up for temporal lobe infarction and epilepsy, last seizure more than ten years ago. She presented with a two-week history of fever, post-prandial vomiting, productive cough and lethargy. Upon arrival to the emergency department, she displayed confusion and restlessness with a GCS of E4V4M5. She was intubated for severe metabolic acidosis (pH 7.27, HCO 5.1, Lactate 14.3) and required inotropic support.

CTA Abdomen showed enteritis and small bowel obstruction without transition point or evidence of mesenteric ischemia. Due to feeding intolerance, she required total parenteral nutrition. CT Brain showed new hypodensity at the left head of caudate, basal ganglia, and left external capsule, with a background of left parietooccipital encephalomalacia. Neurology consultation was sought in ICU for co-management. Given the recurrent lactate acidosis and imaging findings suggestive of new strokes, she was started on IV L-Arginine 0.5G/KG (20g in 50cc D5%) OD for two days. Due to limited stocks, this was switched to oral Arginine 5g QID for 5 days, then 5g BD. Coenzyme Q10 and carnitine were not available. She underwent tracheostomy due to ventilator-associated pneumonia. Her metabolic acidosis and feeding intolerance showed improvement with supportive measures and L-Arginine therapy. She was eventually discharged with walking aid. One month later, she showed remarkable improvement walking independently, whilst on self-purchased oral arginine, carnithine, and coenzyme Q10.

CONCLUSION:

Management of acute crisis in MELAS is mainly supportive. Initiation of treatment including L-Arginine may reduce morbidity. Though relatively inexpensive, these treatments are not easily available in KKM hospitals.

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AN INDOLENT YET SINISTER ADVERSE EFFECT OF IL-5 MONOCLONAL ANTIBODY-BENRALIZUMAB

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INTRODUCTION

Benralizumab, an anti-eosinophil monoclonal antibody targeting the alpha chain of the interleukin-5 receptor, is prescribed as an add-on maintenance therapy for severe eosinophilic asthma. Commonly reported adverse effects include nasopharyngitis, asthma exacerbations, upper respiratory tract infections, and bronchitis. In this case report, we present a rare occurrence of idiopathic intracranial hypertension (IIH) triggered by Benralizumab.

CASE PRESENTATION

We detail the presentation of a 43-year-old woman with a medical history including diabetes mellitus, migraine, obesity, and severe bronchial asthma. She presented with a persistent headache over a 2-month period, predominantly affecting her frontal region and interfering with daily activities, lasting up to a week each time. These headaches differed from her usual migraine, accompanied by nausea and photophobia, exacerbated by straining. She denied any projectile vomiting, fever or visual impairment. Interestingly, the onset of these headaches coincided with her monthly benralizumab injections for severe asthma. The patient's medication regimen included 10 miligram daily and oral metformin 1 gram twice daily.

Physical examination revealed morbid obesity (Body-Mass Index of 45 kg/m²) without any significant neurological deficits, and fundoscopy showed no signs of papilledema. The brain computed tomography scan was unremarkable. Therapeutic lumbar puncture showed an opening pressure of 27 cm H₂O and closing pressure of 19 cm H₂O, with subsequent improvement in headache severity. Analysis of cerebrospinal fluid samples showed no abnormalities except for the elevated pressure.

A diagnosis of idiopathic intracranial hypertension (IIH) was considered, and treatment commenced with acetazolamide 250 milligrams twice daily. Follow-up appointments indicated well-controlled headaches with acetazolamide, and the patient was advised on weight reduction therapy as part of IIH management. The benralizumab was continued with close monitoring.

CONCLUSION

The timing of Benralizumab injections in relation to the headaches suggests a potential association with Benralizumab-induced IIH. The mechanism of benralizumab in IIH may not

be fully elucidated and requires further research. This case illustrates the possibility of benralizumab induced IIH as an adverse effect of IL-5 drugs.

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“LOCK JAW” MASQUERADING AS GUILLAIN-BARRE SYNDROME

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INTRODUCTION

Guillain-Barre Syndrome (GBS) is a polyneuropathy characterized by flaccid paralysis and sensory disruption. GBS presenting with masticatory disturbance and “lock jaw” mimicking temporal mandibular joint disorder (TMJ) is an uncommon manifestation leading to diagnostic difficulties.

REPORT

We present the case of a 31-year-old female with no previous medical history, who initially presented to the Otorhinolaryngology department due to inability to bite and fully open her mouth, which she described as “her jaw was locked”. She was treated as temporomandibular (TMJ) dysfunction but symptoms did not improve. She subsequently noticed bilateral facial weakness followed by numbness of her hand and foot, progressive weakness of her bilateral lower limbs and the inability to close her eyes which was when she was referred to us. Further history revealed fever 3 weeks prior to this incident. Examination portrayed symmetrical mild proximal muscle weakness over all 4 limbs, patchy sensory loss over palms and soles with generalized hyporeflexia, bilateral masseter muscle tenderness and bilateral lower motor neuron 7th cranial nerve palsy. Nerve conduction study showed features of demyelinating polyneuropathy (increased conduction velocity, prolonged distal motor latency and F Wave) with sural sparing, which fulfilled the Uncini’s criteria of the diagnosis of AIDP. Besides, her serum Sulfatide IgM, GM2 IgM and GD2 IgM returned as positive consistent with immune related polyneuropathy.

RESULTS

She made a remarkable recovery with a 5-day course of intravenous immunoglobulin (IVIG). A month post IVIG, her MRS score was 0 with subtle bifacial weakness, but she was able to chew and open her jaw without difficulty.

CONCLUSION

Masticatory disturbances and reduction in bite force are relatively uncommon presentations of GBS which might lead to the misdiagnosis of TMJ disorder. This atypical presentations of GBS should always be kept in mind as the prognosis is generally favorable if treatment is instituted promptly.

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AN ISOLATED CASE OF METHANOL POISONING WITH BASAL GANGLIA NECROSIS AND HAEMORRHAGE IN A DISTRICT HOSPITAL IN MALAYSIA

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INTRODUCTION

Methanol is a common household and commercially available chemical. With its ethanol-like colour and odour, its accidental or intentional ingestion can lead to fatal consequences, with high mortality rates being recorded. Typical manifestations include blurring of vision, central scotomata, blindness, hyperpnea, hypotension, inebriation, sedation, coma, or seizures. Isolated cases of methanol poisoning remain a difficult diagnosis to make in rural settings with limited laboratory capabilities. Characteristic findings of bilateral basal ganglia necrosis with putaminal hemorrhage have been described in postmortem studies of methanol-related deaths. This may be a potential area of research.

REPORT

A 39-year-old gentleman, with a history of chronic alcohol use, presented with an acute episode of gasping and generalised tonic seizure, preceded by visual loss and confusion. Pupils were equal but sluggish upon arrival and the fitting aborted with intravenous Valium administration. The patient was intubated for airway protection and poor Glasgow Coma Scale. Initial workup revealed severe high anion gap metabolic acidosis. The serum ketone was 0.7 mmol/l. Bedside serum viral screening tests and urine toxicology tests were negative. An urgent non-contrasted computed tomography (CT) brain showed a right basal ganglia haemorrhage with bilateral basal ganglia hypodensities. He was started on intravenous sodium bicarbonate infusion but had poor response. Suspicion of methanol poisoning then prompted us to start him on Oral Ethanol infusion and initiate haemodialysis, with Fomepizole and Intravenous Ethanol both unavailable in our district hospital. He eventually deteriorated and succumbed within 19 hours of admission. Both serum and urine methanol levels were confirmed to be significantly raised 2 weeks after the patient's demise.

CONCLUSION

Methanol poisoning can present with non-specific signs and symptoms, and diagnosis may be challenging in resource-limited settings. Potential adjuncts to making the diagnosis include non-contrasted CT of the brain, which may show bilateral basal ganglia necrosis with putaminal haemorrhage. Further studies are needed.

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ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODIES AND ACUTE HAEMORRHAGIC ENCEPHALOMYELITIS - MOGAD AND AHM: FRIENDS, LOVERS, OR NOTHING?

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INTRODUCTION

Acute haemorrhagic encephalomyelitis (AHM) has recently been described as an emerging phenotype of Myelin oligodendrocyte glycoprotein antibody- associated disease (MOGAD). However, the potential aetiological link between anti-MOG antibodies (MOG-Ab) and AHM requires further elucidation. We report a case of adult- onset AHM with serum MOG-Ab positivity, discuss the pathogenic relevance of MOG-Ab, and summarise similar cases in the literature.

REPORT

A 35-year-old male with preceding upper respiratory tract infection presented with acute paraplegia and rapid clinical deterioration including bulbar symptoms, respiratory distress, and encephalopathy. CSF analysis demonstrated pleocytosis and elevated protein levels while comprehensive testing for infective causes were unrevealing.

Brain MRI showed multiple T2W/FLAIR hyperintensities in the midbrain, pons, bilateral internal capsules, cerebellar peduncles, globus pallidi, and thalami while MRI spine revealed longitudinally extensive cervicothoracic T2/FLAIR lesions with a classical “H” pattern and involvement of the conus medullaris.

Additionally, multiple T1W hyperintensities with concurrent SWI blooming artifacts indicative of haemorrhages were observed over both globus pallidi, pons, midbrain, left cerebellum, and spinal cord. Collectively, his clinico-radiologic picture was characteristic of AHM.

Further serum MOG-Ab testing returned a low positive result. Despite receiving concurrent IV methylprednisolone and plasma exchange, his condition worsened, eventually resulting in his demise.

DISCUSSION

Two similar cases of adult-onset AHM with positive MOG-Ab have been recently reported with different clinical courses and outcomes.

Timing of MOG-Ab testing is critical due to declining titres, and might explain the relative rarity of reported MOG-Ab seropositivity in AHM. Histopathological disparities between MOGAD and AHM, including early astrocyte injury, raise questions about the pathogenic role of MOG-Ab. Differences in treatment outcomes necessitates tailored approaches.

CONCLUSION

Our case emphasises caution in interpreting MOG-Ab seropositivity in AHM while underscoring the need for heightened awareness and larger-scale prospective studies to further investigate this potential association.

PREVALENCE OF INTRACRANIAL ATHEROSCLEROTIC DISEASE (ICAD) IN ACUTE ISCHEMIC STROKE (AIS) AND TRANSIENT ISCHEMIC ATTACK (TIA) IN MALAYSIA

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INTRODUCTION

Intracranial atherosclerotic disease (ICAD) is a significant cause of acute ischemic stroke (AIS) globally, but its prevalence and impact in Malaysia remain relatively understudied. This abstract aims to summarize the current understanding of ICAD prevalence in acute ischemic stroke cases within Malaysia population.

Recent studies suggest ICAD is accounted for substantial proportion of AIS cases in Malaysia, particularly among individuals of Malay and Indian descent. The prevalence of ICAD-related strokes varies across different regions in Malaysia, influenced by diverse genetic, dietary, and lifestyle factors.

METHODS

A retrospective analysis was conducted on patients diagnosed with AIS and TIA who underwent magnetic resonance angiography in Hospital Sultan Abdul Aziz Shah to assess intracranial vessels for atherosclerotic disease throughout 2023. Data on demographics, stroke risk factors, imaging findings, and stroke outcomes were collected and analysed.

Preliminary findings indicate that ICAD was prevalent in our patients during the study period. Our study population was predominantly from Malay, Chinese and Indian ethnicities. Risk factors associated with ICAD-related strokes included hypertension, diabetes mellitus, dyslipidaemia, and smoking.

RESULTS

A total of 343 cases of AIS and TIA were included in the analysis. Among these cases, 39 (11.36%) were found to have ICAD.

The mean age of patients with ICAD-related strokes was 61.59 years, indicating that ICAD affects individuals predominantly in their sixth decade of life.

Further breakdown of ICAD-related stroke presentations revealed majority 12 out of 39 cases (30.77%) were associated with lacunar strokes, followed by 11 cases (28.21%) involved anterior circulation strokes, 10 cases (25.64%) involved posterior circulation strokes and 6 cases (15.38%) presented as TIAs.

CONCLUSION

These findings highlight diverse clinical manifestations and distributions of ICAD-related strokes within the studied population. The relatively high proportion of lacunar strokes among ICAD cases suggests a significant contribution of small vessel disease secondary to intracranial atherosclerosis.

AN INCIDENTAL FINDING OF FIBROMUSCULAR DYSPLASIA DURING MECHANICAL THROMBECTOMY IN A STROKE PATIENT

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INTRODUCTION

Fibromuscular dysplasia (FMD) is defined as non inflammatory arterial diseases that commonly involves renal and carotid arteries.¹ Cerebrovascular FMD (C-FMD) is as common as the renovascular counterpart. Patient presenting with FMD with ischemic stroke due to arterial stenosis has a similar management of intravenous thrombolysis and/or mechanical thrombectomy to patients without FMD.⁷

(50words)

CASE REPORT

A 45-years old male had a recent ischemic stroke in Hospital Sungai Bakap(HSB).The presentation was left upper limb numbness with NIHSS 1 preceded by two weeks of headache.Computed Tomography(CT) brain showed hypodense area at right frontal, right parietal, right temporo-parietal and right temporo-occipital region.However, no neuromedical consultation made. Subsequently,a day after discharge from HSB, patient presented to Hospital Seberang Jaya(HSJ) with left sided body weakness preceded by dizziness. On examination, patient had power grade 3 for left upper and lower limb. Patient was diagnosed as Right Total Anterior Circulation Infarct (TACI) based on Computed Tomography Angiography (CTA) brain with NIHSS 14.Spontaneous NIHSS improvement from 14 to 7 during sequential assessment.CTA brain noted acute distal M1 thrombus with Internal Carotid Artery (ICA) thrombus following which a mechanical thrombectomy (MT) was conducted in a private hospital with a successful Thrombolysis in Cerebral Infarction(TICI) score of Grade 3. Intraoperative finding revealed corkscrew appearance of right internal carotid artery and proceeded with right cervical carotid stenting for finding suggestive of fibromuscular dysplasia.Intravenous Tirofiban infusion was given post-carotid stenting.NIHSS worsen from 7 to 10 and repeated CT brain showed complicated with cerebral edema. Patient underwent decompressive craniectomy.NIHSS remained same upon discharge . Modified Rankin Scale(MRS) was 2 at 3 months post stroke. Despite of advances in clinical and radiological features of FMD, considerable knowledge gaps remain, necessitating clinical and pathophysiological research into the neurological presentation of FMD.

(232words)

CONCLUSION

In acute stroke setting, intravenous thrombolysis and/or mechanical thrombectomy suggested for patients presenting with FMD or without FMD.⁸

KEYWORDS

Fibromuscular dysplasia, Mechanical Thrombectomy, Corkscrew appearance

DISCLOSURE

Ethics: Written consent from patient for case writing including the radiological images were obtained.

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SOCIODEMOGRAPHIC, SEVERITY, AND QUALITY OF LIFE PROFILES AMONG MIGRAINE PATIENTS AT A MALAYSIAN TERTIARY HOSPITAL

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INTRODUCTION

Migraine is a disabling disease that is a prominent cause of disability. We aim to evaluate the fundamental demographics, comorbidities and medication profiles of migraineurs, which provides insight for future treatment allocation and therapeutic strategies.

METHODS

We performed an observational cross-sectional study at the Hospital Sultan Abdul Aziz Shah, Serdang, from January 2024 to July 2024. The study population were migraine patients attending Neurology Clinic, who underwent comprehensive clinical assessments and completed two self-administered questionnaires during their clinic visits. The instruments utilized were case report forms, Migraine Disability Assessment (MIDAS) score and migraine-specific quality of life Questionnaire (MSQ).

RESULTS

A total of 47 patients participated, 34 female (72.3%) and 13 male (27.7%), with a mean age of 36.1 years. Malay ethnicity constituted 80.9%, while 14.9% were Indian and 4.3% were Chinese. Majority of them had normal body mass index (40.4%) and blood pressure (mean systolic blood pressure=119.9 mmHg and diastolic blood pressures=77.4 mmHg). Most of them suffered from episodic migraine (44.7%), followed by chronic migraine without aura (27.7%) and chronic migraine with aura (14.9%). Most of the patients required at least two prophylactic drugs (70.2%) and 36.6% required more than three reliever drugs. The MIDAS score reflects the disability due migraine with grade four having severe disability and grade one having no disability. The majority of patients were in grade four (38.3%), followed by grade three (29.8%) and grade two (17.9%). The MSQ score reflects the quality of life, with higher scores showing better quality of life. The patients reported the worst scores in the RFR domain indicating restriction in daily activities, followed by the RPR domain which indicates prevention in daily activities (mean score 60.2 and 71.4 respectively).

CONCLUSION

Despite severe migraine impacting quality of life and daily activities, prophylactic medication usage was suboptimal, with excessive reliance on reliever medications. Addressing the underutilization of prophylactic treatments by neurologists is crucial for enhancing migraine treatment outcomes.



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ASSOCIATION BETWEEN RETINAL MICROVASCULAR CHANGES AND DEPRESSIVE SYMPTOMS IN CEREBRAL SMALL VESSEL DISEASE

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BACKGROUND

Depressive symptoms are common complications of cerebral small vessel disease (CSVD), affecting 10%-30% of patients. Traditional assessments rely on neuropsychological scales, lacking objectivity. Retinal microvasculature, mirroring cerebral vasculature, presents a potential biomarker for CSVD-related depression.

OBJECTIVE

This study aims to explore the correlation between depressive symptoms in CSVD and retinal microvascular changes, identifying retinal microvascular biomarkers. Additionally, it investigates related imaging characteristics through multimodal imaging and brain network analysis.

METHODS

148 CSVD patients were enrolled, with 135 included for analysis. Retinal imaging and neuropsychological assessments were conducted. MRI scans and lesion segmentation tools were employed for imaging analysis. Linear and logistic regression analyses were performed to examine the correlation between CSVD depressive symptoms and retinal microvasculature.

RESULTS

CSVD patients with depressive symptoms exhibited widened central retinal venous equivalent (CRVE) and reduced arteriole-to-venule ratio (AVR). CRVE was positively associated with depression severity and CSVD burden. Additionally, wider CRVE correlated with hippocampal atrophy, suggesting its role in depressive symptom onset. Brain network analysis revealed decreased integration and processing capabilities in CSVD patients with depressive symptoms, reflected by CRVE widening. CRVE showed potential as an early biomarker for CSVD-related depression.

CONCLUSION

CSVD patients with depressive symptoms demonstrate widened CRVE and decreased AVR. Widened CRVE suggests heavier CSVD burden. CRVE changes may reflect hippocampal volume alterations, indicating the occurrence of CSVD depressive symptoms. Decreased brain network integration and processing abilities in CSVD patients with depressive symptoms can be reflected by CRVE widening. CRVE may serve as a potential early screening biomarker for CSVD-related depression.

KEYWORDS

Cerebral Small Vessel Disease; Depressive Symptoms; Central Retinal Venous Diameter; Imaging Biomarkers; Brain Network

A PATIENT'S JOURNEY: SEVERE BASAL EXUDATIVE TUBERCULOUS MENINGITIS

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INTRODUCTION

Tuberculous meningitis is the most devastating presentation of Mycobacterium Tuberculosis. Early diagnosis, prompt anti-tuberculosis treatment and corticosteroids are the main determinants of outcome in tuberculous meningitis. Here, we demonstrate an interesting case of severe basal exudative TB meningitis which required prolonged duration of treatment and subsequently recovered.

REPORT

This is a case of 37 years old female presented with bilateral lower limb weakness, lethargic, headache and vomiting for 2 weeks with intermittent fever and weight loss. She was diagnosed as tuberculous meningitis based on lumbar puncture showed positive CSF TB gene Xpert and brain CT showed focal right frontal lesion with early hydrocephalus and started on anti-TB. However, her condition worsened at day 61 of anti-TB. She developed worsening hydrocephalus and required ventriculoperitoneal shunt. Intensive phase was continued for 108 days and planned for 18 months of total duration. Brain MRI showed thick area of basal meningeal enhancement in the region of the basal cistern involving the suprasellar, Sylvian, pontine, interpeduncular, crural, ambient and quadrigeminal cisterns. During follow up, her symptoms improved despite still had residual radiological finding during serial brain MRI. Latest brain MRI showed unchanged residual rim-enhancing lesion and meningeal enhancement around the basal cistern. Her treatment was continued up to 22 months. Currently, patient is asymptomatic and well.

DISCUSSION

Duration of treatment for tuberculous meningitis usually takes up to 12 months. However, it may be prolonged based on the clinical response to treatment. The longer the duration of anti-TB the higher risk for mortality and complications. In this case of basal exudative meningitis, the residual lesions were still seen during follow up MRI, despite clinical improvement. Due to the high mortality and risk of permanent sequelae of tuberculous meningitis, the course of treatment should be individualized.

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POST COVID-19 INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY: A REVIEW

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INTRODUCTION

The Covid-19 pandemic was initially thought to only affect the respiratory system; but has been shown to involve multiple systems including the nervous system, such as peripheral neuropathy with potentially devastating consequences if not identified and treated.

CASE PRESENTATION

We present a case of a 41 year old Malay gentleman, who suffered Covid-19 Category 2 infection in mid-December 2023. Two weeks later, he developed cramping and numbness in the distal parts of his upper and lower limbs. It progressed to weakness and areflexia, later gradually involved the proximal muscles of his bilateral lower limbs. He sought medical attention two months later, where a diagnosis of acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was confirmed by NCS/EMG and MRI of the nerve roots. His Anti-GM1 IgM antibodies was positive and he received a course of immunoglobulin therapy. However, his bilateral lower limb weakness worsened. He responded well to five cycles of plasmapheresis with maintenance steroid therapy; and neurorehabilitation. Periodic follow-up clinical assessment shows improvement in his motor power and he is presently still receiving ongoing support at our centre.

DISCUSSION

The SARS-CoV2 virus can affect the nervous system in various presentations, both acutely and chronically. Currently, there is a lack of local case reports for post Covid 19 inflammatory polyradiculoneuropathy. A small Egyptian study in 2021 reported 39.3% patients had AIDP, 17.9% presented with demyelinating with secondary axonal pattern and 14.3% presented with CIDP-like picture in their adult patients. The study reported 64.3% patients achieved full improvement post high dose steroids with IVIG administration. Only 25% did not show any improvement and 10.7% showed minimal improvement. Other case reports generally show favourable prognosis with steroids, IVIG and plasmapheresis.

CONCLUSION

Identification of post Covid-19 related neurological sequelae should be highlighted to healthcare professionals for prompt diagnosis and treatment to improve overall outcomes.

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SHORT-LASTING, UNILATERAL, NEURALGIFORM HEADACHE ATTACKS WITH CONJUNCTIVAL INJECTION AND TEARING (SUNCT): A FORGOTTEN ENTITY

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INTRODUCTION

SUNCT is an entity of trigeminal-autonomic cephalalgias with very disabling condition and major impact on the patient's quality of life. Typical age of onset is between 30 to 60 years old. It is characterized by sudden brief attacks of severe unilateral trigeminal distribution pain associated with ipsilateral cranial autonomic features. ¹Diagnosis is based on clinical history, typically in the setting of a normal neurological examination and fulfilment of diagnostic criteria ICHD-3.

REPORT

45-year-old woman with underlying chronic sinusitis experienced recurrent episode of sudden unilateral sharp intense headache spreading to the entire head region, occurring 5 to 10 times per day, lasting 4 to 120 seconds each time. It was associated with lacrimation, eye redness, nasal congestion, and ear fullness. There was no vomiting, photophobia, muscle weakness or numbness. Physical examination revealed no neurological deficits. She seek multiple consultations prior and had been treated as migraine/ trigeminal neuralgia/ chronic sinusitis related headache, and was prescribed paracetamol and triptans. However, symptoms were only partially relieved. Contrasted CT brain was normal. Subsequently, she was treated as SUNCT and preventive treatment Lamotrigine 50mg BD was prescribed with a good response.

CONCLUSION

SUNCT remains one of the common primary headache disorder. Based on ICHD-3 criteria, headache needs to be at least 20 attacks; moderate-severe unilateral head pain, lasting 1-600s; with associated cranial autonomic symptoms or signs ipsilateral to the pain; and frequency of at least one a day for more than half of the time. Prompt recognition and treatment is crucial to prevent unnecessary investigation and morbidity. Lamotrigine is the most effective preventive agent, with topiramate and gabapentin also being useful. Intravenous lidocaine may also be helpful as an acute therapy when patients are extremely distressed and disabled by frequent attacks.²

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HEMORRHAGIC CEREBRAL TOXOPLASMOSIS IN AN HIV INFECTED PATIENT

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INTRODUCTION

Cerebral toxoplasmosis is the most commonly found cerebral mass lesion in patients with acquired immune deficiency syndrome (AIDS). The typical computed tomography (CT) and magnetic resonance imaging (MRI) findings of cerebral toxoplasmosis include multiple ring-enhanced regions with surrounding edema, and most patients clinically respond well to anti-toxoplasma therapy within two weeks. However, haemorrhagic changes can be seen following anti-toxoplasma therapy. The radiological and the clinical course of patients who develop haemorrhagic cerebral toxoplasmosis remains unknown.

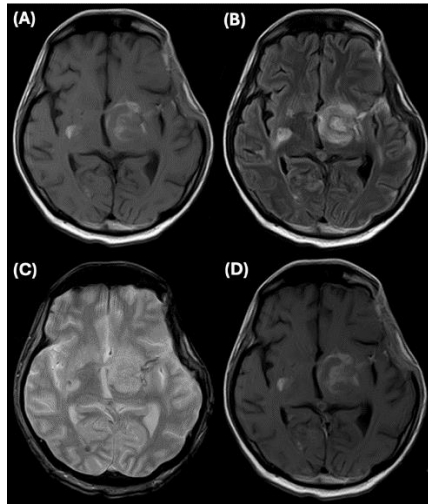
REPORT

A 32-years-old man presented with headache, vomiting and seizure for one week. There was no history of multiple unprotected sexual intercourse or any other high-risk behaviour. The patient was newly diagnosed with HIV/AIDS. Laboratory investigations revealed an aCD4 cell count of 5 cells/ μ l. Initial CT Brain (Figure 1) showed a left basal ganglia intra-axial mass with midline shift and hydrocephalus. A decompression craniectomy and biopsy of the left basal ganglia mass were performed. Histology and immunophenotyping confirmed cerebral toxoplasmosis. Patient was subsequently started on Pyrimethamine, Clindamycin and IV Dexamethasone. Upon commencement of Toxoplasmosis treatment, serial CT imaging showed few new supratentorial hyperdense lesions. MRI confirmed new non-enhancing haemorrhagic lesions with minimal perilesional edema. The CSF culture was negative for bacteria, Mycobacterium, and Cryptococcus.

Figure 1. Axial CT Brain showed left basal ganglia mass with extensive vasogenic edema causing midline shift and hydrocephalus.



Figure 2. Axial MRI Brain in (a) T1-weighted, (b) FLAIR, (c), Gradient Echo, and (d) T1-weighted post-contrast sequences showing new right lentiform nucleus and right occipital non-enhancing haemorrhagic lesions.



CONCLUSION

Hemorrhagic toxoplasmosis is a rare presentation of cerebral toxoplasmosis and should be considered in the differential diagnosis of haemorrhagic cerebral lesions in HIV-infected patients. The intracranial lesions in the present case may have changed from the ischemic lesion induced by arterial inflammations to the haemorrhagic lesion during the course of anti-toxoplasma therapy.

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INCIDENTAL FOREIGN BODIES IN THE GASTROINTESTINAL TRACT OF A VAGRANT FEMALE: AN ADULT NEUROLOGICAL PERSPECTIVE ON UNDERSTANDING PSYCHIATRIC STATES AND BEHAVIORAL PATTERNS

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INTRODUCTION

Homeless individuals often resort to self-harm behaviors, including deliberate foreign body ingestion, leading to frequent Emergency department visits. This population faces an overwhelming burden of medical and psychiatric illnesses. Deliberate foreign body ingestion, commonly observed in adults with mental disabilities and substance abuse issues, necessitates a holistic approach involving endoscopic, medical, surgical, and psychiatric expertise to provide comprehensive care.

REPORT

In our case, a woman in her 30s presented at the Emergency department after swallowing a meat bone, complaining of throat discomfort, breathlessness, and odynophagia. Despite her consciousness, she was only responsive to loud commands. Radiographic imaging revealed both esophageal and abdominal foreign bodies. Following spontaneous expulsion of the primary foreign body, multiple incidental findings persisted in the abdomen. The patient, unfortunately, left against medical advice, preventing further interventions. Clinical examination indicated foreign body sensation and odynophagia. Chest radiography showed esophageal opacities, and subsequent images revealed persistent abdominal opacities. Conservative management led to the expulsion of the primary foreign body within an hour, highlighting the need for ongoing surveillance.

Despite the spontaneous resolution of the primary issue, incidental findings persisted, warranting further investigation. Unfortunately, the patient's premature departure hindered comprehensive interventions. This case underscores the necessity for tailored, multidisciplinary care and continuous psychiatric support for homeless individuals facing such challenges.

CONCLUSION

1. High burden of mental illness among homeless people makes screening for these conditions an essential aspect of care.
2. Deliberate foreign body ingestion is a common phenomenon in homeless population, and requires a multidisciplinary approach, with a combination of psychological therapies and psychopharmacologic interventions.
3. Health care programs should provide tailored services in a multidisciplinary environment, along with medical respite units to reduce re-hospitalization following hospital discharges.

WILSON'S DISEASE IN A 15 YEARS OLD BOY: A RARE CASE

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INTRODUCTION

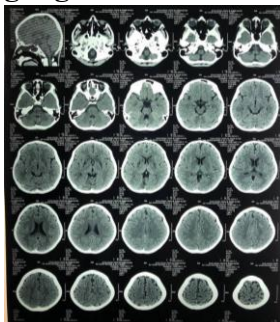
Wilson's disease or hepatolenticular degeneration is an autosomal recessive disease that causes excess copper to accumulate in the body. This disease mainly attacks the liver and basal ganglia of the brain, but can also affect other organ systems.¹ Symptoms can be related to the brain and liver including vomiting, weakness, ascites, swelling of the legs, yellowish skin, and itching. Brain or neurological symptoms include tremors, muscle stiffness, difficulty speaking, personality changes, anxiety, and auditory or visual hallucinations. Diagnosis is difficult and involves blood tests, urine tests, and liver biopsy as well as clinical evaluation. Genetic testing can be used to screen family members of those affected.

REPORT

A 15-year-old pediatric patient came for consultation from a pediatrician, with complaints of slurred speech which he noticed in the last 1 month. The patient had an independent MRI and CT scan which found a blockage in the patient's brain. The patient has also experienced consultations with many doctors, it is said that there is excess copper in the patient. Patients also often complain of weakness, sometimes tremors in the last few months.

The majority of Wilson disease patients with neurological manifestations have been diagnosed with liver cirrhosis. The most common early signs of WD include ataxia, facial awkwardness, dysarthria, hypersalivation, and personality changes.^{2,3} On physical examination of the eye, it was found that there was a ring surrounding the child's cornea. In the eye organ of WD patients, associated with copper deposits on the descemet membrane around the cornea, namely Kayser-Fleischer rings, found in approximately 95% of WD patients. The Kayser-Fleischer ring is considered a relevant criterion for confirmation of Wilson's disease.^{2,4}

Figure 1: Head CT-Scan, Impression: Cerebral infarction in the right and left basal ganglia



CONCLUSION

Wilson disease is an inherited, autosomal recessive disorder of copper metabolism, originating from a genetic defect in the copper-transporting ATPase ATP7B, which is required for biliary copper excretion and loading of ceruloplasmin and other cuprous enzymes with copper. Efforts to use antioxidants (vitamin E and curcumin) in WD therapy are ongoing but further results and recommendations are not yet available. ATP7B mutations, including H1069Q, and R778L, cause accumulation of protein products in the endoplasmic reticulum. Modification of the location of the above-mentioned mutant and its movement to the right cell functional area might restore copper excretion in WD patients.

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UNVEILING THE RESTORATIVE POTENTIAL OF IMATINIB AGAINST 3-NITROPROPIONIC ACID (3-NPA) -INDUCED HUNTINGTON'S DISEASE (HD) IN MICE

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BACKGROUND

Huntington's disease (HD) is a debilitating inherited neurological disorder characterized by motor and cognitive impairments, stemming from mutations in the huntingtin (HTT) gene. These mutations lead to an expansion of CAG repeats in the HTT gene, resulting in a toxic polyglutamine tract in the mutant HTT protein. Despite extensive research into the molecular mechanisms of HD, effective treatments or cures remain elusive. HD manifests with neurobehavioral deficits, motor dysfunction, and heightened levels of reactive oxygen species (ROS).

METHODS

In this study, the neuroprotective potential of Imatinib, a non-tyrosine kinase inhibitor targeting c-Abl, was explored in mice models of HD. Imatinib was administered intraperitoneally at doses of 1 mg/kg and 3 mg/kg. The effects were evaluated using behavioral tests including locomotor activity assessment, Morris water maze, and passive avoidance tests. Additionally, biochemical analyses were conducted to measure acetylcholinesterase (AChE) activity, levels of lipid peroxidation (TBARs), and antioxidant enzyme activity (GSH, SOD, and catalase) in brain tissues. Furthermore, ELISA assays were employed to quantify inflammatory mediators such as NF-kB, IL-1 beta, TNF-alpha, and caspase-3. Histopathological examination using hematoxylin and eosin (H & E) staining was performed to assess neuroprotection.

RESULTS

Imatinib treatment significantly ameliorated locomotor deficits and reduced dementia-like symptoms induced by 3-Nitropropionic acid (3-NPA) in a dose-dependent manner. Moreover, Imatinib administration led to decreased AChE activity and improved cognitive performance in behavioral tests. Biochemical analyses revealed a dose-dependent reduction in TBARs levels and enhanced antioxidant enzyme activity in the brain tissues of treated mice. Additionally, Imatinib treatment resulted in a significant decrease in inflammatory markers, indicating its anti-inflammatory effects. Histopathological examination confirmed the neuroprotective properties of Imatinib in HD.

CONCLUSION

The findings suggest that Imatinib holds promise as a therapeutic intervention for Huntington's disease, demonstrating neuroprotective effects through modulation of various pathways implicated in HD pathology.

KEYWORDS

Huntington's disease (HD), Imatinib, non-tyrosine kinase (c-Abl), neurodegeneration, 3-Nitropropionic Acid (3-NPA).

MULTIPLE SYSTEM ATROPHY-CEREBELLAR TYPE (MSA- C) SURVIVED FOR 6 YEARS AFTER DIAGNOSIS

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INTRODUCTION

Multiple system atrophy (MSA) is a sporadic, progressive neurodegenerative disorder has clinical symptoms characterized by variable combination of Parkinsonism disease like symptoms, cerebellar ataxia & / or autonomic failure. Based on the consensus criteria, patients with MSA are clinically classified into cerebellar (MSA-C) and parkinsonian (MSA-P) subtypes. In addition to major diagnostic criteria including poor response to levodopa, and presence of pyramidal or cerebellar signs (ataxia) or autonomic failure, certain clinical features or "red flags" may raise the clinical suspicion for MSA.

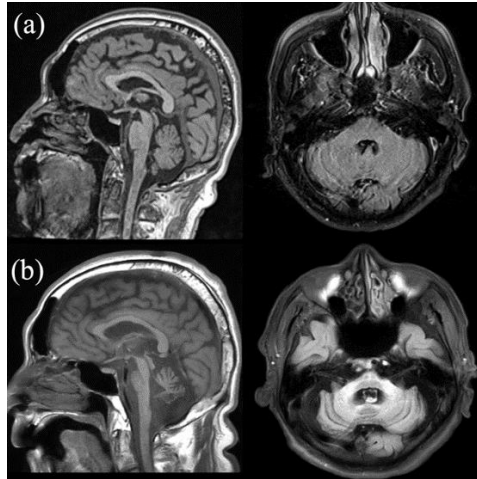
REPORT

In our case report we present a 62-year-old male patient admitted to our hospital due to inability to walk, with poor response to levodopa therapy, whose neurological examination revealed severe Parkinsonism, ataxia and who fulfilled all criteria for MSA, as rarely seen in clinical practice. The brain Magnetic resonance imaging (MRI) showed brain stem and cerebellar atrophy, symmetric cerebral atrophy, as well as the corss sigh in the axial sections of the brain stem. Our patient had early instability, rapid progression, autonomic signs, abnormal posture, bulbar dysfunction, cerebellar dysfunction, and a parkinsonism picture that did not respond to dopaminergic treatment.

CONCLUSION

Multiple system atrophy (MSA) is a rare neurodegenerative disease characterized with glial cytoplasmic inclusion bodies containing alpha synuclein. Clinical features can be manifested as a combination of cerebellar, autonomous and parkinsonian symptoms. It has two subtypes: cerebellar (MSA-C) and parkinsonian (MSA-P). There are very few pathognomonic signs to differentiate MSA-P from Parkinson's disease in the early stage. Rapid progression is one of the very important warning signs for MSA patients. Abnormal postures including Pisa syndrome, anterocollis, and contractures in hands and feet are common in MSA. Development of dysphagia within 1 year of the onset of disease symptoms is reported to be specific (100%) for atypical parkinsonian disorders. Respiratory dysfunction such as inspiratory stridor or sighing is frequent in MSA and rare in PD. MRI is an important tool not only for diagnosis but also for evaluating the clinical features of MSA and the T2-signal changes in the basal ganglia and brain stem on MRI are diagnostically significant.

Figure 1. Brain MRI findings. Mid-sagittal T1-weighted (left side) and Fluid-Attenuated Inversion Recovery images of brain MRI (right side) showed brain stem and cerebellar atrophy 2016 (a). Brain stem and cerebellar atrophy was noticeable in December 2022, and a prominent hot cross bun sign was observed (b).



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INFLAMMATORY DEMYELINATING DISEASE IN A YOUNG GIRL WITH IMPAIRED CONSCIOUSNESS

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INTRODUCTION

Inflammatory demyelinating diseases (IDP) of the central nervous system (CNS) may involve both the brain and spine. Common examples of IDP includes multiple sclerosis, neuromyelitis optica (NMO) and acute disseminated encephalomyelitis (ADEM).

Here, we illustrate the challenges in obtaining the diagnosis in a young girl presented with acute onset of unconsciousness.

CASE REPORT

This is a case of 16-year-old girl who presented with acute impairment of conscious state within a day, preceded by fever and right jaw pain for 2 days. Assessment at Emergency department revealed a stuporous patient with right horizontal gaze preference, neck stiffness, left hemiparesis and bilateral Babinski sign. She was treated for meningoencephalitis. However, the infection screening was negative, with a normal cerebrospinal fluid (CSF) analysis and a negative workup for tuberculosis (TB).

She deteriorated and required mechanical ventilation. Brain MRI with contrast displayed abnormal white matter signal intensities at bilateral deep white matter, cortical and periventricular areas. These areas appear hypointense on T1WI, hyperintense on T2WI, not suppressed on FLAIR and no enhancement on post-gadolinium sequences. Interestingly, there were non-enhancing hyperintense signals within the spinal cord at C2 and C5 vertebra level. She was treated as ADEM and received IV Methylprednisolone for 5 days. She regained full consciousness with the left sided - lower limb strength 2/5, upper limb strength 4/5. She was discharged with tapering prednisolone course as well as intensive physiotherapy.

DISCUSSION

The demyelinating disease of the central nervous system can present with rapid onset of symptoms such as vision changes, weakness, numbness, imbalance, encephalopathy and respiratory distress in severe cases. It can be precipitated by viral or bacterial infections, inflammatory process, genetic predisposition, metabolic and toxic exposure. Yet, some causes are still unrevealed. A high index of suspicion and quick diagnosis and treatment of inflammatory demyelinating CNS disease is crucial to prevent further deterioration as rapid onset of presentation can mimic a vascular events or meningo-encephalitis.

CONCLUSION

A strategy needed to approach a suspected case of demyelinating disease for earlier decision-making to avoid the unbearable complication.

NAVIGATING DIAGNOSTIC DILEMMA: MILLER FISHER SYNDROME IN PREGNANCY MASQUERADING AS STROKE

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INTRODUCTION

Miller Fisher Syndrome (MFS) is a rare variant of Guillain-Barré Syndrome, characterized by the acute onset triad of ophthalmoplegia, ataxia, and areflexia. It is an immune-mediated demyelinating polyneuropathy, often preceded by a viral illness triggering an aberrant autoimmune response, particularly against gangliosides. MFS has a higher incidence among Asian populations compared to Western populations. This case report describes a young woman who initially presented with stroke-mimic symptoms but was diagnosed with MFS after thorough evaluation. Treatment with intravenous immunoglobulin led to clinical improvement and eventual resolution of symptoms after 6 months.

REPORT

A 31-year-old pregnant woman at 26 weeks gestation presented with acute onset of diplopia, generalized weakness, dizziness, nausea and vomiting for 3 days following an upper respiratory tract infection. Examination revealed ophthalmoplegia with restricted eye movements, areflexia and ataxia. Brain CT was normal. CSF analysis showed elevated chloride with anti-GQ1b antibody positivity, confirming Miller Fisher Syndrome diagnosis. She was treated with 5-day intravenous immunoglobulin along with supportive care. Initially her ophthalmoplegia worsened, but subsequently she showed gradual improvement. At 3 months follow-up, she had complete resolution of symptoms. This case highlights the diagnostic challenges of Miller Fisher Syndrome in pregnancy and emphasizes the role of immunotherapy in achieving good clinical outcomes.

CONCLUSION

An acute presentation of diplopia, dizziness and vomiting in a pregnant lady can often misdirect the initial diagnostic considerations towards vascular causes such as posterior circulation stroke or CVT due to the hypercoagulable state associated with pregnancy. Hence, prompt recognition of the characteristic MFS features and knowledge of clinical disease progression are crucial for timely diagnosis and appropriate management of MFS despite the potential for mimicking these vascular presentations.

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PREVALENCE OF LARGE VESSEL OCCLUSION (LVO) AMONG ACUTE ISCHEMIC STROKE (AIS) PATIENTS WITH LOW NIHSS IN MALAYSIA

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INTRODUCTION

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide. The severity of neurological deficit, often measured by the National Institutes of Health Stroke Scale (NIHSS), guides treatment decisions, including the consideration of thrombectomy for large vessel occlusion (LVO). However, there is growing evidence suggesting that some patients with low NIHSS scores may harbor LVO, challenging the current treatment paradigm.

METHODS

A retrospective analysis was conducted on a cohort of acute ischemic stroke (AIS) patients admitted to Hospital Sultan Abdul Aziz Shah, Malaysia, from 2022 to 2023. The study included patients with NIHSS scores ≤ 6 who had large-vessel occlusion (LVO). Imaging findings, specifically the presence of LVO, were extracted from medical records. The prevalence of LVO among AIS patients with low NIHSS scores was calculated, and relevant clinical characteristics were analyzed.

RESULTS

Among the 633 AIS cases included in the study, 29 patients (4.6%) presented with low NIHSS scores and were found to have LVO on imaging. The distribution of LVO mainly in the anterior circulation 27(93%) compared to posterior circulation 2(7%). Among these patients, most patients had middle cerebral artery occlusion (M1 or M2) 16(55%) in comparison to internal carotid artery (ICA) and anterior cerebral artery (ACA) occlusion 16(55%) vs 9(31%) respectively. The mean NIHSS was 2 (SD =1.85).

CONCLUSION

This retrospective reveals a notable prevalence of LVO among AIS patients with low NIHSS scores. These findings underscore the importance of heightened clinical suspicion and advanced imaging modalities, such as CT angiography or MR angiography, in identifying LVO in this patient population. Tailored treatment approaches, including the consideration of thrombectomy, may be warranted to optimize outcomes in AIS patients with low NIHSS scores and LVO. Further research and prospective studies are needed to validate these findings.

DISSEMINATED TUBERCULOSIS MASQUERADING AS A PSYCHIATRIC ILLNESS – A CASE REPORT

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INTRODUCTION

Disseminated tuberculosis (DTB) is rare. It can affect any organ systems. We report a patient who presented essentially for psychiatric symptoms of three months' duration. Only later on, she was diagnosed with a case of DTB affecting the central nervous system as well as the spine and lungs.

CASE PRESENTATION

An elderly lady with behavioral changes (apathy, fear, and restlessness), which started insidiously 3 months earlier and progressively worsened, was referred to us for exclusion of organic brain disorder. Clinical neurological examination and Mini Mental Scale Examination (MMSE) were normal. Except for elevated CRP, ESR and raised CSF opening pressure on lumbar puncture, the autoimmune and para-neoplastic markers, as well as the electroencephalogram (EEG), chest X-ray and CT scan of the brain were normal. The CSF cell counts, and microbiology was also normal. After a short course of empirical intravenous ceftriaxone and acyclovir she was discharged with advice to consult a psychiatrist. During follow up, 8 weeks later she complained of back pain though her abnormal behavior persisted. Investigations revealed a T12 compression fracture with irregularity of the left T12 pedicle and paraspinal fluid collection on MRI spines. A provisional diagnosis of TB spine was made which was confirmed when the pus that was drained from the collection and stained with ZN stain showed Mycobacterium tuberculosis bacilli. During this admission, the CT scan thorax showed left lower lobe consolidation with pleural effusion and right lung nodules. Contrast CT scan brain revealed subtle meningeal enhancement at the right parietal region. Treatment with a 4-drug anti-TB regiment along with a short course of dexamethasone resulted in significant improvement in all her symptoms.

CONCLUSION

This case report indicates that the initial clinical presentation of DTB can be bizarre and misleading resulting in challenges for diagnosing and delay in initiating treatment.

A CASE REPORT ON ANTI-YO ANTIBODY ASSOCIATED PARANEOPLASTIC CEREBELLAR DEGENERATION

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INTRODUCTION

Paraneoplastic neurological syndromes (PNSs) are immune-mediated disorders provoked by tumors expressing neuronal proteins.

REPORT

We report a case of a 47-year-old female presented with progressive imbalance and vertigo, initially treated as vestibular neuritis. Following persistent symptoms, she was referred to a neurologist and eventually diagnosed with possible ataxic Guillain-Barré Syndrome or Miller Fisher syndrome, though treatment was not initiated due to late presentation. Over five months, her condition worsened, leading to significant weight loss, severe cerebellar ataxia, and reliance on a wheelchair. Despite normal initial MRI and basic investigations, subsequent MRI revealed prominent cerebellar atrophy. A positive Anti-Yo antibody test suggested paraneoplastic cerebellar degeneration (PCD), and a PET scan revealed a possible breast malignancy. A biopsy confirmed metastatic adenocarcinoma. Intravenous immunoglobulin and methylprednisolone did not offer much improvement. Due to her frailty, she could not undergo chemotherapy or surgery. PCD is characterized by rapid cerebellar dysfunction often linked to anti-Yo antibodies either from breast or gynecological tumors. The prognosis is generally poor, with most patients remained disabled despite tumor treatment and immunotherapy. Early immunotherapy may offer some benefits, although recovery is rare. Survival varies based on the associated antibody and neoplasm, with poorer outcomes associated with anti-Yo antibodies and advanced age.

CONCLUSION

The prognosis is generally poor, with most patients remained disabled despite tumor treatment and immunotherapy. Early immunotherapy may offer some benefits, although recovery is rare. Survival varies based on the associated antibody and neoplasm, with poorer outcomes associated with anti-Yo antibodies and advanced age. This case highlights prompt recognition and treatment which are crucial to the prevention of significant disability in PCD.

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A RARE PRESENTATION OF ANTI-SULFATIDE IGG POSITIVE IN TUBERCULOSIS

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BACKGROUND

Guillain-Barre Syndrome (GBS) is the most common acute-immune mediated polyneuropathies. It is a rare, but potentially fatal, immune-mediated disease of the peripheral nerves and nerve roots that is usually triggered by infections. We report a rare case of GBS presenting as an acute progressive limb weakness in a Tuberculosis patient.

REPORT

A 63-year-old male complained of a chronic cough for 2 months, associated with a significant loss of appetite and weight. He presented to the Emergency Department with acute shortness of breath, which clinical findings suggestive of left-sided pleural effusion. This was further confirmed with a chest X-ray and diagnostic pleural tapping, which showed an exudative nature. He was able to ambulate well in the ward; however, a few days after admission, he complained of progressive weakness and numbness in his lower and upper limbs. He was unable to walk or grip his bilateral hands. Clinical examination revealed bilateral facial nerve palsy and distal lower motor neuron weakness in both upper and lower limbs. He was areflexic with reduced sensation in his distal hands and legs. A nerve conduction study was conducted, revealing a demyelinating type of sensorimotor polyneuropathy with secondary axonal degeneration. A lumbar puncture was not performed due to lack of consent. He was treated as Guillain-Barré syndrome (GBS) and started on plasma exchange for a total of 5 days. Serum anti-ganglioside tested positive for anti-sulfatide IgG, further confirming the diagnosis. After a few weeks of admission, his sputum Mycobacterium tuberculosis (MTB) culture returned positive. He was treated for smear-negative pulmonary tuberculosis and started on anti-TB medication. He underwent intensive rehabilitation and was discharged well, with minimal neurological deficits after 3 months.

CONCLUSION

This case highlights the importance of maintaining high suspicion of GBS in tuberculosis despite its infrequent correlation. It stresses the importance of prompt intervention to optimize the clinical outcomes.

LIES UNRAVELING TRUTH: ETHICO-LEGAL ANALYSIS OF SALINE PROVOCATION (NOCEBO) TEST IN DIAGNOSING PSYCHOGENIC NONEPILEPTIC SEIZURE

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INTRODUCTION

Saline provocation is a nocebo diagnostic test used to distinguish psychogenic nonepileptic seizures from epileptic seizures. Its practice in neuropsychiatry has been controversial and raises ethical concern. A 17-year-old gentleman with recurrent seizure-like episodes was initiated on levetiracetam by his general practitioner and was admitted to our institution during a breakthrough seizure. He has history of febrile seizure and persistent depressive disorder. We performed an in-patient video-monitored encephaloelectrogram (EEG) along with a saline provocation test. The test was positive, leading to the deprescription of his anti-seizure medication and referral to the psychiatric team. In this abstract, we examine the ethical and legal concerns surrounding the use of nocebo test in this case.

METHODS

We conducted a retrospective ethical analysis using the Four Quadrant Approach and a doctrinal legal research on laws, legislation and policies guiding the saline provocation test.

RESULTS

The saline provocation test is an invasive technique with a high benefit-risk ratio. Deception is central to the test, risking erosion of the fiduciary doctor-patient relationship. Additionally, the patient's subjective experience of the pseudoseizure and the accompanying physical injury should not be overlooked. Lastly, obtaining only verbal consent and using a non-protocolized approach undermine the standard of care in performing the test.

CONCLUSION

Saline provocation test for psychogenic nonepileptic seizure is a controversial diagnostic procedure subjected to ethico-legal scrutiny. We recommend that the institutions establish a written policy and require practitioners to obtain written informed consent prior to conducting the test.

MILLER FISHER SYNDROME MIMICKING BRAINSTEM STROKE SYNDROME

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INTRODUCTION

Miller Fisher syndrome is a rare variant of Guillain Barre syndrome, an autoimmune demyelinating disease that affects almost 100000 worldwide every year. Miller Fisher syndrome classically presents with ataxia, areflexia and ophthalmoplegia. We present to you 2 cases of Miller Fisher syndrome mimicking brainstem stroke.

CASE PRESENTATION

A 58-year-old Malay female with underlying hypertension presented with 5 days history of giddiness and vomiting, associated with generalised weakness. On examination, power over all limbs are full, however, she was unable to perform tandem gait. Cranial nerves examination revealed bilateral internuclear ophthalmoplegia. A CT brain was done showing no abnormality. She was treated as posterior circulation stroke and an MRI brain was ordered. In the ward, her ophthalmoplegia progressed to bilateral vertical gaze restriction and complete palsy of right eye movement leading to the diagnosis of complex ophthalmoplegia. Further examination revealed absent reflexes over all limbs. An urgent brain MRI/MRA was performed which was unremarkable.

The second case entails a 41-year-old Malay male with underlying hypertension who presented with unsteady gait for 2 days. On examination his power of all limbs were full with no cerebellar signs, however it was difficult to elicit reflexes. A plain brain CT showed no abnormalities. Similarly, he was treated as posterior circulation stroke. However, in the ward, he developed complex ophthalmoplegia.

In both cases, the diagnosis was revised to Miller-Fisher syndrome guided by the development of complex ophthalmoplegia. Other supporting features were cytoalbuminological dissociation on CSF examination of case 1 and anti GQ1b Ab positivity in case 2.

CONCLUSION

These 2 cases illustrate the importance of proper eye examination and the need for a sensible list of differentials when dealing with acute eye movement abnormalities which can mimic a posterior circulation stroke syndrome.

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OUTCOME OF INTRAVENOUS THROMBOLYSIS IN HYPERACUTE STROKE TREATMENT IN TERTIARY CENTRE: A 3 YEAR EXPERIENCE IN HOSPITAL SULTAN ABDUL AZIZ SHAH

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INTRODUCTION

Intravenous thrombolytic therapy is an advancement of hyperacute stroke treatment with strong association of good functional outcome. Hospital Sultan Abdul Aziz Shah is a leading tertiary center which provides hyperacute and comprehensive stroke treatment in Malaysia. This study aims to assess functional outcome of thrombolysis using Modified Rankin Score (mRS) score at 90 days including safety outcome as intracranial bleeds and all-cause mortality as well as specific predictors for both outcomes.

METHODS

This is a single-center retrospective analysis to assess overall functional and safety outcome among eligible hyperacute ischemic stroke patients treated within 4.5 hours after stroke with intravenous thrombolysis. Data were collected and analyzed from Hospital Sultan Abdul Aziz Shah (HSAAS) stroke registry that include all intravenous thrombolysis stroke patients from the year of 2020 to 2023. Data then analyzed using IBM SPSS Statistic Version 29.0.0 (241).

RESULTS

Good functional outcome at 90 days defined as mRS 0-2 was seen in 82 (43.6%) patients and poor functional outcome (3-6) was seen in 20 (10.7%) patients. Univariate and Multivariate analysis of the study variables was done to detect the significant independent predictors of the functional outcome. Diabetes melitus (P value 0.039*OR 1.381 (95% C.I)) and hypertension (P value 0.038*OR 1.464 (95% C.I) both were the significant independent predictor of poor functional outcome.

On the other hand, mRS prior discharge is a single most important strong predictor not only for good functional outcome at 90 days (P value <0.001*OR .3.167 (95% C.I)), but also safety outcome in all-cause mortality within 90 days (P value 0.02*OR 1.415 (95% C.I)).

CONCLUSION

Intravenous thrombolytic therapy improves the functional outcome of acute ischemic stroke patients. Also, hypertension, dyslipidemia and mRS at discharge could be used as independent predictors of the functional and safety outcome.

A CASE OF EARLY ONSET PARKINSON'S DISEASE WITH SNCA DUPLICATION IN A BIDAYUH GENTLEMAN FROM SARAWAK

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INTRODUCTION

Monogenic Parkinson's disease in which a single pathogenic mutation can be identified is accountable for 5-10% of Parkinson's disease (PD) cases. SNCA mutations are the second most common cause of autosomal dominant inherited PD¹. With Sarawak being home to many indigenous ethnic groups, these vast under represented population and its genetic prevalence of monogenic PD remains unknown. In a recent study by Tay et al there were no reported SNCA mutations found in a Malaysian cohort² highlighting its rarity. We report a case of a sporadic SNCA duplication presenting as a typical early onset Parkinson's disease (EOPD) and describes his associated clinical features.

CASE REPORT

The patient was a 54-year-old gentleman of Bidayuh ethnicity, indigenous to Sarawak in Borneo and East Malaysia. His initial symptoms started at age 36 with left upper limb resting tremors and also a progressive onset of slowness in gait affecting his occupation as a Farmer. Family also reported he had dream enactments and sleep vocalizations resembling Rapid Eye Movement (REM) sleep behaviour disorder preceding his motor symptoms for years. He was from a non-consanguineous parental union and did not have any relevant family history. His motor symptoms progressed to bilateral involvement and was eventually referred to a Sarawak General Hospital Neurology Unit which led to a diagnosis of EOPD at the age of 39.

The results of laboratory tests including a full blood count, metabolic renal and liver profiles were normal. As well as a plasma ceruloplasmin levels and 24-hr urine copper excretion were within normal limits. A brain MRI with T1/T2 weighted sequences showed no abnormal signals in the basal ganglia. As part of a genetic study, molecular testing was sent to University Malaya Medical Centre in 2021 and screening of common EOPD-associated copy number variations (CNVs) was performed using the multiplex ligation-dependent probe amplification (MLPA) assay. Based on the CNV screening, the patient was found to carry a rare SNCA gene duplication.

The patient was initiated on levodopa-benserazide(200/50mg) and dopamine agonists with ropinirole and was maintained with minimal dose increments and able to achieve a good treatment response with improved motor function for the first 5 years of his follow up. As his disease progressed beyond year 6 on treatment, he started developing motor response fluctuations with wearing off and dose failures. Higher doses of Levodopa up to 1.2g/day in divided doses evoked a mild peak dose choreiform dyskinesia in the upper and lower limbs. Throughout the course of the patient's disease the patient developed prominent psychiatric symptoms, including anxiety and psychosis which persisted with medication adjustments and required low dose Quetiapine for symptom control. His cognition function remained intact with a Mini-Mental State Examination (MMSE) score of 26/30. His motor complications evolved to develop truncal axial deformity with camptocormia and gait freezing which was unresponsive to levodopa and rendered him severely disabled. He also experienced significant and symptomatic postural hypotension towards the later stages and unfortunately died at home at the age of 54.

CONCLUSION

We present, to our knowledge a firstly reported case of early onset Parkinson's disease with a rare SNCA duplication in an indigenous Bidayuh ethnic gentleman from Sarawak. The patient's clinical phenotype was of a typical PD motor features and non-motor features¹. Further epidemiologic and genetic studies are required to better understand and provide insights into the genetic prevalence and spectrum in under-represented ethnic groups in this region.

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CLINICAL FEATURES, EEG CORRELATES, AND OUTCOMES OF PATIENTS ADMITTED WITH MENINGITIS IN THE MEDICAL WARDS OF HOSPITAL CANSELOR TUANKU MUHRIZ, MALAYSIA

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Introduction

Meningitis is a central nervous system infection prevalent in developing countries, including Malaysia. Despite its significance, local data on the clinical characteristics of meningitis are scarce. This study collected and analyzed data on patients with a clinical diagnosis of meningitis to determine their treatment outcomes.

Method

This retrospective study collected data from January to December 2023 for consecutive patients diagnosed with meningitis and admitted to the medical wards of Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia. Exclusion criteria included brain tumors, drug intoxication, brain surgery, or metabolic encephalopathy.

Results

The study recruited 23 patients with a mean age of 45.13 years (SD $\pm$ 20.32). The majority of patients (69.6%) were male, and the median duration of hospitalization was 13 days (IQR 8-18). The predominant clinical features at presentation were altered behavior and seizures. Normal brain imaging findings were observed in 12 patients (52.2%). The median cerebrospinal fluid (CSF) protein level was 470 mg/dL (IQR 291-608), and the mean CSF glucose level was 4.14 mmol/L (SD $\pm$ 1.11). The mean sodium level was 139 mmol/L (SD $\pm$ 1.11), and the mean total white cell count was $12.4 \times 10^9/L$ (SD $\pm$ 6.12). EEG abnormalities were detected in 18 patients (78.3%), with generalized slowing being the most common finding, observed in 12 patients (52.5%). Following treatment, 20 patients (87%) showed improvement, while 2 patients succumbed, and one patient remained bedbound.

Discussion

The timely diagnosis of meningitis relies primarily on clinical features, supported by laboratory and radiological findings. Although EEG is not typically used for diagnosing meningitis, it can provide additional information regarding the extent of cerebral dysfunction. Despite negative cultures, most patients recovered fully with empirical ceftriaxone and acyclovir treatment. Early recognition of the main clinical features of meningitis is crucial for timely treatment to prevent morbidity and mortality.

Conclusion

This study highlights the importance of early diagnosis and intervention in managing meningitis. Clinical features, laboratory results, and radiological findings play an essential role in the diagnosis, while EEG can be a valuable tool to assess the severity of cerebral dysfunction and potential complications. Most patients respond well to empirical treatment, emphasizing the need for prompt medical therapy to improve the outcome.

EXECUTIVE FUNCTION AMONG MALAYSIAN CHILDREN WITH EPILEPSY

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INTRODUCTION

This study aims to determine the prevalence of executive function (EF) deficit and its associated risk factors among children with epilepsy (CWE) in UMMC. CWE frequently encounter challenges in executive function, which can have a considerable effect on their overall well-being. These challenges may involve limitations in cognitive functions like focus, short-term memory, critical thinking, and making decisions.

METHODS

Cross-sectional study of all CWE aged 5 to 18years old with at least 6months' duration of epilepsy attending mainstream school seen in UMMC clinic in 2023 were recruited. Executive function was measured using the parent-proxy and child self-report of Behaviour Rating Inventory of Executive Function (BRIEF), Quality of life was measured using the parent-proxy and child self-report of Quality of Life Measurement for Children with Epilepsy (CHEQOL-25) questionnaire. Strength and Difficulty (SDQ), and Parenting Stress Index (PSI) were also administered as part of the evaluation.

RESULTS

A total of 121 CWE and their parents participated in the study. Executive dysfunction on the BRIEF is indicated by T scores ≥ 65 . In general, all the subscales and indices for BRIEF has a mean T-score of <65 . Global Executive Composite (GEC) which is the overall index of the BRIEF score; mean 56.07 (SD: 9.57). There is no significant change in the quality of life of CWE with BRIEF T-score of <65 or ≥ 65 . The contributing factor to abnormal BRIEF score were found out to be i) SDQ hyperactivity in Behaviour Regulation Index (BRI) ($p=0.020$), Emotional Regulation Index (ERI) ($p<0.001$), Cognitive Regulation Index (CRI) ($p<0.001$) and GEC ($p<0.001$); ii) SDQ conduct in ERI ($p=0.022$), iii) PSI parent-child dysfunctional interaction in BRI ($p=0.037$), and GEC ($p=0.024$); iii) Chinese ethnicity in BRI ($p=0.015$).

CONCLUSIONS

Our result shows that hyperactivity is the main contributing factor in executive function deficit. Parental stress and ethnicity may also affect CWE executive function. In children with hyperactivity and executive function deficits, there is a significant impact on their daily functioning and overall development. These deficits can affect various aspects of their lives, such as their ability to pay attention, solve problems, plan and organize tasks, control impulses, and manage their emotions.

VALIDATION OF THE HATTORI SCORE AS A SCREENING TOOL FOR DRAVET SYNDROME IN TWO MALAYSIAN TERTIARY CARE CENTRESPooven Raj Selva Rajah¹, Chow Su Ying¹, Khadijah Husainy², Nor Azni Yahya², Sindhu Viswanathan¹¹ Paediatric Department, Hospital Pulau Pinang, Pulau Pinang, Malaysia.² Paediatric department, Hospital Raja Perempuan Zainab II, Kota Bharu, Malaysia.**INTRODUCTION**

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy. Early diagnosis leads to appropriate anti-seizure medications institution, but is often delayed. The Hattori score (HS) is a screening test with high sensitivity and specificity for DS, especially when scored above 6. Its clinical components include seizure onset age, presence of more than 5 seizures, presence of myoclonic, focal or hemiclonic seizures, or prolonged seizures (> 10 minutes) and hotwater bath seizures. We sought to retrospectively analyse and validate HS as a screening test for patients with DS in two tertiary Malaysian hospitals.

METHOD

We screened the paediatric neurology database at Hospital Pulau Pinang and Hospital Raja Perempuan Zainab II for patients with confirmed DS and reviewed demographic and epileptology data. We interrogated records for Hattori score clinical criteria and ages at which these criterion weremet. We calculated the earliest age at which HS reached ≥ 6 , indicating a high specificity (>94%) for DS. This was compared to the age of first clinical DS suspicion.

RESULTS

We studied 23 patients (7 male) with median age of 10.3 years (3 -21 years). Mean seizure onset was at 5.7 months (2-11 months). The median age at which HS of more than 6 was achieved 9.5 months (4-34months) versus the median age of first clinical suspicion of DS, which was 24 months (5 months- 13 years). The discrepancy between these two ages was on average 14.5 months. 22/23 (96%) patients' clinical suspicion of DS was after a first neurologist review.

CONCLUSION

Hattori score accurately predicted DS with a 14.5 month lead time. HS should be introduced to clinicians managing paediatric seizures to identify and timely escalate these patients to neurologists. This may improve clinical outcomes as neurologists have more access to appropriate anti-seizure medications for these children.

USE OF TELEMEDICINE BY PARENTS OF AUTISTIC CHILDREN DURING THE COVID-19 PANDEMIC AT HOSPITAL SULTAN ISMAIL JOHOR BAHRU

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INTRODUCTION

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition. Early and regular intervention play a crucial role in improving the behavioural, social, and academic outcome. The COVID-19 pandemic disrupted traditional hospital services, necessitating innovative approaches such as telemedicine to deliver interventions for children with ASD.

METHODS

A quasi-experimental design was used whereby one group was studied before and after a telemedicine intervention. The sample population was drawn from parents of children with newly diagnosed ASD, who underwent online parental training (telemedicine) for six (6) months between July 1, 2021, and December 31, 2021 at Hospital Sultan Ismail Johor Bahru. Participants' children were between 2-6 years' old. The total number of participants was 125. Data on socioeconomic circumstances, parental perception of the telemedicine intervention, and parental competence were collected via a questionnaire given to parents during clinic visits, after written informed consent was obtained. The intervention was in three parts, delivered online by a consultant developmental paediatrician or developmental paediatrics clinical fellow. All parts incorporated question and answer sessions. (1) Part 1: Three-hour educational talk focusing on symptoms, diagnosis and management of ASD, school placement, welfare registration, coping strategies and sibling matters, (2) Part 2: Three-hour seminar, including videos and practical sessions, focusing on parent coaching and strategies to improve social and communication skills in minimally verbal children, (3) Parent-mediated Connect and Communicate (PCCP) workshop: Five-hours of parent coaching using the DIR® Floortime model, a structured play therapy model to improve children's social communication skills. Developmental progress pre- and post-intervention were assessed using standardised tools (Symbolic Play Test, CAPUTE Scales, and Brigance Early Childhood Screens III), during follow up. Additional pre- and post-intervention data were collected through review of electronic medical records.

RESULTS

More than three-quarters (76.0%) of parents reported increased knowledge about their child's condition, and 72.8% reported improved confidence in managing their child's behaviour, following the telemedicine intervention. Over half (52.0%) experienced reduced anxiety, while 36.8% felt better understood by others. Approximately four out of five (80.8%) agreed that the series of talks and parental guidance had a positive and significant impact on their child's progress. Furthermore, overall parental competence, as measured by the Parenting Sense of Competence (PSOC) scale, indicated an increase in competence, whereby the overall median score was 56 (interquartile range: 44 to 68). There were significant improvements in



developmental progress of the children, as measured by developmental quotients (DQ) pre- and post-telehealth intervention ($p < 0.05$).

CONCLUSION

Telemedicine was well-received by parents of children with ASD, leading to increased parental competence and significant developmental progress in these children. These findings underscore the potential of telemedicine as an effective approach for supporting autistic children in Malaysia and highlight the need for its widespread adoption.

KEYWORDS

Autism spectrum disorder (ASD), telemedicine, parental perception and competence, developmental progress

JUVENILE MYASTHENIA GRAVIS: A CROSS SECTIONAL STUDY OF CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES IN A TERTIARY PAEDIATRIC NEUROLOGY CENTER IN MALAYSIA

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INTRODUCTION

Juvenile myasthenia gravis (JMG) is an autoimmune condition affecting the neuromuscular junction in those below 18 years old, most commonly associated with anti-acetylcholine receptor antibodies (AChRAb). It is termed as ocular myasthenia gravis (OMG) when only ocular muscles are affected, and systemic myasthenia gravis (SMG) when systemic muscles are involved. This study describes the clinical characteristics and treatment outcomes of a cohort of JMG in Malaysia.

METHODS

The electronic medical records were searched from 1st January 2019 until 1st May 2024 for all patients diagnosed with JMG attending the paediatric neurology clinic of Hospital Tunku Azizah, Kuala Lumpur. Clinical information including age of onset, ethnicity, gender, duration of follow up, family and personal history of autoimmune disease, clinical subtypes, preceding events, initial manifestations, AChRAb testing, repetitive nerve stimulation results, treatment, complications and outcome were collected. Outcome at the last clinic visit was determined according to Myasthenia Gravis Foundation of America Post-Intervention Status (MGFA-PIS).

RESULTS

38 JMG patients were identified of which 60% had OMG and 40% had SMG. SMG showed a female preponderance (73% female) but OMG showed a male preponderance (70% male). 79% had AChRAb positive with no significant preceding events, personal or family history of autoimmunity. All patients presented with ptosis with 9 (24%) having systemic symptoms at onset and another 6 (16%) developing systemic symptoms later. Most received treatment (36/38). All those treated received pyridostigmine; half received IVIG (18/36); some received steroids (26/36); azathioprine (8/36); and only 3/36 had thymectomy. 9 with SMG had systemic crises of which 4 patients required intubation. Most had optimal outcomes (71%) while most with non optimal outcomes had an improvement in clinical status (21%).

CONCLUSION

Most JMG patients in this cohort have similar characteristics to other international cohorts and most have optimal outcomes with treatment.

FACTORS PREDICTING POOR MENTAL HEALTH AMONG PARENTS OF PRESCHOOL CHILDREN WITH AUTISM SPECTRUM DISORDER

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INTRODUCTION

Families of children diagnosed with autism spectrum disorder (ASD) experience more dysfunction and instability than “typical” families, leading to an increase in parenting stress. Parents who are unable to cope with parenting stress may resort to maladaptive coping mechanisms or exhibit psychological symptoms such as depression and anxiety. This study aims to explore the incidence of depression, stress, and anxiety among parents of children with ASD and the factors affecting it.

METHODS

This was a cross-sectional descriptive study which recruited parents of preschool children aged 30-72 months who are diagnosed with ASD. The subjects were recruited from the child developmental clinic of a tertiary hospital run by developmental paediatricians. Parents were asked to fill in a questionnaire which included baseline demographics, Parent Sense of Competence-Revised (PSOC-R) scale, Depression Anxiety Stress Scale-short form (DASS), Strength and Difficulties Questionnaire (SDQ) and Social Responsiveness Scale (SRS).

RESULTS

A total of 99 parent-child dyads were recruited into the study. Most children were male (76.8%), and the questionnaires were answered mainly by their mother (67.7%). A significant number of parents had symptoms of moderate to extremely severe depression (28.3%), anxiety (48.5%), and stress (20.2%). The PSOC had a median score of 72 (minimum 27, maximum 94). Demographic variables such as the child's age, parental gender, race, family income, education, and employment were not associated with increased DASS scores. PSOC scores were negatively correlated with depression subscale scores. Higher SRS and SDQ scores were positively correlated with poorer mental health.

CONCLUSION

Parents with poorer mental health had a lower sense of competence and had children with more behavioural problems and social communication impairment. Parental training, which would increase parent competence and self-confidence, might be beneficial in improving mental health. Active screening of mental health should be done among parents of autistic children with severe dysfunction.

HYPOTONIC MALE INFANT WITH NEURODEVELOPMENTAL DELAY; THINK OF MCT 8 DEFICIENCY

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INTRODUCTION

Thyroid hormones play a vital role in human brain development, regulating neural cell migration and differentiation, synaptogenesis, and myelination. MCT8 deficiency is caused by genetic abnormalities in the thyroid hormone transporter, monocarboxylate transporter 8 (MCT8)¹. This X- linked recessive disorder is characterized by severe intellectual disability and hypotonia which impair the life expectancy of patients with MCT8 deficiency¹.

REPORT

We report a case of a 10-year-old boy who is the first child of non-consanguineous young parents who presented with global developmental delay and only came to our attention at 10 months of age. He failed to thrive but had no obvious feeding difficulties. On examination, he was a floppy infant with central hypotonia and poor head and truncal control. He had variable limb tone with some dystonic posturing intermittently and brisk reflexes but no clonus. His MRI brain revealed slow myelination for his age and no evidence of structural brain anomalies. Interestingly, his thyroid function revealed normal TSH, low T4, and high T3. A molecular test of the SLC16A2 gene was done, which then confirmed the diagnosis of MCT-8 specific thyroid hormone cell membrane transport deficiency.

CONCLUSION

In the past decade, despite various new publications on MCT 8 deficiency, no therapeutic strategies have been registered for this neurocognitive debilitating disease, which results in a decreased life expectancy for patients². Yet, it is important to have a high index of suspicion, as a simple evaluation with a thyroid function test, including T3 levels, can lead to proper genetic testing to establish a fast and accurate diagnosis without the need for unwarranted testing. In addition, at-risk families could receive proper genetic counselling once a diagnosis is established.

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CURIOUS CASES OF INTRACTABLE HICCUPS AND VOMITING

Muhamad Azamin Anuar, Mardhiah Majid, Shafiq Kamarudzaman, Rohaya Mohamad, Nor Azni Yahaya

BACKGROUND

The area postrema syndrome (APS) represents a distinctive diagnostic criterion for a variant of neuromyelitis optica spectrum disorders. While hiccups and vomiting are nonspecific symptoms in medical practice, chronic and intractable occurrences should raise suspicion for APS. This neurological condition involves inflammation and demyelination of the area postrema, a region in the dorsal medulla oblongata responsible for regulating vomiting and other autonomic functions.

CASE PRESENTATION

We present the cases of two paediatric patients, aged 9 and 11 years, who presented with persistent and worsening hiccups and vomiting despite empirical treatment for common conditions. Initially, diagnostic investigations were directed towards ruling out gastrointestinal, respiratory, and urinary tract disorders. However, as symptoms progressed, the patients exhibited additional signs, including dysphagia and bulbar dysfunctions, alongside relative weakness in the upper limbs.

Upon consultation with paediatric neurology specialists and subsequent neuroimaging with MRI scans of the brain and cervical spine, both patients revealed characteristic demyelinating lesions localized to the area postrema. Furthermore, serological testing confirmed the presence of anti-aquaporin-4 antibodies, supporting the diagnosis of APS.

While immunotherapy was promptly initiated in both cases, one patient unfortunately succumbed to complications arising from newly diagnosed hypertrophic obstructive cardiomyopathy (HOCM), identified post plasma exchange therapy. Conversely, the second patient demonstrated favourable response to treatment and is currently undergoing outpatient follow-up, showing signs of improvement.

CONCLUSION

The presented cases underscore the importance of considering APS in the differential diagnosis of chronic and intractable hiccups and vomiting, particularly in paediatric patients. Early recognition and intervention are crucial in preventing delays in diagnosis and treatment, as misdiagnosis can lead to adverse outcomes. Heightened clinician awareness of APS and its clinical manifestations is paramount to facilitate timely management and improve patient prognosis.



THESE CHILDREN DON'T FEEL PAIN

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BACKGROUND

Hereditary Sensory and Autonomic Neuropathy (HSAN) IV is a rare autosomal recessive disorder characterized by a reduction in both myelinated and non-myelinated nerve fibres of peripheral nerves, resulting in diminished or absent pain sensation and increased self-mutilated behaviours. This condition poses significant challenges in diagnosis and management, underscoring the need for increased awareness among paediatricians.

METHODS

We conducted a retrospective study of five cases, ranging in age from 5 to 13 years, to elucidate the clinical features and diagnostic investigations associated with HSAN IV. The cases presented a spectrum of manifestations, from oral and digital signs to severe complications such as unexplained fractures. All patients exhibited congenital insensitivity to pain and anhidrosis. Notable oral self-mutilations included autoextraction of teeth and severe bite injuries, with one patient developing osteomyelitis and three others experiencing Charcot arthropathy. Tragically, one patient succumbed to septic shock secondary to chronic *Staphylococcus aureus* skin infection. Nerve conduction studies revealed normal findings in three patients, while all patients tested positive for NTRK1 gene mutation, confirming the diagnosis of HSAN type IV. Additionally, all patients presented with patterns of learning disability.

CONCLUSION

Our study underscores the critical importance of early diagnosis and the implementation of specific management strategies to mitigate the characteristic oral, digital, joint, bone, and skin trauma associated with HSAN IV. Timely recognition of this condition can facilitate the implementation of preventive measures and appropriate interventions to improve patient outcomes and quality of life.

EFFECTIVENESS OF PARENT TRAINING IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND AVOIDANT RESTRICTIVE FOOD INTAKE DISORDER AT CHILD DEVELOPMENT CLINIC, HOSPITAL PULAU PINANG (CDC HPP)

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INTRODUCTION

Avoidant Restrictive Food Intake Disorder (ARFID) is characterized by persistent disturbance in feeding resulting in inability to meet nutritional and/or energy needs. ARFID is common among children with autism spectrum disorder (ASD). Unrecognized and untreated ARFID leads to various macronutrient and micronutrient deficiencies resulting in serious complications. This study aims to assess the effectiveness of parent training on dietary modifications in this group.

METHOD

This is a quasi-experimental study involving 40 children aged 3-11 years old with ASD and ARFID seen at CDC HPP from 1st March 2024 until 28th February 2025. Recruited parents complete Brief Autism Mealtime Behaviour Inventory (BAMBI) questionnaire and 24-hour dietary intake before and 6 months post intervention. Interventions include an individualised dietary consultation, 2- hour virtual interactive session and monthly follow up phone calls for 6 months. Pre and post intervention data including children's growth parameters, mealtime behaviours, macronutrients and energy intake will be analysed using paired t-test.

RESULTS

This study is still ongoing. Preliminary pre-intervention results for 10 patients reported mean energy intake of 1540 kcal/day which is adequate for recommended nutritional intake (RNI). Their mean protein intake was 54.9g/day, fat intake was 56.7g/day and carbohydrate intake was 200.6g/day. All the macronutrient intakes were more than the RNI. All of them have no or very minimal vegetable intake. All parents scored more than 34 in BAMBI, signifying significant mealtime behaviours. 50%, 20% and 30% of them had z score below -2 for weight, height and BMI respectively. There is 1 child (8.3%) with anemia, 1 with iron deficiency and another 1 with vitamin D insufficiency. Our limitation includes reporting bias in dietary recall by parents.

CONCLUSION

There is a high prevalence of nutritional deficiency in children with ASD and ARFID. Preventive measures including dietary intervention are much needed to prevent serious complications.

**PREPARING PARENTS OF CHILDREN WITH AUTISM SPECTRUM
DISORDER (ASD) FOR ADOLESCENCE: CHILD DEVELOPMENT CENTER
HOSPITAL PULAU PINANG (CDC HPP) EXPERIENCE**

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INTRODUCTION

The increasing number of children with ASD reaffirms the need to improve targeted interventions and transition supports. Information about parents' need and expectation for their children with ASD is lacking. This study aims to identify parents' need in preparing their child with ASD for adolescence and to ascertain correlation between children's ASD severity and cognitive function with parenting stress.

METHODS

Descriptive study of all 36 parents with children of ASD aged 9 to 12 years, attending "Supporting Pre teens with ASD" workshop. Pre and post workshop self constructed questionnaires, Autism Parenting Stress Index (APSI) form, Social Responsiveness Scales 2 (SRS-2) and Raven's 2 are completed. Parents' are also interviewed to identify their needs in preparing their child for adolescence. Data analysis is done via thematic analysis and multiple regression analysis by using SPSS.

RESULTS

This study is still ongoing. Our preliminary findings showed that all parents have concerns in social skills, mental health, local health care and educational service. 75% of the parents think social skills involving interpersonal relationship and coping skills are needed. 50% of children involved were categorized as having ASD level 1 (SC I RRB II) and level 2 (SC II RRB II) severity respectively. The APSI scores are low (range: 6-13) and parents reported more stress in dealing with core symptoms of ASD.

CONCLUSION

Social skills are the primary concern of parents of children with ASD. This aspect of training is much needed for children with ASD to transition into adolescence.

JAMUAR SYNDROME: A CASE REPORT ON AN EXCEEDINGLY RARE DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY DUE TO A GLYCOSYLATION DISORDER

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BACKGROUND

Developmental and epileptic encephalopathies (DEE) occur when developmental impairment is beyond that expected from the epileptic activity alone¹ often with a genetic aetiology². Jamuar syndrome is an exceedingly rare autosomal recessive DEE due to variants in *UDGH* gene. Here, drug resistant epilepsy (DRE), axial hypotonia, severe global developmental delay and limited lifespan are seen. No precision therapy is yet available.

REPORT

We describe a non-consanguineous Iban infant with infantile spasm syndrome at 5 months. He had mild motor delay but soon regressed with acquired microcephaly. His spasms were refractory to glucocorticoids and he developed DRE. This included generalized motor seizures including clonic seizures involving facial muscles and limbs and status epilepticus of focal tonic to bilateral tonic-clonic seizure, lasting 30 minutes. He trialed a combination of six anti-seizure medications including vigabatrin, valproate, phenobarbitone, levetiracetam, topiramate and clobazam but remained encephalopathic and hypotonic, warranting assisted feeding via Ryle's tube. He continued to regress and succumbed due to aspiration pneumonia at 13 months.

Extensive investigations encompassing blood counts, electrolytes and renal and liver profiles, serum ammonia, lactate, inborn error of metabolism, and cerebrospinal fluid screens were negative. MRI brain at 9 months revealed cerebral atrophy, ventriculomegaly and delayed myelination. His initial electroencephalogram hypsarrhythmia evolved into bilateral posterior quadrant epileptiform discharges. A singleton whole exome sequencing revealed a recurrent, homozygous, likely pathogenic variant in *UDGH* gene (NM_003359.4: c.1174C>T).

CONCLUSION

UDGH codes an enzyme aiding glucuronidation and is a precursor of glycosaminoglycans synthesis. *UDGH* dysfunction, particularly with loss of function variants, leads to glycosylation disorders. Functional studies on our patient's variant³ suggest loss of function, in keeping with the newly described Jamuar syndrome³. Even though, there are no precision therapies yet, this homozygous variant, highly likely indicates parental carrier status and has significant repercussions for reproductive counselling and prenatal testing for future pregnancies.

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AUTISTIC REGRESSION AS A PREDICTOR OF NON-VERBAL ABILITY AMONG CHILDREN WITH ASD

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BACKGROUND

Autism spectrum disorders (ASD) represent a heterogeneous group of developmental disabilities characterized by social and communication impairments and restricted repetitive behaviours. About one third of children with ASD had history of development regression. Regression in language is most commonly reported by parents. However, little was known about the association between regression and social cognitive function.

METHOD

A cross sectional descriptive study was conducted at the Child Development Clinic. Systematic random sampling was used to enrol 50 ASD children (44 boys, 6 girls, mean age 7.4 ± 0.4). Their cognitive function was assessed with Raven's Progressive Matrices. Caregiver were given Social Response Scale-2 (SRS-2) to assess the child social difficulty. Independence T test was used to compare the mean standard score for Raven's Progressive Matrices and SRS-2 among children with regression versus without regression.

RESULT

Among 50 participants, 40% was found to have language regression. There was homogeneity of variance as assessed by Levene's Test for Equality of Variances (Raven's $p = 0.6$; SRS-2 $p = 0.9$). Therefore, an independent t-test was run on the data with a 95% confidence interval (CI) for the mean difference. For children without regression the Raven's mean standard score (76.8 ± 28.1) is significantly higher than those with regression (56.9 ± 26.0), $t(79) = 3.2$, $p = 0.002$. Whereas SRS-2 score showed no significant different between both groups (without regression 68.8 ± 8.4 ; with regression 71.7 ± 8.8 ; $t(79) = -1.5$, $p = 0.134$).

CONCLUSION

ASD regression children with autistic regression has significant lower non-verbal ability; however, the regression do not predict the severity of social impairment.

EXPERIENCE WITH DUCHENNE MUSCULAR DYSTROPHY PATIENTS IN HOSPITAL TENGKU AMPUAN AFZAN KUANTAN, PAHANG

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INTRODUCTION

Duchenne Muscular Dystrophy (DMD) represents a formidable challenge in the realm of genetic disorders, its X-linked recessive nature imparting a distinctive profile of slowly advancing muscle weakness. This hallmark symptomatology, often discernible as early as 2 to 3 years of age, primarily afflicts the male population, although its impact is not exclusive, as female carriers may also exhibit subtle motor impairments alongside cognitive difficulties.

REPORTS

In our clinical domain, we have had the opportunity to engage with six patients grappling with dystrophinopathies, encompassing five cases of DMD and one case of Becker's Muscular Dystrophy.

The onset of symptoms within this cohort has demonstrated a broad spectrum, spanning from as early as 2 years to as late as 5 years, with a mean onset age of 3.6 years. Similarly, the age at which these conditions are formally diagnosed showcases considerable variance, ranging from 4 to 9 years, with an average diagnostic age of 6.6 years. Despite this divergence in presentation, a consistent observation across all cases was the presence of hyperCKaemia and transaminitis during the initial assessment, underscoring the biochemical perturbations intrinsic to DMD pathophysiology.

Noteworthy genetic aberrations were identified in two patients' multiplex-ligation dependent probe amplification (MLPA) method, characterised by deletions encompassing exon 10-11 and 61-70 and another patient had negative MLPA, prompting a referral to the genetic team into specialist testing including single point mutation. Furthermore, the ambulatory status of these patients exhibited considerable heterogeneity, with five individuals demonstrating varying degrees of mobility, whereas one patient necessitated wheelchair assistance due to significant musculoskeletal compromise.

CONCLUSION

Moving forward, our endeavour lies in fostering heightened community and healthcare personnel awareness surrounding DMD, advocating for early referral pathways and genetic counselling to facilitate prompt intervention and tailored rehabilitative strategies. The initiation of steroid therapy emerged as a pivotal determinant in the preservation of ambulatory function and mitigation of cardiorespiratory profiles, with a mean initiation of 7.2 years observed within our cohort. Though concerted efforts aimed at expediting diagnosis, optimising therapeutic interventions, and fortifying patient support networks, we aspire to redefine the trajectory of



DMD management, fostering improved outcomes and quality of life for affected individuals and their families

Keywords

DMD; HTAA; Pahang

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NOVEL CASE OF UNC13A HOMOZYGOUS LOSS OF FUNCTION CAUSING EARLY INFANTILE DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY (EIDEE) WITH PROMINENT MYOCLONIC SEIZURES AND CONGENITAL MYASTHENIA

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INTRODUCTION

UNC13A homozygous loss of function variant have been associated with dysmorphism, extreme muscle weakness, myasthenic features and encephalopathy/brain abnormality. We report a novel case of UNC13A who had EIDEE with prominent myoclonic seizures as the main phenotype.

REPORT

A 1-year-old-boy born term to consanguineous parents (first cousin), developed recurrent myoclonic jerks since day 3 of life which improved with intravenous phenobarbitone. Cerebrospinal fluid examination, karyotyping and metabolic investigations were normal. He required nasogastric tube feeding upon discharge due to poor sucking.

At 2 months old, he was referred for worsening myoclonic jerks, which were multiple daily and persistent since neonatal period. Upon examination, he had microcephaly, expressionless facies, ptosis, marked generalized hypotonia and hyporeflexia. Other features include wide nasal bridge, high arched palate, flexion contractures over both knees, and long slender overlapping digits. Electroencephalogram showed burst suppression pattern with epileptic myoclonus, and periods of prolonged attenuation lasting up to 1 minute. Phenytoin worsened his seizures, and no response was seen with pyridoxine and folinic acid. His seizures were best controlled with combination of levetiracetam and phenobarbitone. Whole exome sequencing confirmed homozygous variant in *UNC13A c.1903_1951del(p.Glu635Ter)*, a null variant predicted to cause nonsense mediated decay and loss of function. Repetitive nerve stimulation revealed significant decremental response confirming congenital myasthenia. Treatment with Salbutamol and pyridostigmine were stopped prior to any clinical effect due to intolerable side effects.

On follow-up, he had severe failure to thrive and remained encephalopathic with barely any spontaneous movement. His daily myoclonus was milder with some spontaneous reduction.

CONCLUSION

Our case shared features previously described in UNC13A homozygous mutation including extreme muscle weakness, myasthenia, encephalopathy, dysmorphism and burst suppression pattern on electroencephalogram. EIDEE with prominent myoclonic seizures can be a prominent feature of homozygous UNC13A loss of function variant, hence expanding the phenotypic spectrum of this variant.

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METHADONE INDUCED TOXIC LEUKOENCEPHALOPATHY: A CASE REPORT

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INTRODUCTION

Poisoning accounts for about 7% of all accidents in children under 5 years and is implicated in about 5% of all childhood deaths in developing countries. Evidence has shown that the incidence of poisoning with opium derivatives is growing especially methadone. Goals are mainly to treat the increased intracranial pressure and minimize secondary neurologic insults. Unfortunately, there are no specific treatment guidelines available. Common MRI findings include diffuse symmetrical T2- weighted hyperintensity of the cerebral white matter.

CASE REPORT

We report a 2-year-old girl who was premorbid well, who presented with loss of consciousness following an accidental methadone ingestion. She was unwell 1 day prior to presentation, requiring regular paracetamol. Father mistakenly served 10mg of syrup methadone which was presumed to be paracetamol. With the initial GCS of 3/15, bradypnea and cyanosis she was intubated as there were no response to naloxone. She then developed seizures that prompted imaging. The CT brain showed left parieto-occipital lesion which represented infarction and presence of bilateral cerebellar lesions possibility related to methadone induced toxic encephalopathy. She was extubated after cerebral protection. However, remained encephalopathic with spontaneous eye opening, unable to speak and no movement against gravity. We proceed with MRI Brain on day 4 of admission which showed abnormal signal hyperintensities at bifrontal, bilateral high parietal and left parieto- occipital region, involving both grey and white matter. Despite intensive rehabilitation she remained encephalopathic with poor motor recovery. We decided to commence IV methylprednisolone 10 mg/kg TDS on day 5 of admission, she had increase in facial expression response to parents but motor function remained. We prolonged the corticosteroids for a total of 5 days and weaned over the next 6 weeks. At 6 months review she crawled and sat without support, tolerated normal adult diet not requiring a feeding tube and spoke fluently. Her interaction with sibling exceeded parents' expectation but still demonstrated poor fine motor recovery.

CONCLUSION

The triad of toxin exposure, neurobehavioral symptoms, and classic radiographic findings should raise suspicion for methadone induced leukoencephalopathy. Leukoencephalopathy can be very debilitation with a varied neurodevelopmental outcome if treatment is delayed. We suggest early treatment with corticosteroids which may help improve long term outcome, however this needs to be further studied.

GLS-RELATED NEONATAL (LETHAL) ENCEPHALOPATHY IN A PAIR OF SIBLINGS

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INTRODUCTION

Recent research has identified a significant genetic defect – a loss-of-function mutation in the *GLS* gene, which responsible for encoding glutaminase.¹ This mutation disrupts the conversion of glutamine into glutamate, leading to profound consequences, characterized by severe neonatal encephalopathy and respiratory insufficiency. In this study, we shed light on the plight of a pair of siblings inherited homozygous *GLS* mutation.

METHOD

Case report

RESULTS

We reported a pair of siblings from a consanguineous family. The genetic result of *GLS* mutation came back after the first sibling passed away. The first sibling was encephalopathic, hypotonic and poor respiratory effort at birth, needing ventilation. She developed refractory seizures shortly after birth with evidence of active ictal discharges despite multiple antiseizure medications. Neuroimaging showed simplified gyral changes and cerebral oedema. The treatment was re-directive and she passed away at day-40 of life because of severe respiratory insufficiency and encephalopathy. The second sibling was born two years later, presenting with similar manifestations. Parents were counselled about the illness and the genetic result. They understood about the grave outcome of the illness. The boy passed away at day-10 of life.

DISCUSSION

Our case report mirrored those of previously reported cases, albeit rare, with both siblings succumbing shortly after birth due to complications arising from the condition.^{1,2} This poignant case underscores the urgent need for further understanding of *GLS*-related encephalopathy and highlights the critical role of genetic testing in neonatal care. The genetic testing could provide the families with an explanation and closure.

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THERAPEUTIC PLASMA EXCHANGE (TPE) IN CHILDREN WITH MYASTHENIC CRISIS

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INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder affecting neuromuscular junction. The disease causes fluctuating and varying degrees of weakness in ocular, bulbar, limb, and respiratory muscle. The most serious complication of MG is myasthenic crisis. This condition characterized by generalized severe muscle weakness, resulting in respiratory distress that increase both morbidity and mortality. An appropriate therapy is necessary to treat patients with myasthenic crisis. Treatment option that can be use is therapeutic plasma exchange (TPE).

REPORT

A 17-year-old girl presented with severe muscle weakness since two days before admission. She complained of difficulty in breathing. The patient began to complain that her eyes were difficult to open since two weeks before. She complained of fluctuating drop eyes and the symptom got improvement in the morning. She complained of difficulty chewing, swallowing, and fluctuating slurred speech. These symptoms relieved with rest.

Physical examination showed ptosis. She had limited movement of both upper and lower extremities, with the muscle strength of both upper extremities were 3333/3333 and lower extremities were 3333/3333. The physiological reflexes were decrease with negative Babinsky reflexes in both legs. The were no clonus. The Wartenberg test was positive.

Prostigmin test showed positive result. Anti-acetylcholine receptor was 30,12 nmol/L. A chest CT-scan showed thymic hyperplasia. The patient diagnosed with myasthenic crisis. She was treated by three cycles of TPE during hospitalization along with oral pyridostigmine 7 mg/kg/day divided in four doses and oral methylprednisolone 1 mg/kg/day divided dose. The myasthenic crisis showed improvement after receiving three cycles of TPE. The symptoms relieved after TPE treatment.

Figure 1: Prostigmin Test



CONCLUSION

Myasthenic crisis requires aggressive management. Therapeutic plasma exchange (TPE) has proven to be an effective treatment for patients with myasthenic crisis and prevent further mortality.

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EARLY SIGNS AND ACTIONS: NAVIGATING AUTISM DIAGNOSIS IN EARLY CHILDHOOD

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INTRODUCTION

Autism Spectrum Disorder (ASD) is characterised by significant challenges in social communication and restricted repetitive behaviours. Early diagnosis and intervention are critical to improve long-term outcomes for children with ASD.

REPORT

This is a case report of a 3-year-old girl, the eldest of two siblings, referred by a medical officer in Klinik Kesihatan for a suspected case of autism spectrum disorder. She was born full-term to a mother who experienced anaemia during pregnancy, the child presented with developmental delays in speech noted from the age of 2, lacking the ability to combine two words and showing minimal social reciprocity. Behavioural observations included a lack of eye contact, repetitive movements such as hand flapping, hypersensitivity to certain sounds like a vacuum cleaner, and distress over unmet requests. Clinically, while her gross and fine motor skills were adequate, her social interactions and verbal communications were significantly impaired, with developmental speech approximating that of a 12-month-old. Following initial assessments, the child had been receiving occupational therapy for nearly two months, with a recent initiation of speech therapy. The family also received a referral to a psychologist for behavioural interventions, emphasizing the collaborative management of suspected ASD cases.

The case highlights the astute decision-making by the medical officer in recognizing early signs of ASD and the importance of swift referral for specialist evaluation and early intervention, which are crucial for better prognostic outcomes. This case also emphasizes the need for heightened vigilance among healthcare providers to detect early signs of autism for timely interventions. Furthermore, it illustrates the importance of involving both parents in therapeutic sessions to enhance the effectiveness of interventions.

CONCLUSION

This case is a powerful reminder of the crucial impact of early detection and comprehensive management in caring for children with ASD.

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NAVIGATING DELAYED PRESENTATION: SELECTIVE MUTISM COMPLICATING THE RECOGNITION OF AUTISM SPECTRUM DISORDER

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INTRODUCTION

The intricate dynamics of diagnosis in autism spectrum disorder (ASD) can be exacerbated by the presence of other co-occurring conditions. These 2 cases enable us to delve into selective mutism (SM), which is characterised by a consistent failure to speak in specific social situations despite speaking in other contexts. This presents a challenge in recognition. Initially described in 1877 by Kussmaul, SM has evolved from being viewed as a voluntary behaviour to a reaction pattern to overwhelming or threatening contexts, as highlighted in the DSM-5.

REPORT

The first case which features an 8-year-old girl underscores the challenges of identifying ASD amidst the background of SM and restrictive food intake. Her case was first highlighted at 4 years 9 months due to her restrictive food intake which resulted in faltering growth. Upon further exploration, her autistic traits with significant rigidities to textures as well as routines had been present before age 2. As she was communicative with her family members but was particular with peers, allowances had been made for her not speaking in public. However it was after a year of school, the persistent interaction challenges were evident even with familiar faces.

The second case, involves a 7-year-old girl who presented after being in primary school for a year. Despite manifesting limited interaction with peers, rigidity, texture aversion and emotional dysregulation, she presented late due to initial misinterpretation of her SM, since age 3-and-a-half, as extreme shyness. She also had difficulties with reading and writing, but had a strong grasp of mathematics. The presence of dyslexia made it more challenging. Her journey highlights the nuanced interplay between ASD, selective mutism, and other comorbidities such as specific learning disorder, emphasising the importance of early recognition and intervention.

CONCLUSION

These cases show the complexities of an ASD diagnosis in girls with SM. They emphasise the necessity of awareness among healthcare professionals to recognise the masking effect of SM in the timely identification and intervention of ASD. It is important to mitigate the impact of delayed presentation and thus diagnosis, on the developmental trajectories of these young people.

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METHOTREXATE LEUKOENCEPHALOPATHY IN CHILDHOOD ACUTE LEUKAEMIA: THE UNIVERSITY OF MALAYA MEDICAL CENTRE EXPERIENCE

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INTRODUCTION

The reported incidence of methotrexate-related neurotoxicity among paediatric patients receiving chemotherapy for acute lymphoblastic leukaemia (ALL) is 3-7%. We sought to describe the clinical characteristics and outcomes of methotrexate leukoencephalopathy (MTX LE) in paediatric patients who had received treatment for ALL on the MA-SPORE 2010 or 2020 protocols in a Malaysian tertiary centre.

METHODS

Retrospective chart review of patients referred to the Paediatric Neurology service in the University of Malaya Medical Centre between 1 January 2014 and 31 January 2024 due to leukoencephalopathy following ALL treatment with intravenous and intrathecal methotrexate.

RESULTS

Symptomatic leukoencephalopathy manifested in 3% of paediatric ALL patients (8/252) after a median of 243 days (range 28-438 days) from ALL diagnosis and 7 days following intravenous or intrathecal methotrexate. Males predominated at 87.5% ($n=7$) and there was a Malay majority of 87.5% ($n=7$). Signs included encephalopathy ($n=5$), motor deficits ($n=3$), and seizures ($n=2$). Mean follow-up was 4.2 years (range 0.33-9.1 years). Persistent neurological deficits were observed in 6 patients (75%), with 50% ($n=4$) having a modified Rankin score of ≥ 4 . 37.5% had cognitive deficits ($n=3$), 25% had dystonia requiring ≥ 4 antidystonia medications ($n=2$), 12.5% developed epilepsy requiring two antiseizure medications (ASM) ($n=1$), 12.5% developed refractory epilepsy requiring 4 ASM and vagal nerve stimulation ($n=1$). 2 patients made full recovery. 42.9% of those with persistent deficits had a diagnosis of T-cell ALL ($n=3$), with hyperleukocytosis (mean total white cell count $536.1 \times 10^9/L$) in 2 patients and central nervous system involvement in 2 patients.

CONCLUSION

50% of patients in our cohort had moderate to severe neurodisability following MTX LE, contrasting with the general consensus that methotrexate neurotoxicity is transient. Genetic susceptibilities might account for this difference.

TUBERCULOSIS MENINGITIS COEXISTING WITH HIV INFECTION: A CASE REPORT

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INTRODUCTION

HIV-associated tuberculous meningitis (TBM) poses significant diagnostic and therapeutic challenges and carries a dismal prognosis. HIV-infected patients present more frequently with extra-meningeal tuberculosis and systemic features of HIV infection.

REPORT

A 6-year-old boy was admitted at our institute, complaints of severe headaches for 2 months, fever for 3 months temperature 38°C. Weakness over left upper limb followed by lower limb and diarrhea for 30 days. Convulsion, generally, 30second, frequency 3-5x/day, before and after convulsi was conscious. His parent positive TB and HIV.

Regio colli were multiple enlarged lymph nodes (0.5-1 cm). Ronkhi bilateral at lungs. On neurological examination, gait was hemiparese, tone was decreased over left side, power was 4/3 over left upper and lower limb.

Meningeal sign were positive. Anthropometric was mild underweight. HIV-1 RNA 45,476 copies/ml and 4.7 log copies/ml. CD4 4.3%, absolute CD4 50, CD8 (57.76), and absolute CD8 (679). CSF; count cells 172, PMN (segmen) 146, MN (Limfosit) 26, Protein 137, Glucosa 28. Gen expert negative. The culture CSF Acinetobacter streptococcus alfa hemolytic, culture feses (Klebsiella pneumoniae). CT scan contras: tuberculoma, ventriculomegali, and edema. Roentgen thorax were effusion pleura, cardiomegali. Echocardiografi finding reduced LV function (EF 53%, FS 27%). EEG showed severe generalized hypofunction. Treatment were meropenem, steroid tapping off, fenitoin, furosemide, asetozolamid, captopril, Anti Tuberculosis Treatment, Antiretroviral Treatment, Formula Nutrition. For oral by nasogastric tube.



CONCLUSION

In HIV-associated TBM, clinical course and outcome are influenced by profound immunosuppression at presentation, emphasising the need for earlier diagnosis of HIV infection and initiation of antiretroviral treatment.

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RESCUE MEDICATION PRACTICE IN PATIENTS WITH DRAVET SYNDROME IN A MALAYSIAN TERTIARY HOSPITAL

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INTRODUCTION

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy with recurrent prolonged seizures leading to complications such as hypoxic ischaemic encephalopathy (HIE) and sudden unexpected death in epilepsy (SUDEP). Early initiation of rescue medication DS prevents injury and reduces hospital admissions.

METHODS

We screened the paediatric neurology patient database at Hospital Pulau Pinang for patients with confirmed DS. We reviewed medical records for demographic data and epileptology of our cohort. We analysed age of seizure onset, first prolonged seizure or status epilepticus (≥ 5 minutes), number of seizures beyond 30 minutes and age at which rescue medication was introduced.

RESULTS

We studied 17 DS patients (4 male, 24%) with median age of 12.7 years (3- 21 years). One patient died, aged 16, due to probable SUDEP. Median age of first clinical suspicion of DS was 2.5y (5m-13y). 16/17 (94%) had recurrent status epilepticus. Mean age of first status was 6.8 months (3-11months). 8/16(50%) patients had at least one seizure lasting 30 minutes or more. All 16 received rescue medication prescription by age 4. 5/16 (31%) were prescribed their rescue medication immediately after the first prolonged seizure.

The remaining 11 (69%) had a mean time lag of 12.7 months between first status and rescue medication prescription. 6/11 went on to have 17 further prolonged seizures. 8/11 received their first prescription after a paediatric neurology consult. One patient sustained HIE due to status epilepticus complication, despite rescue medication.

CONCLUSION

Timely rescue medication introduction is delayed in more than half our DS patients, often until neurology consult. This has potential serious implications. The practice and protocol of giving rescue medication after single prolonged seizure should be emphasized among clinicians. Individualised written seizure management plans may have a role in terminating seizures that do not respond to first dose of rescue benzodiazepines.

HAEMOPOEITIC STEM CELL TRANSPLANT, A PAUSE FOR CEREBRAL ADRENOLEUKODYSTROPHY: A CASE REPORT

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INTRODUCTION

X-linked adrenoleukodystrophy (X-ALD) is a rare inherited condition. It is a peroxisomal disorder leading to intracellular accumulation of very long chain fatty acid (VLCFA). X-ALD has 3 main disease entities comprising myeloneuropathy, cerebral leukodystrophy and primary adrenal insufficiency. Cerebral ALD presentation includes cognitive symptoms such as declining school performance and behavioural issues and neurological symptoms such as seizures and visual impairment.

REPORT

We present a 7-year-old boy who came in with status epilepticus, due to presumed meningitis and symptomatic hyponatraemia. He developed diplopia with left 6th cranial nerve palsy and bilateral papilloedema post extubation. MRI brain revealed a swollen splenium of corpus callosum with patchy enhancement with white matter hyperintensities in both parieto-occipital lobes and medial temporal lobes, suggestive of posterior reversible encephalopathy syndrome (PRES), with a differential of reversible splenial lesion syndrome (RESLES). He made a complete neurological recovery with resolution of eye signs 5 months later. He presented again with a hyponatraemic seizure and a new complaint of skin hyperpigmentation 8 months after initial presentation. Repeat MRI Brain demonstrated worsening white matter hyperintensities extending to midbrain and optic tract, suggestive of demyelination. The diagnosis of cerebral ALD and adrenal insufficiency was confirmed when his VLCFA showed increment in values and a pathogenic variant was noted in *ABCD1*. His cognition and neurological examination remained normal. He underwent haplogenic haemopoietic stem cell transplant (HSCT) with father as donor. Family screening revealed carrier parents and confirmed X-ALD in his asymptomatic 3-year-old younger brother, who is being worked up for HSCT.

CONCLUSION

X-ALD has a heterogenous presentation and a high index of suspicion is warranted when boys present with MRI brain white matter changes, especially in the presence of adrenal insufficiency. X-ALD causes neurodisability and death when untreated. HSCT prevents disease progression and is available in Malaysia.

VEHICULAR ENTRAPMENT AND HEAT RELATED INJURY (VEHRI) - A SUBSET OF HEAT RELATED INJURY OR AN IMPORTANT DOMAIN ON ITS OWN?¹A Wannard; ¹Tan KA¹Department of Paediatrics, Hospital Sultanah Bahiyah, Km 6 Jalan Langgar, Alor Setar, Malaysia.**INTRODUCTION**

When the core body temperature rises above 40°C, individuals will experience loss of consciousness and at risk of developing multiorgan failure secondary to heat stroke. The mortality and morbidity are high following the injury. The issue of asphyxia would further compound the problem if individuals who suffered from heat stroke were found within a confined space for long. We report a boy who suffered VEHRI manifested remarkable dyskinesia movements and made a good recovery with supportive care.

REPORT

A five-year-old boy was trapped in a car boot under the hot sun for approximately 3 hours. Child was found limp and required extensive resuscitation. He developed shock, acute rhabdomyolysis with acute kidney injury as well as myocardial dysfunction, needing inotrope and ventilation support. During the recovery phase, he developed dyskinesia with vigorous hand shaking and agitation pointing towards extra-pyramidal symptoms. However, magnetic resonance imaging (MRI) of this patient showed symmetrical white matter hyperintensities particularly over bilateral frontal, parietal, occipital, subcortical and deep white matter suggestive of leukoencephalopathy. He made exceptional improvements without noticeable dyskinesia movements before discharge.

CONCLUSION

The neuroimaging result in our patient contrasted with the typical MRI findings in heat stroke survivors which affect mostly the cerebellum. The findings suggest that asphyxia following vehicular entrapment could be an additional factor causing the insult to the patient's brain and other organs besides heat stroke. Therefore, we propose this new term "VEHRI" - for this condition to represent the overlapping nature of the condition between asphyxia due to being entrapped in a confined space and heat related injury.

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UNVEILING THE CLINICAL SPECTRUM: INSIGHTS FROM THE UNIVERSITY OF MALAYA MEDICAL CENTRE'S CASE SERIES ON MOGAD (MYELIN OLIGODENDROCYTE GLYCOPROTEIN ASSOCIATED DISEASE)

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INTRODUCTION

Myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD) is an autoimmune demyelinating disorder increasingly recognized in pediatric patients, presenting unique diagnostic and therapeutic challenges. This case series aims to highlight the varied presentation, disease patterns and treatment strategies & outcomes of 4 patients in our center with MOGAD.

METHODS

This is a retrospective chart review of paediatric patients who tested positive for MOG-antibody (MOG-Ab) following an initial presentation of acute central demyelination. The patients presented between 2017-2023.

RESULTS

MOG-Ab was present in four patients. Mean age of onset was 5 years (range 2-9 years). The initial MOGAD presentations in our cohort were: optic neuritis (ON) alone ($n=3$) and acute demyelinating encephalomyelitis with ON (ADEM-ON) ($n=1$). Mean time from presentation to treatment was 7.25 days (range 3-14 days). All patients received acute treatment with intravenous methylprednisolone; 2 patients received intravenous immunoglobulin. Maintenance therapy was indicated in 2 patients. Monophasic disease was observed in 2 patients, and multiphasic disease in 2 patients. One patient demonstrated persistent neurological deficit.

CONCLUSION

The reported clinical spectrum of MOGAD internationally shows that MOGAD-ON is a more common presenting phenotype in older children (>11 years old). However, in our patient cohort, the majority of patients with ON were of a younger age group. Treatment and prognosis are highly dependent on time from symptoms onset to initiation of treatment, in one of our patients delay in presentation resulted in permanent deficits in vision. It is imperative that children who are suspected to have MOGAD be promptly worked up and treated for better treatment outcomes.

MALAYSIAN PARENTS' PERCEPTION AND EFFECTS OF GASTROSTOMY TUBE INSERTION FOR CHILDREN WITH SEVERE NEUROLOGICAL IMPAIRMENT

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INTRODUCTION

Children with severe neurological impairment (SNI) are often associated with swallowing dysfunction and dysmotility which lead to feeding difficulties often requiring gastrostomy. Previous studies have shown that parents are often resistant to gastrostomy resulting in a delay of gastrostomy tube insertion.

METHOD

This was a cross sectional cohort study on children with SNI with swallowing impairment. A questionnaire on parental perception of gastrostomy feeding was obtained. Parents rated on visual analogue scale of quality of life and health perceived by parent and WHOQOL-BREF for parents' general quality of life and Parenting Stress Index at baseline, and at 3-6 months after tube insertion.

RESULT

A total 28 patient were recruited for this study. The median time for decision of gastrostomy insertion is about 2.1month. There was a significant association between longer duration in making decision on gastrostomy on parental perception on whether they felt they were not given a choice on gastrostomy decision, and if they felt they were not well informed on procedure. The mean visual analogue scale for Quality of life and health related quality of life of children have significant improvement of the score after gastrostomy tube insertion. Parents reported significant improvements in physical health, psychological health, social functioning, environment compared with results at baseline. 96.4% of the parent were satisfied with gastrostomy tube insertion. There were 93% of mother reported less respiratory infection and 96.4% of parents would have implemented gastrostomy tube earlier.

CONCLUSION

Most of our parents reported high satisfaction post-gastrostomy with improvement in the quality of life for both children and parent. Parents who did not feel empowered in the decision-making process of gastrostomy took longer to make the decision for gastrostomy highlighting the importance of adequate information is given during gastrostomy counselling.

A CASE WITH ACUTE POST-MEASLES ENCEPHALITIS ASSOCIATED WITH ACUTE LEUKOENCEPHALOPATHY WITH RESTRICTED DIFFUSION

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INTRODUCTION

Virus associated encephalopathy has a wide spectrum of manifestations. Measles infection is relatively rare in our community because of the local national immunization policy. However, incidents of measles infection could still happen due to vaccine refusal by individual parents. The complications could be associated with high morbidities and mortality. We reported a boy who is an unvaccinated foreigner presented with a complicated measles infection.

CASE REPORT

A 7-year-old boy developed measles infection after having a sick contact to his brother upon arrival to Malaysia. He presented with classical measles manifestations with status epilepticus to a district hospital, needing intubation. After 3-day cerebral protection, his conscious level and respiratory effort were poor for extubation. Neuroimaging revealed features were consistent with acute leukoencephalopathy with restricted diffusion. Measles Ig M was highly positive with elevated protein and neopterin in the cerebrospinal fluid. Immunoglobulin, vitamin A and dexamethasone were administered for the diagnosis of measles infection and immune-mediated encephalitis. Before departing back to his own country, he had modified Rankin score 5 and he remained encephalopathy, with spasticity predominantly affecting both upper limbs.

CONCLUSION

Acute post-measles encephalitis is rarely reported and it was found to have good outcome with glucocorticoid treatment. However, our patient's neurological outcome was poor because the illness was complicated with acute leukoencephalopathy with restricted diffusion, following status epilepticus. As measles infection is preventable by vaccination, it is important to advocate the vaccination to all children.

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SEIZING 'FAR AWAY': AN APPROACH OF NEONATAL SEIZURE IN LIMITED RESOURCE SETTING IN BORNEO

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INTRODUCTION

Neonatal seizures are the commonest neurological emergency and are associated with poor neurodevelopmental outcome. While they are generally difficult to diagnose and treat, they pose a significant clinical challenge for physicians especially in limited resource setting.

REPORT

This report describes a case of a male newborn who have KCNQ2 developmental and epileptic encephalopathy. A term male infant born to a Chinese parent, with uneventful antenatal and intrapartum period. Mother noticed abnormal movement since day 6 of life, however did not seek any treatment as it was subtle and lasted few seconds. He developed multiple focal seizure with lateralization of eye 1 months later, hence brought to hospital. The seizure was stimulus sensitive and required various of anti-epileptic medication to control the seizure. Referral to pediatric neurologist was made and urgent EEG showed multiple epileptic discharges, consistent with epileptic encephalopathy. MRI brain suggestive of corpus callosum hypoplasia. He was discharged later with levetiracetam and carbamazepine. Eventually, Clonazepam was added. Throughout review in clinic, his seizure was controlled with 3 antiepileptic medicines. He also has global developmental delay and under multidisciplinary follow up.

CONCLUSION

Further genetic screening was done later and pathogenic variant of KCQN2 detected. KCQN2 is associated with autosomal dominant. Although variant is a known variant and most likely the variant is de-novo, parenteral testing is recommended.

KEYWORDS

Neonatal seizure, epileptic encephalopathy, KCQN2, autosomal dominant

CHEMICAL STABILITY OF MIDAZOLAM INJECTION SOLUTION FOR INTRANASAL USE AS PAEDIATRIC HOME RESCUE MEDICATION BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

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INTRODUCTION

Numerous studies showed that injection Midazolam solution administered via nasal route is effective and safe to be used as home seizure rescue medication at pre-hospital setting. Repacking the injection Midazolam solution into a glass amber bottle equipped with an inner plug of syringe adapter can avoid the skill requirement in breaking the glass ampules and ensure timely administration of seizure rescue medication in an emergency situation. However, there is a lack of information on the long term stability of undiluted injection Midazolam solution stored in a glass amber bottle under different temperature.

METHODS

A specific stability-indicating high-performance liquid chromatography coupled with UV detection method was developed for midazolam hydrochloride and validated for selectivity, linearity, sensitivity, precision, and accuracy. Injection Midazolam solution packed in glass bottles were stored under refrigeration (2-8 °C) and room temperature (30±2 °C). Stability analysis in this study was conducted at 8 time points- immediately after preparation (day 0), 2 weeks, 1 month, and then monthly until 6 months.

RESULTS

Concentrations of injection Midazolam solution decreased over 6 months. Stability was defined as retention of at least 90% of the initial drug concentration. Stability was maintained up to 3 months in the glass amber bottle under both storage conditions. Concentrations were superior under room temperature (30±2 °C) compared to refrigeration (2-8 °C).

CONCLUSION

Undiluted Midazolam injection solution 5mg/ml remained chemically stable up to 3 months in glass amber bottle. The preparation of the easy-to-use midazolam solution will empower parents or caretakers to use intranasal Midazolam in the pre-hospital setting and ensure timely administration of seizure rescue medication at emergency.

KETAMINE: AN EFFICACIOUS AGENT IN REFRACTORY SEIZURE MANAGEMENT POST NAJA KAOUTHIA (COBRA) ENVENOMATION

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INTRODUCTION

Status epilepticus (SE) is a neurological emergency defined as either a single seizure lasting longer than 5 minutes or two or more consecutive seizures within 5 minutes without full consciousness in between. Refractory status epilepticus (RSE) occurs when SE fails to respond to first line benzodiazepine and a second-line anti-seizure medication. Response to conventional RSE treatment varies between patients. Ketamine, an NMDA receptor antagonist with anti-seizure properties is an adjunct therapy for refractory seizures. We used intravenous ketamine infusion in a child with RSE, post Naja kaouthia (cobra) envenomation induced cardiac arrest.

REPORT

We present a pre-morbidly healthy 6-year-old girl who developed RSE following cobra envenomation. Her first generalized tonic-clonic (GTC) seizure occurred 50 minutes post-envenomation. She experienced an in-hospital two-minute cardiac arrest after the first appropriately dosed intravenous benzodiazepine and subsequently sustained another 12 minutes of arrest five minutes later. She then developed refractory myoclonic seizures for 20 hours despite loading doses of intravenous Levetiracetam, Phenobarbitone and Midazolam infusion of up to 8 mcg/kg/min. Her seizures showed minimal response to Propofol infusion. Ketamine infusion was initiated at 20 hours of insult with cessation of myoclonic jerks within minutes. CT brain performed after cessation of seizures showed cerebral edema over the right hemisphere. Bedside EEG showed diffuse slowing with bilateral independent lateralized epileptiform discharges over the left fronto- central and right anterior temporal regions. She required a frontal decompressive craniectomy at Day 3 post envenomation. She remained seizure- free, despite subsequent tapering off ketamine infusion.

CONCLUSION

Naja kaouthia envenomation is not known to directly induce seizures but can lead to arrhythmias causing cardiac arrest, leading to cerebral hypoxic insult and subsequent RSE. Intravenous ketamine infusion should be considered early in hypoxic insult induced RSE

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UNVEILING RARE PRESENTATION OF SCURVY: MUSCULAR WEAKNESS IN THE PAEDIATRIC POPULATION

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INTRODUCTION

Vitamin C deficiency is relatively rare in developed nations; however, it continues to pose a significant health concern among the paediatric population. This abstract delves into the rare manifestation of vitamin C deficiency, with muscular weakness emerging as the primary symptom.

METHODS

A retrospective case review was performed. Informed consent was obtained from the parents of patients.

CASE REPORT/ RESULTS

We describe 5 cases of vitamin C deficiency presenting with musculoskeletal manifestation in early childhood. Our patients were aged between 3 to 8 years of age. All presented with an inability to ambulate and complaints of non-specific limb pain. All patients appeared miserable. However, none exhibited classical gum manifestations. Systemic and neurological examinations were normal. One child had Autism spectrum disorder; however, the other four had a very restricted diet. Baseline investigations and infective markers were negative. Serum vitamin C levels were low in all five patients. All five patients showed rapid and good response to oral vitamin C treatment. Upon subsequent follow up after 4-6 weeks, all children showed near complete recovery of symptoms and were able to ambulate.

CONCLUSION

Vitamin C deficiency needs to be considered in children presenting with non-specific symptoms of refusal to ambulate/ musculoskeletal weakness paired with rigid food intake. A clear and thorough history should provide us with the clinical suspicion of scurvy.

HIPPOCAMPAL SECONDARY NEURODEGENERATION AFTER CORTICAL ISCHEMIC STROKE: MECHANISMS AND THERAPEUTIC OPPORTUNITIES

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INTRODUCTION

Stroke is strongly associated with cognitive decline and dementia. Indeed, significant impairment in at least one cognitive domain was reported in approximately 70% of stroke survivors who achieve full clinical recovery. Whilst stroke in brain regions involved in cognition (i.e. hippocampus) are rare, impaired cognition, decreased hippocampal function and hippocampal neurodegeneration are common after stroke. There is emerging evidence suggesting that stroke triggers a wave of secondary damage that causes the progressive and inexorable loss of brain tissue at sites connected to the area damaged by the initial infarction, a phenomenon termed as secondary neurodegeneration.

METHODS

Our studies to date have aimed on characterising the cognitive deficits associated with post-stroke secondary neurodegeneration as well as neuropathological changes.

RESULTS

Using the rodent touchscreen platform for cognitive assessment, we demonstrated that unilateral cortical photothrombotic stroke at the motor and somatosensory cortices causes impairments in visual discrimination, cognitive flexibility and associative memory up to 84 days post-stroke. Notably, we reported similar cognitive deficits in mice and humans in the chronic phase post-stroke using the touchscreen-based paired-associate learning task. We have also shown that cortical stroke is associated with persistent neuronal loss, neuroinflammation, accumulation of neurotoxic proteins and cerebrovascular dysregulation at sites of secondary neurodegeneration, including the hippocampus, out to 84 days post-stroke.

CONCLUSION

Treatments that target inflammatory processes, clearance of neurotoxic proteins and cerebrovascular repair or regeneration may be quite promising in protecting stroke-induced secondary neurodegeneration. Given the delayed and long-term progression of secondary neurodegeneration, there is opportunity for therapeutic intervention to target these neuropathological changes and improve post-stroke outcomes.

EFFECTS OF SEIZURE ON COGNITIVE DECLINE IN AN ALZHEIMER'S DISEASE WITH EPILEPSY RODENT MODEL

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INTRODUCTION

Alzheimer's disease (AD) and epilepsy are complex and prevalent neurological disorders that are known to impact cognition. However, Alzheimer's disease with epilepsy (ADE) may present a unique interacting relationship, potentially exacerbating the cognitive decline further than their respective individual disorders. Nevertheless, the effects of seizures on cognition in AD are scarcely studied, and thus, the underlying mechanisms of this relationship are yet to be determined. This study aimed to determine the effects of acute kainic acid-induced seizures on learning and memory paradigms in a Sprague-Dawley (SD) model of induced-ADE.

METHODS

AD was induced in 8 to 10-week-old SD male rats via bilateral intracerebroventricular injection of 3mg/kg Streptozotocin. Cognitive tests such as Morris Water Maze, Novel Object Recognition, Elevated Plus-Maze, and Passive Avoidance Test were performed 3-5 weeks after AD induction. On the 5th week, seizures were induced via kainic acid (10mg/kg +5mg/kg, 30 minutes apart) intraperitoneal injection. In the 7th–9th week, cognitive test paradigms were conducted again.

RESULTS

The results showed that in the 7th–9th week, ADE animals had better learning and memory outcomes across the cognitive paradigms than AD animals but worse cognitive outcomes than the seizure non-AD animals. Thus, based on our results, seizures did have an effect on cognition across all parameters, but contrary to our hypothesis, seizures did not exacerbate the cognitive decline of AD. This could be attributed to the seizure-induced hyperexcitability behavior in the model that confounds the subtle learning and memory impairment induced by the AD at 7-9 weeks post AD-induction.

CONCLUSION

In conclusion, seizures may have an effect on AD-induced cognition, albeit seizure hyperexcitability and early preceding neuropathological findings should be taken into account.

INVESTIGATION INTO THE ROLE OF ORPHAN G-PROTEIN COUPLED RECEPTOR GPR151 IN OBESITY ASSOCIATED HABENULAR COGNITIVE DEFICITS

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INTRODUCTION

Obesity is a multifactorial non-communicable metabolic disorder that plagues the modern world in the 21st century. Currently, there are abundance of literature focusing on metabolic etiology of the disorder especially with regards to high fat diet, yet the cognitive processes leading to vicious cycle of energy consumption and obesity remain under studied. Two phenomena have been observed in high fat diet induced obesity including risk prone behavior and unusual reward perception such as altered delay discounting (the forfeit of larger delayed reward in favor of immediate small reward) but underlying molecular mechanisms require further elucidation. We target the habenula, an anti-reward epithalamic structure as a region of interest with highly conserved function and genetics across vertebrates.

METHODS

Establishment of high fat diet group

Fear behavior assessment: Conditioned place avoidance (CPA) to examine fear (risk) avoidant behavior
qPCR: expression of GPR151 in habenula

RESULTS

In our study, we managed to demonstrate fear learning deficits after 2 weeks of high fat diet in zebrafish model, where we found a post-conditioning reduction in avoidant behavior in CPA. By employing qPCR, we found that dorsal habenular abundant GPR151 mRNA expression was downregulated in high fat diet group fish compared to the control.

CONCLUSION

Hence with the finding of altered expression of GPR151, we concluded that habenular GPR151 expressing neurons have a role in habenular cognitive domain and obesity likely alters the function of habenula via GPR151. Future neuronal activity studies will be used to validate the association of GPR151 deficient habenula with cognitive deficits found in high fat diet group via calcium imaging and behavioral assay on GPR151 deletion mutants.

BEHAVIOUR AND HIPPOCAMPAL PLASTICITY IN A KETAMINE-BASED MODEL OF SCHIZOPHRENIA

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INTRODUCTION

Schizophrenia is a complex, chronic and relapsing mental health disorder that often presents with positive, negative and cognitive symptoms. Due to its complex nature, developing a suitable animal model that can represent the pathophysiology and other aspects of the disease is challenging yet crucial for the clinical and progression of illness studies. Ketamine, a non-competitive antagonist for the N-methyl, D-aspartate (NMDA) receptor was found to be a suitable drug for developing psychotic activities due to its strong psychotomimetic properties. We aimed to study the behavioural and hippocampal neuroplasticity in different doses of the ketamine-induced schizophrenia model.

METHODS

To develop schizophrenia, the rats model was administered with different doses of ketamine (10, 50 and 100 mg/kg) via intra-peritoneal (*i.p.*) for 10 days. The effects of different doses of ketamine on the locomotor and motor activities of the models were further studied using an open field test (OFT). The effects of ketamine on emotional behaviours, such as anxiety and depression, were also assessed using the forced swim test (FST) and the elevated plus maze (EPM). The Morris Water Maze (MWM) test was used to observe the models' spatial memory and learning processes. Finally, *in vivo* electrophysiological recording was done to study the hippocampal neuroplasticity.

RESULTS

Our findings indicated that administration of all doses of ketamine (10, 50 and 100 mg/kg) for 10 days leads to hyperactivity in the rats model and increased anxiety and depression-associated behaviours in the rats. The result also demonstrated that all doses of ketamine affected spatial memory and learning and caused long-term memory deficits in the rat model.

CONCLUSION

This model, however, has been invaluable in advancing our understanding of schizophrenia and in the development of potential treatments.

IN VITRO EPILEPSY MODEL USING INTRACELLULAR CALCIUM FLUCTUATION MEASUREMENT

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BACKGROUND

Most in vitro epilepsy models are based on measurement of epileptiform activity, whether in slice or neuron culture. Traditional electrophysiological techniques are not yet able to measure neuronal activities in cells that less active electrically. Significant intracellular calcium fluctuation happened in neurons, it can resembles neuron activity and also appear along with neuronal depolarization. Calcium oscillation correlates with burst of neuronal action potential depicting epileptiform activity. Alternative approach to measure neuronal depolarization neuron is by observing the intracellular calcium fluctuation, this can be visualized by calcium fluorescence. Cell line SH-SY5Y is easy to handle and able to differentiate to be a stable neuron culture. This culture can be used to evaluate neuronal death or injury in degenerative disease, cerebral ischemia, and epilepsy.

This research aimed to find the optimal dose of kainic acid applied to SH-SY5Y culture as an in vitro epilepsy model by observing intracellular calcium fluctuation

METHOD

Cell line SH-SY5Y culture were carried out until reach 80% confluency, then observed for next 3 days until intervention. The cell cultures were divided into five groups : control group and epilepsy model group, consist of 4 subgroup with various doses of kainic acid (4 μ M , 8 μ M , 16 μ M , dan 20 μ M). Every group consist of 5 samples. Kainic acid was given for 48 hours, then we performed calcium assay to detect intracellular calcium flux fluctuation using Fluo-4. Observation was done with confocal laser scanning microscopy periodically for 52 seconds with 13 second interval.

RESULT

Intracellular calcium fluorescence was highest with kainic acid dose of 20 μ M, compared to other groups of all time of observations, followed by dose 4 μ M, 8 μ M, control group, and 16 μ M, subsequently. Calcium fluorescence at dose 4 μ M were higher than dose 8 μ M and 16 μ M. Kainic acid dose were positively correlated with the increase of intracellular calcium fluorescence, with the closest correlation found at dose 20 μ M.



CONCLUSION

Cell line SH-Sy5Y culture can be used as an in vitro epilepsy model. We found that kainic acid dose of 20 μM was the optimal dose to raise intracellular calcium fluctuation resembles epileptiform activity. Further research with narrower time interval and longer duration of observation is needed, millisecond time interval and few minutes duration is recommended to have a better calcium fluctuation result.



α 7NACHR ACTIVATION PREVENTS NEUROINFLAMMATION ASSOCIATED WITH CEREBRAL ISCHEMIA REPERFUSION INJURY IN ZEBRAFISH MODEL

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INTRODUCTION

Ischemic stroke is characterized by an abrupt cessation of blood flow in an artery to the brain. Activating the α 7-Nicotinic Acetylcholine Receptor (α 7nAChR) during post-stroke reperfusion injury has been shown to provide neuroprotective effects in stroke-induced injury in rats, but whether this strategy can be used as pre-treatment remains unknown.

METHODS

In this study, PNU282987 (α 7nAChR agonist) was administered intraperitoneally as a pre-treatment. The hypoxia/reoxygenation model in zebrafish was established by perfusing pure nitrogen gas in a hypoxia chamber for 10 minutes, followed by an hour of recovery/reperfusion in a beaker. The zebrafish locomotor activity was examined after 1 hour in the recovery tank, with parameters examined including total distance travelled, maximum acceleration, meandering, and turn angle. The mitochondrial dehydrogenase activity were used to assess brain damage along with the survival rate. Real-time quantitative RT-PCR was used to determine the gene expression levels of inflammatory markers TNF α , IL-6, IL-10, NF κ B, and STAT3.

RESULTS

Hypoxia/reoxygenation significantly increased the expression of proinflammatory markers such as TNF- α , IL-6, and NF κ B while α 7nAChR agonist reduced these markers. However, there was no improvement in agonist group locomotor activity and brain damage, implying that the neurological impairment was not fully reversed following PNU282987 pre-treatment. Nevertheless, agonist treatment significantly increased the zebrafish survival rate following the ischemic reperfusion injury.

CONCLUSION

This study suggests that activating α 7nAChR as a pre-treatment may protect against ischemic/reperfusion injury in zebrafish by modulating neuroinflammatory activity.

HABENULAR ORPHAN G-PROTEIN COUPLED RECEPTORS AS NOVEL THERAPEUTIC TARGETS FOR NEUROPSYCHIATRIC DISORDERS

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INTRODUCTION

The habenula, an ancient brain structure, is a strategic node in the information flow from fronto-limbic brain areas to brainstem nuclei. The dynamic role of the habenulacircuitry in these processes can be unmasked by monitoring lateral habenula neuronfiring, which increases in response to punishment and decreases during reward.

Many studies have implicated the habenula and connected circuitry in psychiatricdisorders that are associated with dysfunction of the reward system, in particular schizophrenia, mood disorders, and substance-use disorders. Interestingly, the habenula is highly enriched in evolutionarily conserved orphan G protein-coupledreceptors (GPCRs or GPRs).

METHODS

Using pharmacological, behavioural, gene-knockout and *in vivo* neuroimaging approaches, we examined the roles of habenula-specific orphan GPCRs, including GPR54, GPR139 and GPR151, in neuropsychiatric behaviours in zebrafish models.

RESULTS

We found that GPR54 is involved in serotonin modulation and fear expression. Similarly, GPR139 was found to exhibit a modulatory role in fear learning.

Interestingly, GPR139 also exhibits a neuroprotective effect against glutamate excitotoxicity and cognitive impairment. GPR151 has been known as an obesity-riskgene, but we recently found its role in social behaviours and a possible link with cognitive function.

CONCLUSION

Our study presents habenular orphan GPCRs as a promising avenue for understanding neuropsychiatric diseases and developing new therapeutic strategies.

EXPLORING THE EFFECTS OF LOCAL MALAYSIAN FRUIT EXTRACTS ON SEIZURE PARAMETERS IN A ZEBRAFISH LARVAE MODEL

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INTRODUCTION

Previous literature has shown that some fruits may aggravate seizures while some fruits or its phytochemicals may be beneficial against seizures due to its anti-convulsant, anti-oxidant and anti-inflammatory activities. This has led to concerns in consumption of fruits among people with epilepsy, particularly in relation to the interaction with their medication. Currently, the knowledge on which fruits, particularly local Malaysian fruits, that might provoke or prevent seizures are scarce. Hence, we have explored on the three most commonly consumed fruits in Malaysia and investigated their effects on seizure activity.

METHODS

Fruit extracts were prepared from local common fruits (Durian, Mangosteen and Rambutan), using mainly 50% and 95% Methanol as well as water during the extraction process. A zebrafish larvae model was used for toxicity testing, where the larvae were incubated for 96 hours in each fruit extract to determine the safe dose. The anti- and pro-convulsant activity of each fruit extract were analyzed using parameters such as total distance travelled and maximum acceleration. These effects were also analyzed with the co-administration of pentylenetetrazol (PTZ) a known pro-convulsant and diazepam, a known anti-convulsant, in order to determine if the fruit extract aggravated further the proconvulsive or anticonvulsive effect, respectively. Fruit extracts that showed anti- or pro-convulsant activity were further evaluated using neurotransmitter analysis and calcium imaging to determine the mechanism of action of the observed activity.

RESULTS

Durian methanol extracts were observed to be pro-convulsant and further increased the activity of PTZ. Interestingly, all the water extracts (durian, mangosteen and rambutan) was shown to have an effective anti-convulsive activity instead. Neurotransmitter analysis coincided with the changes seen in the GABA and glutamate levels as well as GABA/glutamate ratio in the larvae. Similarly, calcium imaging was able to further showcase the potential of these fruit extracts to aggravate or ease seizure activity, although the significance is debatable.

CONCLUSION

This study might be a guiding light for both people with epilepsy as well as carers to make an informed decision on which fruits to use and which to avoid, in order to maintain a good quality of life.

THE THERAPEUTIC EFFECTS OF *Lactocaseibacillus rhamnosus* ON STRESS-INDUCED ANXIETY: A SYSTEMATIC REVIEW

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INTRODUCTION

Over the past two decades, a rise in stress-induced anxiety, particularly among late teens and early twenties, has become a significant public health concern linked to premature mortality. While anxiolytic medications are the conventional therapeutic approach, their adverse effects and dependency risk necessitate exploring alternative treatments. *Lactocaseibacillus rhamnosus*, a beneficial gram-positive bacterium residing in the human gut, is widely utilised as a dietary supplement and for treating urinary tract infections due to its resilience to gastric and bile acids. This review systematically assessed the potential therapeutic effects of *L. rhamnosus* strains on stress-induced anxiety, leveraging recent discoveries regarding the bidirectional communication along the microbiota-gut-brain axis in neurological conditions.

METHODS

An extensive literature search and selection was systematically conducted using PubMed, EMBASE, and Scopus databases for original studies on *L. rhamnosus* on stress-induced anxiety from 2011 to 2023. The studies included both animal and human subjects.

RESULTS

Out of a total of 1226 records, 20 articles met this review's inclusion and exclusion criteria. The predominant findings indicated the beneficial effects of *L. rhamnosus* in ameliorating behavioural manifestations of stress-induced anxiety. Moreover, investigations highlighted biochemical alterations after *L. rhamnosus* administration, including modifications in neurotransmitter metabolism, specifically GABA and serotonin, and shifts in gut microbiota-derived metabolites, indirectly influencing stress and anxiety levels.

CONCLUSION

Our analysis shows *L. rhamnosus*'s therapeutic effectiveness for stress-induced anxiety, though studies with null findings must be recognised. Discrepancies may arise from factors like bacterial strains, dosage, and anxiety severity. Standardising these parameters in future research can reduce bias. While *L. rhamnosus* shows promise for anxiety treatment, more studies are needed to clarify its role as an adjunctive or substitute therapy for conventional anti-anxiety medications.

EXPLORING THE THERAPEUTIC POTENTIAL OF *Swietenia macrophylla* IN ALZHEIMER'S DISEASE PATHOLOGY: INSIGHTS FROM PRECLINICAL STUDIES

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INTRODUCTION

Globally, approximately 24 million elderly individuals suffer from dementia, commonly associated with Alzheimer's disease (AD). Despite available treatments to alleviate AD symptoms, there's a critical need to develop therapeutics that modify the course of the disease. Phytochemicals are gaining interest for their potential to enhance memory, learning, and cognitive function. *Swietenia macrophylla*, commonly known as mahogany, holds significant medicinal value and is native to tropical and subtropical regions worldwide. The ethyl acetate fraction of SM seeds (SMEAF) contains active compounds with pharmacological properties. In this study, we investigated the effects of orally administered SMEAF (at doses of 200mg/kg and 100mg/kg) over 21 days in BALB/c mice, with Ibuprofen (100mg/kg) as a positive control, to protect against neuroinflammation induced by intraperitoneal Lipopolysaccharide (LPS).

METHODS

Behavioural tests, including novel object recognition and Y-maze tests, were used to assess learning and cognitive function. Gene expression studies focusing on Amyloid Precursor Protein (APP), Microtubule-associated protein tau (Mapt), Cyclooxygenase-2 (COX-2), Brain-derived neurotrophic factor (BDNF), cAMP-responsive element-binding protein-1 (CREB-1) and Neuropeptide-Y (NPY) were performed on brain tissues. Neurotransmitter levels of acetylcholine and Glutamate, along with protein profiling using LCMS/MS, were analyzed in brain tissues.

RESULTS

Results showed that SMEAF at doses of 200mg/kg (HD) and 100mg/kg (LD) significantly improved memory compared to the LPS group. SMEAF treatment also reduced the expression of AD-associated genes like APP and Mapt, as well as COX-2, while increasing neuroprotective factors such as BDNF, CREB-1 and NPY. Acetylcholine and Glutamate expression were significantly increased with SMEAF treatment compared to the LPS group. Heatmap analysis revealed differential protein expression across treatment groups, indicating potential mechanisms in AD pathology for further investigation.

CONCLUSION

These findings underscore the potential of SMEAF as a therapeutic avenue for neurodegenerative diseases like AD, offering promise for future research and clinical applications.

PHILANTHOTOXIN-343: A PROMISING NEUROPROTECTIVE AGENT AGAINST NMDA-INDUCED RETINAL INJURY IN GLAUCOMA

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INTRODUCTION

The overstimulation of N-methyl-D-aspartate receptors (NMDAR) leading to excitotoxicity has been implicated in glaucoma associated with calcium-dependent neurotoxicity. The excitotoxic cascade induces an excessive influx of calcium ions (Ca^{2+}) which leads to apoptotic pathway resulting in retinal ganglion cell death and optic nerve damage. This study aimed to investigate the potential neuroprotective effects of Philanthotoxin-343 (PhTX-343) to prevent retinal injury associated with NMDAR excitotoxicity and oxidative stress, as well as studying the underlying apoptotic mechanism involving calcium regulated proteins.

METHODS

Experimental Sprague-Dawley rats were divided into three groups and were intravitreally administered with (i) phosphate-buffer saline (PBS), (ii) NMDA, and (iii) pre-treatment with PhTX-343 followed by NMDA. After seven days, rats were subjected to visual behavior assessments. Following euthanasia, the retinal and optic nerve tissues were harvested H&E and toluidine blue staining respectively. Retinal tissues were also harvested for biochemical analysis of calcium-regulated proteins and transcription factors, as well as oxidative stress, and apoptotic biomarkers.

RESULTS

Our results demonstrated that pre-treatment with PhTX-343 significantly enhanced rats' visual capacity, prevented optic nerve damage, preserved retinal ganglion cell layer thickness, and increased retinal cell density compared to NMDA-induced rats. PhTX-343 administration also led to increased antioxidant concentrations (glutathione, superoxide dismutase, catalase) and reduced retinal 3-nitrotyrosine levels and inducible nitric oxide synthase. PhTX-343 also suppressed the expression of pro-apoptotic proteins (caspase-3, BAX), while anti-apoptotic protein (BCL) was increased in comparison to the NMDA group. In all parameters, the results for PhTX-343 group was found similar to healthy rats, including the regulation of calcium-regulated (calpain, calcineurin, cabin) and transcription factors (p53, NF-kB).

CONCLUSION

Our study provided evidences that PhTX-343 protected against NMDA-induced RGC apoptosis of the retinal cells through the regulation of specific transcription factors and calcium-regulated proteins, thus preserving visual functions in rats.

DISSECTING THE MOLECULAR CHANGES INDUCED BY PALM ALPHA TOCOTRIENOLS IN HUMAN DIFFERENTIATED NEURONAL CELLS: A QUANTITATIVE PROTEOMICS APPROACH

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INTRODUCTION

Alpha tocotrienol (α T3) is one of the isoforms of tocotrienols besides delta (δ), beta (β) and gamma(Y) tocotrienols. Palm tocotrienols have been studied extensively for their neuroprotective roles in cell-based as well as animal models. Previously, our group has reported that α T3 protects neuronal cells by augmenting intracellular antioxidant enzymes and suppressing oxidative stress. Moreover, our studies also demonstrated protective effects on dopaminergic neurons via alterations in dopaminergic markers such as alpha-synuclein, dopamine and tyrosine hydroxylase. Therefore, this study is aimed to explore the differential protein expression implicated by α T3 in protecting human neuronal cells.

METHODS

A label-free quantitative double mass spectrometry was used to analyse the proteins extracted from α T3 treated cells and untreated control cells. Briefly, human SH-SY5Y neuroblastoma cells were cultured and differentiated to mimic human dopaminergic neurons. Then, the differentiated neurons were treated with α T3 for 24 hours and proteins were extracted, digested and cleaned up before analysis in LC-MS/MS. The protein sets treated with α T3 were compared to those of untreated controls using a two-tailed *Student t-test* to identify proteins significantly modulated by α T3 in differentiated SH-SY5Y cells. Proteins were considered significantly regulated if the difference between the two treatment groups yielded a p-value less than 0.05 ($p < 0.05$). These significant proteins were further analyzed using bioinformatics databases such as KEGG, STRING and SR PLOT to uncover the Gene ontology (GO) annotations and Pathway Enrichment analysis to elucidate the differentially modulated pathway resulting from α T3 treatment.

RESULTS

Our research revealed that α T3 exerted regulation over a total of 158 significant proteins in human-differentiated neurons. Among these proteins, 84 experienced upregulation, while 74 were down-regulated. Analysis using Gene Ontology (GO) terms unveiled notable alterations in the mRNA catabolism pathway within the biological process category, as well as changes in structural constituents within the ribosome. Additionally, Pathway enrichment analysis highlighted a significant modulation of the ribosome pathway. Further dive into the proteins that regulated the ribosome, we found about 30 ribosomal proteins were differentially regulated by α T3 in human neuronal cells. These proteins have been identified to be involved in various reactions in protein translation including translation initiation, CAP-dependent translation initiation and rRNA processing in the nucleus and cytosol. Our study indicates that the



differential regulation of ribosomal proteins by α T3 could impact the synthesis of proteins crucial for synaptic plasticity and neuronal remodelling. This, in turn, may facilitate processes such as learning, memory formation, and adaptation to new environments. Furthermore, changes in the expression of ribosomal proteins also indicate the synthesis of proteins that support neuronal survival such as in neuron growth, proliferation and survival.

CONCLUSION

In our prior investigation, we established that treating human neuronal cells with α T3 notably protected neurons via enhancing cell viability and antioxidant enzyme levels while reducing reactive oxygen species. The current exploration through proteomics analysis revealed significant changes in the ribosome pathway, impacting various protein synthesis and translation that are significant in neuronal health and survival. This study serves to complement our previous research in elucidating the molecular mechanisms influenced by α T3 in human neuronal cells.

ARTEMISININ AMELIORATES THE NEUROTOXIC EFFECT OF 3-NITROPROPIONIC ACID: A POSSIBLE INVOLVEMENT OF THE NRF2/HO-1 AND ERK/BDNF SIGNALING PATHWAYRichmond Arthur¹, Uma Shanker¹, Puneet Kumar^{1*}¹*Department of Pharmacology, Central University of Punjab, Bathinda, India***INTRODUCTION**

Neurodegenerative disorders like Huntington's disease (HD) continue to be a major threat to human health, with oxidative stress, neuroinflammation, and apoptosis all playing important roles in their development.

METHODS

The protective effect of artemisinin (ART) alone and in combination with the ERK antagonist PD98059 against 3-nitropropionic acid (3-NP) induced cell death and oxidative stress in SH-SY5Y cells was determined using the MTT and DCFH-DA assays, respectively. *In vivo*, using a 21-day treatment period, the possible neuroprotective effects of ART (10, 20, and 40 mg/kg *i.p.*) against the neurotoxicity generated by 3-NP (10 mg/kg *i.p.*) was evaluated in Wistar rats by assessing behavioral parameters on day 1, 14 and 21. Biochemical, inflammatory, apoptotic markers, and histopathological changes were assessed using striatal samples obtained from the brain of experimental animals on day 22.

RESULTS

ART significantly mitigated the neurotoxic effect of 3NP in SH-SY5Y cells. However, ART's neuroprotective activity was reduced in the presence of PD98059. Moreover, ART treatment for 21 days substantially alleviated the behavioral impairments associated with 3-NP toxicity. It reduced the oxidative stress induced by 3NP, as evidenced by the lower levels of MDA and nitrite, and improved catalase and SOD activity. ART effectively suppressed neuroinflammatory (IL-6) and apoptotic markers (caspase 3 and 9) while increasing the levels of the neurotrophic factor BDNF. The histological changes brought on by the 3-NP treatment were reversed by ART.

CONCLUSION

Artemisinin could exert its neuroprotective effect via antioxidant, anti-inflammatory, and antiapoptotic properties with a possible involvement of the Nrf2/HO-1 and ERK/ BDNF pathway.

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PROTECTIVE EFFECT OF A REDUCED PDLIM5 EXPRESSION AGAINST PHENCYCLIDINE-INDUCED COGNITIVE IMPAIRMENT

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BACKGROUND

Phencyclidine (PCP) is used to model cognitive deficits related to schizophrenia. The *PDLIM5* is significantly associated to schizophrenia from various studies. This study investigated the effect of PCP administration on *PDLIM5* gene expression in the brain and whether a reduced *PDLIM5* expression in brain has a protective effect against PCP-induced spatial learning and memory impairment.

METHODS

The *PDLIM5* knockout mice, C57BL6/J strain, was directly obtained and purchased from the Mouse Biology Program, University of California, Davis which then shipped to Malaysia. Only wild-type (WT) and heterozygous (HET) mice were used for the experiment. A drug regime of PCP dose at 10 mg/kg in the regime of 7 days daily injection, intraperitoneal, and followed by 1 day withdrawal period was used to induce the cognitive deficits. There were two comparison groups: 1) WT vs. HET mice, 2) WT-PCP vs. HET-PCP mice. Morris water maze (MWM) was conducted to measure spatial learning and memory performance and forced swimming test (FST) used to indicate hopefulness behaviour. Brain samples were collected for the gene expression analysis. Student's *t*-test and two-way ANOVA statistical analyses were carried out appropriately.

RESULTS

Gene expression analysis demonstrated that the *PDLIM5* is expressed in various brain regions. PCP administration increased *PDLIM5* expression in the prefrontal cortex, hippocampus, and amygdala. In the behavioural analysis, HET mice showed higher motivation to escape in the FST compared to WT mice. When treated with PCP, HET mice exhibited less impairment in spatial learning and memory compared to control both phase of acquisition and probe phases of MWM.

CONCLUSION

The findings suggest that decreased *PDLIM5* expression has a protective effect against PCP-induced cognitive deficits. This study highlights the potential therapeutic implications of targeting *PDLIM5* for the treatment of cognitive impairment related to schizophrenia.

KEYWORDS

Schizophrenia, memory, phencyclidine

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THE NEUROPROTECTIVE ROLES OF XANTHONES IN ALZHEIMER'S DISEASE: A SYSTEMATIC REVIEW

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INTRODUCTION

Xanthones, natural secondary metabolites, hold significant potential as neuroprotective agents owing to their notable biological impact on Alzheimer's disease (AD). Yet, their precise mechanisms in AD remain elusive. This study aimed to systematically review the neuroprotective role of xanthones in both *in vitro* and *in vivo* models related to Alzheimer's disease, thus elucidating their roles in AD.

METHODS

A literature search was conducted in the Medline and Scopus databases using specific keywords to identify relevant articles published until June 2023. After eliminating duplicates, all retrieved articles were imported into the Rayyan software. Screening of article titles was performed according to predetermined inclusion and exclusion criteria. Bias assessment was conducted for the relevant full-text articles using the Office of Health Assessment and Translation (OHAT) tool.

RESULTS

A total of 21 papers were included in this review. Xanthones have demonstrated various pharmacological effects on AD. In cell culture studies, xanthones exhibited anti-cholinesterase activity, thereby protecting against acetylcholine loss. They also manifested neuroprotective properties by enhancing cell viability and reducing the accumulation of β -amyloid and tau aggregation. In addition, administration of xanthones in animal models resulted in a reduction in neuroinflammation by decreasing microglial and astrocyte burden. In terms of molecular mechanisms, xanthones prevented neuroinflammation through the modulation of signaling pathways, including TLR4/TAK1/NF- κ B, MAPK and caspases-related pathways.

CONCLUSION

Despite the various neuroprotective effects associated with xanthones, there is a scarcity of studies elucidating their underlying mechanisms in AD. Further studies are warranted to comprehensively grasp their potential neuroprotection to AD.

KEYWORDS

xanthone, Alzheimer's disease, memory impairment, dementia, neuroprotection

UNRAVELLING THE NEUROPROTECTIVE PROPERTIES OF *Ficus deltoidea* Jack IN ALZHEIMER'S DISEASE-LIKE RAT MODEL: INSIGHTS FROM HISTOLOGICAL AND MOLECULAR PERSPECTIVES

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INTRODUCTION

Dementia, notably Alzheimer's disease (AD), presents a significant challenge for aging populations due to its progressive cognitive decline caused by neuronal degeneration. The hallmark attributes of AD include amyloid beta plaques and neurofibrillary tangles caused by hyperphosphorylation of tau. Multiple studies have explicitly investigated tau phosphorylation, revealing that phosphorylated tau is significantly elevated in the majority of AD brains. Current medications for AD offer limited palliative care, underscoring the urgent need for multifaceted therapies targeting various AD pathogenic pathways. Natural products have been vastly researched for their potential in AD drug development and, hence, in this study, the therapeutic potential of *Ficus deltoidea* (FD) is highlighted by determining its neuroprotective effects on hippocampal histology and AD-related protein expression in an AD-like rat model.

METHODS

This study induced AD-like conditions in male albino Wistar rats using D-galactose (D-gal) and aluminium chloride (AlCl₃), known as senescence and neurotoxic agents, respectively. The AD- induced rats were orally administered with FD extract at varying dosages for 12 weeks. Subsequent investigations including Morris water maze (MWM) test, hippocampal tissue examination via Nissl staining and measurement of hyperphosphorylated tau (p-tau) expression were performed to assess the neuroprotective effects of FD.

RESULTS

MWM results demonstrated that AD-induced rats exhibited impaired spatial learning and memory, which were significantly improved with FD co-administration. The AD-induced rats



showed a significant loss of pyramidal neurons in the cornu ammonis 1 (CA1) sub-region of the hippocampus. However, FD administration successfully reversed these morphological aberrations. Furthermore, FD-treated rats exhibited an apparent decrease in p-tau expression in their brains.

CONCLUSION

The administration of FD resulted in a lower p-tau level, which improved learning and memory, along with reduced neuronal loss. These findings indicate that early intervention with FD may serve as a preventive measure against AD and offer therapeutic benefits for AD medication development.

EVALUATING THE PATHOGENIC ROLE OF SYNTHESIZED HUMAN NEUROMELANIN ANALOGUES THROUGH INTRANIGRAL INJECTION IN MICE AND ITS IMPLICATION IN PARKINSON'S DISEASE

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INTRODUCTION

Parkinson's disease is an age-related neurodegenerative disorder where neuromelanin (NM) containing catecholaminergic neurons are preferentially lost. Like iron, the amount of intraneuronal NM in the substantia nigra (SN) increases as the person ages. When NM is released extra-neuronally by degenerating neurons, it aggravates neuroinflammatory and neurodegenerative processes. As human NM is practically insoluble and its isolation has ethical concerns, this study focuses on developing a PD model from synthesized human NM that may mimic human NM.

METHODS

Two synthesized human NM analogues 1 (PheoDAβLg Fe0.5%) and 2 (PheoDAfLg Fe0.5%) were selected based on previous in-vitro studies. 1 µl of 0.5mg/ml or 0.25mg/ml NM analogues 1 and 2 were injected in SN through stereotaxic injection in 5-7 months male ICR mice. The rotarod, grip strength, and round beam walk test analyzed motor impairment. On the 21st day, animals were perfused, and immunohistochemistry was performed to analyze astrogliosis and TH⁺ neuronal loss. Moreover, Perl's and Masson-Fontana staining were done to evaluate the presence of iron and NM, respectively.

RESULTS

NM Analogue 1 (0.5mg/ml and 0.25mg/ml) induced significant astrogial activation, increased ferric iron and induced TH-positive neuronal loss. NM Analogue 2 (0.5mg/ml and 0.25mg/ml) induced significant motor impairment, astrogial activation, and TH-positive neuronal loss. However, no significant dose-dependent effect was observed. Masson-Fontana staining for NM was not prominent, suggesting phagocytosis and degradation of NM analogues by microglia.

CONCLUSION

Synthesized human NM analogues 1 and 2 induced neuroinflammation and neurodegeneration in mice SN, similar to human NM.

EFFECTS OF CLITORIENOLACTONES FROM *Clitoria ternatea* ROOT ON CALCIUM CHANNEL MEDIATING HIPPOCAMPAL LONG-TERM POTENTIATION IN RATS INDUCED CHRONIC CEREBRAL HYPOPERFUSION

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INTRODUCTION

Chronic cerebral hypoperfusion (CCH) is a common mechanism of acute brain injury due to impairment of blood flow to the brain. Moreover, a prolonged lack of oxygen supply may result in cerebral infarction or global ischemia, which subsequently causes long-term memory impairment. Research on using *Clitoria ternatea* root extract for treating long-term memory has been studied extensively. However, the bioactive compound contributing to its neuroprotective effects remains uncertain. In the present study, we investigate the effects of clitorienolactone A (CLA) and B (CLB) from the roots of *Clitoria ternatea* extract on hippocampal neuroplasticity in rats induced by CCH.

METHODS

Bioactive compounds of CLA and CLB were isolated from the *Clitoria ternatea* roots extract using column chromatography. The rat model of CCH was induced using two-vessel occlusion surgery (2VO). The rats were divided into four groups of treatment: Sham+veh.; 2VO+veh.; 2VO+CLA 10mg/kg; 2VO+CLB 10mg/kg. The effect of CLA and CLB on *in vivo* hippocampal synaptic plasticity was assessed using electrophysiological technique. The calcium imaging technique was performed to evaluate the effects of CLA and CLB on the changes of calcium channel. *In silico* study was performed to assess the binding energy of CLA and CLB against glutamatergic receptor subtypes using AutoDock 4.0.

RESULTS

The CCH rats that received 10mg/kg of CLA and CLB significantly reversed the impairment of hippocampal long-term potentiation following 2VO surgery. Furthermore, incubation of CLA and CLB (5 μ M) significantly sustain the increment of intracellular calcium in rat's cortical neurons during hypoxia condition. Following *in silico* study, the results found that both CLA and CLB exhibited lower binding affinity against GluN2A and GluN2B subunits.

CONCLUSION

Our findings demonstrated that bioactive compounds from *Clitoria ternatea* improved long-term memory deficits in the chronic cerebral hypoperfusion rat model via calcium uptake. Hence, CLA and CLB could be potential therapeutic tools for treating cognitive dysfunction.

KEYWORDS

Clitorienolactones, *Clitoria ternatea*, Chronic cerebral hypoperfusion, Neuroplasticity

Basic Neuroscience

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COGNITIVE PERFORMANCE IN A RAT MODEL OF CEREBRAL SMALL VESSEL DISEASE (CSVD): A MORRIS WATER MAZE ANALYSIS

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BACKGROUND

Cerebral small vessel disease (CSVD) is becoming acknowledged as a significant contributor of cognitive impairment in the elderly. Our study explores the relationship between CSVD pathogenesis, endothelial dysfunction, and cognitive performance, with a focus on Nuclear Factor- Kappa Beta signaling as a potential therapeutic target. Because age and hypertension are the primary risk factors for CSVD, this study compared the spatial learning and memory of various age groups of spontaneously hypertensive stroke-prone (SHRSP) rats, which serve as an animal model of early stage CSVD, to normotensive, Wistar-Kyoto (WKY) rats.

METHODS

The Morris water maze (MWM) test was performed to evaluate spatial learning and memory abilities using three trials: visible platform, hidden platform, and a probe. In this MWM test, the rats (35 SHRSP rats and 39 WKY; three age groups (8, 12, and 42 weeks) underwent daily training trials for five days, and followed by a day-six probe trial to evaluate their memory retention

RESULTS

At 8 and 14 weeks of age, the rats from SHRSP and WKY groups had similar swimming speeds and escape latencies. By 42 weeks of age, the SHRSP rats presented fluctuating escape latencies, which could indicate potential learning and memory issues, in contrast to the WKY rats' steady performance. In probe trial test (day 6), the SHRSP rats spent an equivalent time in the target quadrant with hidden platform as the WKY rats at ages 8, 14 and 42 weeks.

CONCLUSION

Even though CSVD rat models experienced cognitive decline by 42 weeks of age, they maintain their spatial learning and memory abilities without significant impairment. Therefore, future examination into histopathological neurodegeneration, as well as the localization and over- expression of endothelial functional markers could provide insights into the white matter vulnerabilities, and consequently, the underlying mechanisms of CSVD.

KEYWORDS

cerebral small vessel disease, cognitive performance, spontaneously hypertensive stroke-prone rat, morris water maze, wistar Kyoto

SUBACUTE EFFECTS OF METHIOPROPAMINE ON BEHAVIOUR AND DOPAMINE NEUROTRANSMITTER SYSTEM IN MICE

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INTRODUCTION

Methiopropamine (MPA), a derivative of methamphetamine (METH), is one of the new psychoactive substances (NPS) which are mostly synthetic drugs sold as legal alternatives to illicit drugs to circumvent the existing law. MPA was discovered in 1942 but became increasingly popular in 2012 due to easy access to their supply through the internet. However, limited research and its close resemblance to METH have raised concerns about its harmful effects to the brain. This study investigated the subacute effects of MPA on the monoamine neurotransmitter systems in relation to the behavioural changes observed through a battery of tests in mice.

METHODS

Male Swiss Albino mice were randomly divided into four groups (n=10) which received daily intraperitoneal injections of either normal saline, METH at 1 mg/kg or MPA at 1 or 3 mg/kg once daily for seven days. The animals were subjected to novel object recognition (NOR), open-field (OFT), 8-radial arm maze (8-RAM) and forced swim (FST) tests at the end of the treatment. At the end of the tests, animals were killed and brain were collected for quantification of monoamine neurotransmitters using HPLC with electrochemical detector and identification of gene expression state using microarray analysis.

RESULTS

Mice treated with MPA and METH demonstrated intact non-spatial memory on day 7 but MPA at 3 mg/kg significantly ($p<0.05$) caused memory deficits 24 hours post-withdrawal using NOR test. Similarly, the higher dose of MPA impaired reference and working memory errors comparable to METH based on the 8-RAM test. MPA did not induce depressive-like behaviour as evident by unaltered immobility time in the FST. In the OFT, MPA at 3 mg/kg reduced anxiogenic behaviour but did not affect locomotor activity. In the prefrontal cortex (PFC), a significant ($p<0.05$) reduction in dopamine levels accompanied with an increased dopamine turnover rate was observed following subacute exposure to 3 mg/kg of MPA without significant alterations to other neurotransmitters. The microarray analysis demonstrated a substantial upregulation in monoaminergic neurotransmission pathway in the PFC for the group treated with 3 mg/kg MPA.

CONCLUSION

Subacute MPA treatment induced behavioural changes possibly mediated through the disruption of dopaminergic neurotransmission, an effect that is similar to that of METH exposure. This study contributed to further understanding of behavioural and physiological consequences associated with MPA use which poses a risk of neurotoxicity.

REVEALING HIDDEN THREATS: PLATELET DERIVED-MICROPARTICLES AS KEY PREDICTORS FOR CARDIO-CEREBROVASCULAR DISEASE RISK FACTOR IN INDIVIDUALS WITH CEREBRAL SMALL VESSEL DISEASE

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INTRODUCTION

In the context of age-related cerebral small vessel disease (CSVD), such as white matter hyperintensities, often incidentally discovered during neuroimaging, and frequently associated with cardio-cerebrovascular risk factors, this study investigates the unique correlations between these risk factors and CSVD prevalence among asymptomatic working-aged adults in an unexplored suburban region on the northeast coast of the peninsular Malaysia.

METHODS

Sixty subjects (mean age: 39.83 ± 11.50 years) with low to moderate cardio-cerebrovascular disease risk, as predicted by QRISK3, underwent 3T magnetic resonance imaging (MRI) brain scans and peripheral venous blood collection for circulating microparticles (MPs) enumeration, specifically focusing on platelet-derived MPs (CD62P) as a novel biomarker. A comprehensive biostatistical approach incorporating correlation analysis (CA), decision tree analysis (DTA), and artificial neural networks (ANN) such as principal component analysis (PCA) and multilayer perceptron (MLP) was employed to identify factors contributing to CSVD prevalence.

RESULTS

CSVD was found in 20 (33.3%) subjects (mean age: 46.00 ± 12.00 years). CA revealed strong correlations with age, hypertension, smoking status, and family history. DTA identified aging and CD62P as the most significant predictors for CSVD. MLP and PCA confirmed that aging and CD62P were the primary disease risk predictors, achieving an 88.3% accuracy in this study population.

CONCLUSION

This investigation highlights the potential of CD62P as a novel biomarker for CSVD and offers valuable insights for clinicians in enhancing the quality of assessment, prevention, and therapeutic strategies, particularly for asymptomatic and economically active working adults.

TEARS OF MELIOIDOSIS: A RARE PRESENTATION OF LACRIMAL GLAND MELIOIDOSIS WITH INTRACRANIAL EXTENSION

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INTRODUCTION

Abscesses are known complications of melioidosis, an infection caused by a gram-negative bacillus, known as *Burkholderia pseudomallei*. Ocular involvement is infrequent, with melioidosis-related lacrimal glands abscess being rare and possibly underreported in our literature, carrying a high rate of mortality and morbidity, especially with intracranial involvement resulting in neuromelioidosis.

REPORT

We present a middle-aged man with diabetes mellitus presenting with myriad of symptoms including fever, sore throat and headache for a week, with bilateral periorbital swelling specifically starting over superolateral aspect of the orbits. Clinical assessment demonstrated bilateral proptosis with complex ophthalmoplegia with chemosis and blepharitis. Blood culture grew *Burkholderia pseudomallei* and CT venogram of the brain and orbits confirmed cavernous sinus thrombosis.

Despite being on Meropenem and low-molecular-weight heparin, he developed focal clonic seizures in the right upper limb with preserved awareness. A contrast-enhanced MRI brain showed new bilateral subdural effusions with numerous rim-enhancing abscesses over bilateral lacrimal gland and bilateral temporalis muscle. Left parietal burr hole drainage, along with incision and drainage of bilateral upper eyelid abscesses were performed, resulting in marked clinical and radiological improvement. He completed eight weeks of intensive phase antibiotics and was started on eradication phase prior to his discharge.

CONCLUSION

If inadequately treated, lacrimal gland abscesses can lead to intracranial abscesses, meningitis and thrombosis as seen in our patient. A timely diagnosis and prompt initiation of targeted antimicrobial therapy, complemented with intensive care unit management are critical interventions in managing severe melioidosis, improving survival among patients. Early MRI also guided our treatment, demonstrating the advantage of MRI compared to conventional CT scans and should be advocated in every patient with suspected neuromelioidosis.

REPURPOSING ANAKINRA FOR NEUROINFLAMMATION MEDIATED ALZHEIMER'S DISEASE: *IN VITRO* AND *IN VIVO* EFFECTS

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INTRODUCTION

Alzheimer's disease (AD) is a leading cause of dementia and appears to be a growing burden due to the lack of drugs which can treat and cure AD. Neuroinflammation has been identified to play a significant role in many neurological conditions including AD and has been seen as an early event in AD pathophysiology. Of late repurposing drugs that were previously approved by the FDA has gained interest as it removes many of the time and financial barriers for bringing a drug to market. Insights of the past 4 to 14 years show that microglia activation and neuroinflammatory processes are locked in a vicious cycle with amyloidosis, and, hence, new pharmacotherapies should target both these processes. Anakinra is an interleukin-1 receptor antagonist (IL-1Ra) that competitively inhibits the binding to the interleukin-1 type 1 receptor (IL-1R1) thus blocking the effects of interleukin (IL)-1 (IL-1), specifically in the inflammatory system. It maintains the balance effects of inflammatory cytokines by reducing the IL-1, known as primary pro-inflammatory cytokines. Anakinra is an approved drug for several inflammatory diseases involving inflammation in the periphery like rheumatoid arthritis, Crohn's disease, and psoriasis but are also lately used in the brain to reduce the effects of Mediterranean fever, neurotrauma, and on certain forms of epilepsy in children. Thus, the aim of this study is to study the neuroprotective effects of Anakinra as an anti-neuroinflammatory agent in preventing AD associated neuroinflammation.

METHODS

In the *in vitro* part of the study, BV2 murine microglial cell line were incubated in the presence of LPS (0.01 to 100 µg/mL) for 24 h. The cell viability was measured using MTT assay. The release of NO and ROS were detected using the Griess test and DCFDA reagent assay, respectively. The mRNA levels were determined using RT-PCR and the genes tested were NF-κB1, TNF-α, IL-1β, IL-6, and NOS2 genes. For the *in vitro* study, a zebrafish larvae model was employed where ACR was exposed at a dose of 1 mM to 3 days post fertilization (dpf) zebrafish larvae for 3 days whereas anakinra (5, 10 & 20 µM) was treated for 24 hr. After the treatment period, larvae from all groups were assessed for cognitive impairments via behavioral studies and then processed for RT-PCR. The genes assessed were NF-κB, TNF-α, IL-1β, BDNF, and CREB1 genes.

RESULTS

In the *in-vitro* studies, anakinra has been observed to diminish the gene expressions of tumor necrosis factor-alpha (TNF-α) and nitric oxide synthase 2 (NOS2) stimulated by

lipopolysaccharide (LPS). Anakinra also reduced the LPS-induced production of nitric oxide (NO) and reactive oxygen species (ROS). Thus, the hypertrophic state of LPS-activated BV2 microglial cells was reversed by anakinra. Furthermore, acrylamide(ACR)-induced activation of NF- κ B, TNF- α and IL-1 β were down-regulated while cAMP response element binding protein (CREB) expression levels were markedly enhanced in ACR-treated zebrafish larvae. It was also observed that anakinra improved the uncoordinated swimming behaviors in ACR-exposed zebrafish larvae. Overall, anakinra demonstrated potential anti-neuroinflammatory and anti-oxidative effects.

CONCLUSION

These research findings suggest that anakinra demonstrated a time- and concentration-dependent anti-neuroinflammatory effect across multiple targets which reinforces the notion of repurposing anakinra for AD treatment.

THE ROLE OF OREXIN SIGNALLING IN FEAR MEMORY AND LEARNING IN ZEBRAFISH

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INTRODUCTION

Fear and fear-like behaviors are crucial for survival because they promote adaptive reactions to potential threats. Various brain mechanisms underpinning fear and its control have been extensively investigated over the years. Recently, there has been a surge of curiosity on the potential role of appetite-regulating hypothalamic neuropeptides in fear-like activities. Fear and fear-related behavior are influenced by appetite-regulating neuropeptides, which affect physiological and pathological processes. These neuropeptides, such as ghrelin, leptin and orexin, interact with brain fear circuits, influencing anxiety and stress reactions. Anxiety disorders and mood abnormalities can be exacerbated by dysregulation, which links hunger and emotional states.

The complicated neuroconnectivities between appetite-regulating peptides and fear-related behaviors suggest their possible involvement in fear-related disorders such as anxiety disorders, phobia and related psychiatric conditions. Understanding these connections may open up new therapeutic pathways for the treatment of fear-related diseases, such as repurposing existing medications that target appetite-regulating peptides.

METHODS

To determine the connection of starvation and the neuropeptide orexin and if orexin plays a role in fear memory consolidation: Orexin mRNA levels were quantified in comparison to starved zebrafish brain. Fear learning and memory was assessed in starvation treatment and administration of orexin agonist and antagonist of zebrafish. Conditioned place avoidance assay was conducted using alarm substance as the aversive stimuli to validate the potential involvement of orexin neurons in fear learning and memory.

To determine the involvement of habenula neurons in orexin modulation: Using a neuronal marker; c-fos, habenula neuronal activities were quantified by RTPCR with different treatments. Also to add, pERK was used to further validate the neuronal activities of the habenula as well via immunostaining.

RESULTS

Higher expression of orexin-A mRNA levels was detected in starved fish. Then, orexin and starvation significantly affect fear memory in zebrafish by lacking in avoiding the 'punished zone' in the CPA assay, suggesting fear memory impairment. Regardless, the role of orexin signaling in fear memory remains to be elucidated. In unconditional fear experiment, fish treated with orexin-A did not have an impact.



The involvement of the habenula in conjunction of orexin mediating the activities only in aversive situation via c-fos expression marker. pERK expression was also observed in the habenula in all aversive situations and in starvation only treatment.

CONCLUSION

Orexin and starvation indeed affect fear memory in zebrafish. AS induced CPA assay showed orexin agonist treated zebrafish impairs expression of fear memory by decreased/minimal avoidance behaviour and starved zebrafish showed reduced expression of fear memory similarly. While blocking orexin receptor showed the opposite effect on the CPA assay. c-fos expression in the habenula was high upon AS exposure along with orexin-A treatment, suggesting orexin system may have involved in the aversive process in the habenula. However, it is still not known if there is any direct connection and mechanism of orexin and the habenula neurons in this experiment. But, mapping of neural activity in the presence of orexin-A using c-fos showed potential connections of orexin and the habenula. Another marker is used to validate the neural activity of the habenula in starved condition and orexin-A treated zebrafish which is pERK. pERK expression in the ventral habenula established that the connectivity between orexin modulation in the habenula in aversive stimulation. Nevertheless, there are many neural pathways remain unclear and more exploration can be conducted in understanding further the specific role of orexin in fear memory.

KEYWORDS

Starvation, orexin, fear memory, aversive learning, conditional fear, habenula, neuroactivity

***Channa striatus* PREVENTS PENTYLENETETRAZOLE-INDUCED SEIZURES AND MODULATES INFLAMMATORY MARKERS**

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INTRODUCTION

Epilepsy occurs as a result of a hypersynchronized burst of neuronal activity in the brain. In most cases, the cause of epilepsy is unknown, but neuroinflammation is postulated to be one of the mechanisms involved in epileptogenesis. Therefore, ameliorating neuroinflammation could potentially improve neuroinflammation-mediated epilepsy. In Malaysia, *Channa striatus* (CS) fish is traditionally used for general wound healing among the older generation because of its anti-inflammatory and anti-nociceptive properties. We aim to investigate if CS has anti-epileptogenic and anti-inflammatory properties against pentylenetetrazol-induced seizures.

METHODS

We performed an LC/MS study on crude CS extract to determine the bioactive components present in the extract. Toxicity studies were performed on the adult zebrafish to determine a safe dose of CS extract to be used. Then, anti-epileptic studies were performed using adult zebrafish challenged with a proconvulsant, pentylenetetrazol (PTZ), after 24 hours of CS treatment of different concentrations. The expression of inflammatory genes and genes implicated in epilepsy was evaluated. Neurotransmitter analysis (GABA, inhibitory γ -aminobutyric acid, and excitatory glutamate, Glu) and brain protein expression were also assessed.

RESULTS

We identified a total of 31 compounds in the crude CS extract, where 2 of them, taurine, and leucine, have been previously shown to be anti-epileptic. Furthermore, we found that CS extract treatment reduced seizure severity significantly at 40 mg/L and prolonged the onset of PTZ-induced seizures in zebrafish significantly at doses of 10-80 mg/L. A decrease in gene expression was found, which is significant with CREB1, IL-1, NF-KB, and NPY genes. However, the GABA/Glu ratio did not change at all doses of CS extract. The brain protein expressions of syntaxin binding protein 1a and solute carrier family 1 member 2b were decreased by CS extract treatment. They are mapped onto the synaptic vesicle cycle pathway and associated with neuroinflammation-mediated epilepsy.

CONCLUSION

These results demonstrated the therapeutic potential of CS extract in treating neuroinflammation-mediated epilepsy by showing the ability of CS extract to reduce seizure severity, prolong latency time of seizures and decrease the expression of inflammatory genes and genes implicated in epilepsy.

MECHANISTIC INSIGHTS INTO THE ROLE OF GPR139, AN ORPHAN RECEPTOR, IN MODULATING THE ANTI-ADDICTIVE EFFECT AND KRATOM-DERIVED ALKALOID (MITRAGYNINE)

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INTRODUCTION

Opiate addiction presents a concerning public health challenge, worsened by the rise in infectious diseases and overdose fatalities. Despite the introduction of Harm Reduction movement like methadone and buprenorphine, their potential for addiction and adverse effects remains a significant concern. *Mitragyna speciosa* (kratom) has recently garnered attention as a potential alternative treatment option due to its opioid-like properties, however, kratom's addictive property and growing numbers of its abuse cases limit its therapeutic potential for opioid addiction. Mitragynine is the main psychoactive alkaloid of kratom and acts as a partial agonist at the mu opioid receptor (MOR). Additionally, the discovery of GPR139, a novel G-protein coupled receptor, has sparked interest in its potential role in modulating the effects of opioid drugs, particularly in the habenula, a brain region implicated in aversive behaviours and decision-making. The habenula acts as a crucial focal point in our study due to its role in the modulation of drug-seeking behaviours.

Our investigation aims to bridge the gap in understanding the pharmacological mechanisms of mitragynine and its potential as a therapeutic agent. Through a comprehensive exploration of the MOR-GPR139 complex, we aim to uncover novel insights into the neural circuitry underlying opioid addiction and withdrawal. We aim to elucidate whether blocking GPR139 could mitigate the adverse effects associated with mitragynine, potentially paving the way for a safer and more effective treatment approach for opioid dependence.

METHODS

To characterize the binding properties of mitragynine to the MOR-GPR139 complex, our study employed a dual approach involving both cellular and organismal models. Initially, HEK293-T cells were co-transfected with expression vectors containing human GPR139 or human MOR, alongside reporter gene vectors, enabling the assessment of mitragynine's interaction with these receptors. Subsequently, an MTT assay was employed to optimize the dosage of mitragynine treatment and the GPR139 antagonist. Dual-Luciferase Reporter Assay System will be utilized to determine luciferase activity and normalize with Renilla luciferase activity.

Concurrently, utilising zebrafish as an in vivo model, a conditioned place preference assay was conducted to evaluate the addictive properties of mitragynine, with morphine serving as a positive control. Multiple doses of mitragynine, ranging from 1 mg/L to 3 mg/L, were administered to observe dose-dependent addictive behaviour. This bridges insights from cellular binding studies with behavioural observations in zebrafish.

RESULTS

MTT treated cells showed dose and time-dependant inhibition in HEK293-T cells proliferation after treatment with mitragynine at varying time points. Cell proliferation was more greatly inhibited at 48h and 72h compared to 24h at which its proliferation decreased greatly at treatment with 50 μ M of mitragynine.

Addictive behaviour was not observed in zebrafish exposed to 1mg/L and 2mg/L of mitragynine compared to morphine. While zebrafish treated with 3mg/L of mitragynine exhibited aversive behaviour towards the drug.

CONCLUSION

While conclusive data is pending, our preliminary findings suggest that mitragynine may not induce addiction in zebrafish. This initial observation lays the groundwork for further investigation into the addictive potential of mitragynine as an analgesic. We aim to dive into the effects of mitragynine post-physical trauma to elucidate its potential role in triggering addiction pathways. This integrated approach provides a comprehensive understanding of mitragynine's pharmacological effects, from receptor-level interactions to behavioural responses, contributing to the broader understanding of its potential as a treatment option for opioid dependence.

THE ROLE OF SPEXIN IN FEMALE INFERTILITY

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INTRODUCTION

Infertility is a major global health issue that affects millions of people of reproductive age and roughly one in every six people are struggling to conceive. World Health Organization has defined infertility as the inability to conceive after 12 months of unprotected sexual intercourse. Women usually tend to suffer more due to the society stigma. Spexin, a novel neuropeptide that has been associated with various important neuroendocrine functions, including metabolism, stress, and reproduction. Recent reports have implicated the possible role of spexin in reproductive disorders. Therefore, the present study aims to understand the possible association of spexin with female infertility.

METHODS

In the present study, 70 females diagnosed with infertility and 50 reproductively healthy females were recruited from University Malaya Medical Center (UMMC). The plasma spexin levels were measured using spexin enzyme linked immunosorbent assay (ELISA). The effect of the demographic data was further investigated on the plasma spexin levels in both infertile and fertile women.

RESULTS

The ELISA assay revealed that plasma spexin levels were significantly ($p < 0.05$) higher in infertile patients as compared to the healthy ones. No significant differences in plasma spexin levels were observed between obese and non-obese patients of both groups. Positive correlation was shown between plasma spexin levels and age, menstrual cycle phases in both infertile and healthy groups as well as duration of infertility.

CONCLUSION

This is the first study reveals the significant association between spexin and infertility in females, suggesting its possible role in regulating reproductive function and may serve as an independent biomarker for female infertility diagnosis.

MORPHOLOGICAL AND ELECTROPHYSIOLOGICAL ANALYSIS OF DOWN SYNDROME CEREBRAL ORGANOID

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INTRODUCTION

Down syndrome (DS) is a neurodevelopmental disorder resulting from trisomy of human chromosome 21. Neuropathological features of DS encompass abnormal neuroanatomical structures, altered brain cell populations, and dysregulated neural gene expression, leading to defective neural circuitry, impaired neurotransmission, and synaptic dysfunction. These abnormalities manifest clinically as cognitive and memory impairments, language difficulties, behavioral challenges, and early-onset dementia. However, our understanding of DS neuropathology primarily relies on DS mouse models due to the scarcity of human samples. This study aims to investigate the morphological and electrophysiological development of DS using human induced pluripotent stem cell (hiPSC)-derived cerebral organoids (COs), which mimic embryonic human brain development.

METHODS

HiPSCs from disomic control and trisomic DS ($n=3$) were derived into COs for up to 4 months. We monitored CO growth by capturing images at regular intervals and analyzed their morphological features using ImageJ software. Additionally, we conducted single-unit recordings to assess COs' electrophysiological activity and analyzed the frequency of action potentials in response to electrical stimulation. Each experiment was performed with at least two independent batches, and statistical analysis was conducted using an unpaired t-test.

RESULTS

Trisomic DS COs exhibited a significant reduction in area and diameter ($p<0.05$) from day 14 to 4 months compared to disomic controls. This morphological change mirrors the neuroanatomical abnormalities observed in DS postmortem brains, characterized by decreased brain weight and volume. Furthermore, single-unit recordings revealed a significantly lower frequency of action potentials in DS COs, indicating impaired neuronal firing and synaptic function. This electrophysiological finding is consistent with DS's overactive inhibitory GABAergic neurotransmission theory, as observed in DS human and mouse models.

CONCLUSION

Our study demonstrates that trisomic DS hiPSC-derived COs exhibit reduced size and impaired electrophysiological function, reflecting the neurodevelopmental deficits observed in DS. This hiPSC-derived CO model offers a valuable in-vitro platform for DS research.

UPGRADING THE EFFECTIVITY OF ANTI-SEIZURE MEDICATIONS FOR STATUS EPILEPTICUS WITH NANOFORMULATION - A SYSTEMATIC REVIEW

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INTRODUCTION

Status epilepticus (SE) presents a life-threatening medical emergency condition characterized by prolonged seizures, leading to severe neuronal damage, morbidity and mortality, if not promptly treated. Immediate intervention is crucial, yet current anti-seizure medications (ASM) face limitations such as poor bioavailability, as many are orally prescribed, or otherwise in need for invasive administration routes such as intravenous ASMs. Nanoparticle-based drug delivery systems offer a promising approach in overcoming these challenges by enhancing drug solubility, stability, and brain bioavailability.

METHODS

This systematic review examines recent advancements in nanoformulations of ASMs for SE management. A comprehensive search using Google Scholar, PubMed, Scopus, and Science Direct, using the search term [nano particle OR nanoparticle OR nanoformulation OR nano formulations] AND [status epilepticus] were done, and 12 relevant studies were identified, highlighting various nanoparticle types, formulation methods, administration route, pharmacokinetic parameters, and stability.

RESULTS

ASM nanoparticles demonstrate advantageous characteristics for drug delivery, including their small size, high surface area, and tuneable physicochemical properties. These attributes facilitate efficient drug transport across biological barriers, precise targeting, and controlled release, ultimately augmenting drug efficacy while mitigating adverse effects. By optimizing release profiles and employing non-invasive administration routes like intranasal delivery, nanoformulated ASMs emerge as a promising immediate therapeutic strategy for SE management.

CONCLUSION

Nevertheless, further research is important to refine nanoformulation parameters, evaluate long-term safety considerations, and substantiate clinical efficacy. Thus, nanoparticle-based ASM delivery harbors considerable potential for transforming future SE treatment paradigms, offering prospects for enhanced patient outcomes and quality of life.

THERAPEUTIC EFFECT OF STINGLESS BEE HONEY ON COGNITIVE IMPAIRMENTS OF ALUMINIUM CHLORIDE AND D-GALACTOSE INDUCED RODENT ALZHEIMER'S MODEL

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INTRODUCTION

Alzheimer's disease (AD) is a long-term, progressive neurological condition that impairs memory and cognitive function. It is the most prevalent type of dementia, making up to 70% of cases, and is defined by the build-up of tau tangles and amyloid-beta (A) plaques in the brain. According to predictions, the number of AD cases will triple by 2050, placing a considerable burden on healthcare systems and families around the world.

METHODS

The study used 63 adult Sprague-Dawley rats that weigh 180 – 200g. Rats randomly divided into 6 groups with eight rats in each group. Group I assigned as control. Group II assigned as negative control or known as AD- like model, Group III assigned as positive control or known as AD+Donepezil, Group IV, V and VI assigned as treatment group. Donepezil (DPZ) prepared in distilled water, respectively. D-galactose and AlCl₃ prepared in 0.9% saline. The animals behavioural reactions to D-gal and AlCl₃ treatment were evaluated using two behavioural assays, conducted in the following order: first, measuring locomotor activity in OFT, and then MWM task for memory and learning.

RESULTS

Rats treated with SBH showed improved spatial memory as indicated by increased time spent and number of crossings in target quadrant during assessment in MWM. Learning ability of AD rats treated with SBH was also improved in MWM. Cognitive abilities of AD model rats were severely affected. Similar behavioural alterations in AD model induced by co-administration of AlCl₃ and D-gal. Cognitive deficits, decreased cholinergic activity, and AD-like lesions in brain, were also observed after combined administration of AlCl₃ and D-galactose. In AD model rats, nuclear membrane was not clear and neurons had flame-like irregular shape. In AD+DPZ rats, damaged and degenerated neurons were observed having irregular and indistinct morphology. One of the main findings of present work is that DPZ was not able to prevent the neurodegenerative mechanism induced by AlCl₃+D-gal. However, SBH not only treated the behavioural but also histopathological alterations in brain of AD-like model rats.

CONCLUSION

The present study suggests that SBH, a potent antioxidant, has an ability to treat oxidative. Neurotherapeutic agents such as SBH could be used in the earlier stage of the disease to stop the progression of the neurodegenerative process.

ALPHA-TOCOPHEROL RESCUES INTERFERON-INDUCED MOOD DISORDERS IN MICE

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INTRODUCTION

Interferon-alpha (IFN-alpha) is commonly used to treat severe disorders such as hepatitis C, cancer, and multiple sclerosis. However, clinical use has been linked to serious neuropsychiatric adverse effects such as depression, anxiety, and, in severe cases, suicide ideation. These incidents could have hampered the therapy's efficacy. Elevated IFN-alpha levels are known to promote oxidative stress, which leads to monoamine depletion, hyperactivation of the HPA axis, and disruption of the cytokine network, all of which are related with depression and anxiety. The most commonly found isomer of the Vitamin E family, alpha-tocopherol, has been shown to have potent antioxidant and anti-inflammatory properties. The purpose of this study was to see if alpha-tocopherol could relieve IFN-induced mood disorders in mice.

METHODS

Male ICR mice were given 10 daily intraperitoneal injections of IFN-alpha (36 ug/kg) or saline. Alpha-tocopherol (50 or 100 mg/kg, p.o.) or its vehicle were co-administered with i.p. IFN- for 10 daily doses in distinct groups of mice. Each mouse was subjected to open field test, social interaction test, and tail suspension test at the end of the last dose. Each animal's behaviours were captured and analysed.

RESULTS

When compared to the saline control group, mice treated with IFN-alpha were significantly travelled less distance in the open field test. In the social interaction test, mice given IFN-alpha exhibited a shorter social interaction time than saline-treated mice. In the tail suspension test, the IFN-treated group had considerably longer immobility time. Interestingly, co-administration of -tocopherol reduced IFN-induced depressed and anxiety-like behaviours.

CONCLUSION

Our data suggest that alpha-tocopherol can inhibit the onset of anxiety- and depressive-like reactions in mice produced by repeated IFN- therapy, possibly through its well-known antioxidative and anti-neuroinflammatory effects.

EFFECT OF JAVANESE MUSIC ON ANXIETY AND DEPRESSION-LIKE BEHAVIOUR AFTER CHRONIC STRESS: AN ANIMAL STUDY

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INTRODUCTION

Chronic stress is a significant contributor to anxiety and depression-like behaviors in rodents, mirroring aspects of human psychopathology. Non-pharmaceutical therapy, including music therapy, has shown promise in alleviating these conditions. This study explores the potential effect of Javanese traditional music on anxiety and depression-like behaviors in rats subjected to Unpredictable Chronic Mild Stress (UCMS).

METHODS

Male Wistar rats were divided into four groups, including the normal control group (CG1), not given any treatment (n=6); negative control group (CG2), given UCMS only (n=6); intervention group 1 (IG1), given UCMS and classical music (n=6), intervention group 2 (IG2): given UCMS and Javanese traditional music (n=6), each of which was given the intervention for 21 days. Anxiety-like behavior was measured with the Elevated Plus Maze (EPM) test and depression-like behavior with the Sucrose Preference Test (SPT) and Forced Swim Test (FST).

RESULTS

The potential effects of Javanese traditional music on anxiety-like behavior were explored, revealing a significant increase in the total time spent in the open arms ($p=0.000$) and a concurrent decrease in the total time spent in the closed arms ($p=0.000$) when compared to a negative control group. Additionally, reductions in depression-like behavior were observed, evidenced by elevated sucrose preference ($p=0.000$) and decreased immobility time ($p=0.004$). Lastly, there were no significant differences between the effect of Javanese traditional music and classical music on anxiety and depression-like behaviors.

CONCLUSION

The findings suggest that Javanese traditional music holds promise in alleviating anxiety and depression-like behavior in *Rattus norvegicus* following UCMS exposure. Moreover, there is no difference between the effect of Javanese traditional music and classical music.

DIFFERENTIAL EFFECT OF *IN VITRO* RUXOLITINIB TREATMENT ON NEURAL STEM/PROGENITOR CELL (NSPC) AND OLIGODENDROCYTE PRECURSOR CELL (OPC)

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BACKGROUND

Dysregulation of JAK-STAT signaling pathway is implicated in several disorders including myeloproliferative diseases and autoimmune disorders. A potent and selective inhibitor of Janus-associated kinase (JAK) enzyme, ruxolitinib (Rux), was previously approved by FDA for treatment against the aforementioned diseases. Additionally, there is increasing experimental usage of Rux to modulate aberrant JAK-STAT signaling in the central nervous system (CNS). Despite the interest, the potential cytotoxic effect of Rux on the various cell types within the heterogenous CNS microenvironment remains unknown. Two stem and progenitor cell populations, namely the neural stem/progenitor cells (NSPCs) and oligodendrocyte precursor cells (OPCs), are important for long-term maintenance and post-injury recovery response of the CNS. In addition, JAK-STAT signaling pathway has been shown to play crucial roles in the survival and proper functioning of these stem cell population. Therefore, this study aims to investigate the effect of Rux on proliferating and differentiating NSPC and OPC populations.

METHODS

Cultured rat NSPCs and OPCs were treated with various concentration of Rux (2 μ M to 20 μ M). The effect of Rux on proliferating NSPCs (nestin⁺) and proliferating OPCs (PDGF-R- α ⁺) was assessed via a 3-day Rux treatment, whereas its effect on differentiating NSPCs (neurofilament⁺) and differentiating OPCs (MBP⁺/PDGF-R- α ⁺) was assessed following a 7-day treatment. The cultures were then subjected to cytotoxicity assessment. Firstly, quantification of cells following treatment was performed via immunocytochemistry staining. Besides, the effect of Rux treatment on cell death was assessed using YO-PRO-1/PI dual-staining. Finally, the impact on DNA synthesis was assessed through BrdU assay.

RESULT

Rux treatment does not affect NSPC cultures within the dosage range tested. Conversely, Rux treatment negatively impacted OPCs. Specifically, Rux at a dosage above 10 μ M significantly reduced the number of proliferating OPCs. This reduction was associated with induction of



apoptosis rather than disruption in DNA synthesis. On the other hand, Rux treatment across all tested dosages was found to induce necrosis among differentiating OPCs, thereby significantly reducing their numbers.

CONCLUSION

Taken together, Rux within the range of 2 μ M to 20 μ M does not appear cytotoxic to NSPCs. On the other hand, OPCs appear to be vulnerable to the cytotoxic effect of Rux, with proliferating and differentiating OPCs exhibiting differential vulnerability to Rux treatment. These findings suggest a differential mechanism of actions of Rux on the heterogenous cell types within the CNS.

KEYWORDS

ruxolitinib, JAK inhibitor, cytotoxicity, oligodendrocyte precursor cell, neural stem/progenitor cell

NOVEL THERAPEUTIC OPTION USING SYNTHETIC MRNAS TRANSCRIPTION FACTOR IN REPROGRAMMING STEM CELL INTO INSULIN PRODUCING CELLS

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INTRODUCTION

Diabetes Mellitus (DM) is a prevalent chronic metabolic disorder impacting 422 million individuals globally, with an annual death toll of 1.6 million. Autoimmune β -cells destruction and insulin resistance define diabetes pathologically. This study centers on differentiating pluripotent stem cells into insulin-producing cells using synthetic mRNA as treatment instead of donor islet cell transplantation. Terminal cell differentiation can be orchestrated via temporal expression of transcription factors, initiating trans-differentiation.

METHOD

The primary objective is to differentiate mesenchymal stem cells into functional β -cells by modulating key transcription factors: PDX1, PAX4, NGN3, MafA, and GLIS3, pivotal in natural pancreatic β -cells differentiation. This study involves three distinct phases: (1) synthesis of synthetic mRNA, (2) *in vitro* investigations, and (3) *in vivo* transplantation. The successful transfection assessment encompasses gene expression analysis, cell viability, apoptosis assay, immunohistochemistry staining, and glucose-stimulated insulin assay.

RESULTS

Results reveal increased viability of terminally differentiated cells (>80% vs. 72.71% control), affirming the safety of mRNA-mediated differentiation. RT-PCR demonstrates amplified insulin mRNA expression in PNMPG-differentiated β -cells ($P < 0.05$), emphasizing effective insulin induction. *In vivo* analysis examines weekly glucose readings and oral glucose tolerance test (OGTT) data to evaluate differentiated cell impact, revealing encouraging glucose regulation trends. Moreover, C-peptide, insulin receptor and insulin level exhibit significant differences in the differentiated cells compared to control groups ($p < 0.05$).

CONCLUSION

In conclusion, synthetic mRNA transcription factors drive huMSC differentiation into β -cells, elevating cell viability and β -cell marker expression. This innovative approach holds potential as an alternative Diabetes Mellitus treatment.

KEY WORDS

Diabetes Mellitus, mesenchymal stem cell, β -cells, synthetic mRNA, cell differentiation

COGNITIVE ENHANCEMENT AND ANTIOXIDANT PROPERTIES OF WIN55,212-2 ON COGNITIVE IMPAIRMENTS INDUCED BY ALUMINUM CHLORIDE AND D- GALACTOSE IN RATS.

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INTRODUCTION

Globally, Alzheimer's disease (AD) is the prevailing progressive neurodegenerative disorder related to ageing, currently lacking a cure. Aluminium has been reported to act as a neurotoxic metal, whereas D-galactose (D-gal) has been established to be an ageing agent. WIN55,212-2 (WIN), is a potent cannabinoid agonist that has been reported to partially restore neurogenesis in aged rats. To investigate the therapeutic potential of WIN for AD, the current work created an AD-like rat model of neurotoxicity and cognitive impairment caused by AlCl₃ and D-gal.

METHODS

Male albino Wistar rats were given D-galactose at 60 mg/kg intraperitoneally and orally administered AlCl₃ at 200 mg/kg daily for 10 weeks. Five behavioural assessments were performed. Subsequently, commencing from week 8 of the experiment, rats were co-administered with WIN (0.5, 1 and 2 mg/kg) and donepezil 1 mg/kg until week 11. Behavioural assessments of the rats and oxidative stress biomarkers: Malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione (GSH) were assessed.

RESULTS

The results revealed that rats treated with AlCl₃ 200 mg/kg/day and D-gal 60 mg/kg/day showed cognitive impairments in both spatial and non-spatial learning and memory tests, which is also associated with increased oxidative stress ($p < 0.05$) and decreased ACh level ($p < 0.05$) in their brains. However, administration of WIN (0.5 mg/kg/day, 1 mg/kg/day and 2 mg/kg/day) doses reversed the cognitive impairments and the associated AD-like pathologies. As there were increases in the levels of ACh, SOD and GSH, while a significant decrease in the levels of MDA was also observed.

CONCLUSION

WIN's capacity to lower oxidative stress and hence improve cognitive function may be linked to demonstrating the effectiveness of medication. These results offer scientific proof in favour of the investigation of cannabinoid agonists as potent substances for the treatment of cognitive impairments associated with AD.

CO-CULTURE WITH GLIOBLASTOMA INDUCES MORPHOLOGICAL CHANGES AND APOPTOSIS IN CHOLINERGIC CELLS THROUGH REGULATION OF INFLAMMATION-RELATED PROTEINS

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INTRODUCTION

While interactions between glioblastoma (GBM) and neurons can promote tumour progression, these may affect cholinergic neuronal integrity, leading to dementia-like symptoms. These symptoms often occur early in GBM tumour progression, before the first diagnosis of GBM. Although clinical and *in vivo* studies have supported these observations, the fundamental mechanisms of these interactions remain obscure. This study aims to elucidate the mechanisms underlying the co-culture interactions between cholinergic and GBM cells.

METHODS

The retinoic acid-induced cholinergic-differentiated SH-SY5Y cells were co-cultured with GBM cell lines, LN-18 and T98G respectively, and subjected to flow cytometry, JESS Western and LC-MS/MS analysis.

RESULTS

Co-culture with GBM cells resulted in significant reduction in soma diameter, neurite length and arborization of cholinergic cells. Subsequent analysis revealed that co-culture interactions with GBM cells led to mitochondrial membrane depolarisation and apoptosis in cholinergic cells. Interestingly, this was accompanied by upregulation of autophagy markers in co-cultured GBM, without significant changes in cell cycle and proliferation level, suggesting that autophagy induction during co-culture interactions supported GBM growth. Proteomics profiling followed by PANTHER analysis revealed the upregulation of proteins associated with apoptosis, cytokine-mediated inflammation and cytoskeletal regulation pathways in cholinergic cells co-cultured with LN-18 and T98G, respectively. Meanwhile, proteins involved in cell cycle and PI3K signalling pathways were expressed in co-cultured GBM cells.

CONCLUSION

Collectively, the present findings indicated that co-culture with GBM cells elicited autophagic responses, leading to morphological changes and inflammation-mediated apoptosis in the cholinergic cells. This consequently sustained the co-cultured GBM cell progression through modulation of cell cycle and PI3K pathway-associated proteins. Overall, these findings can contribute to future identification of early detection biomarkers and potential therapeutic targets for GBM.

EFFECTS OF CBD-ENRICHED HEMP EXTRACT AND CBD ISOLATE ON ANXIETY AND RECOGNITION MEMORY IN CHRONIC UNPREDICTABLE MILD STRESS-INDUCED RATS

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BACKGROUND

Anxiety disorder is one of the most common psychiatric conditions, often resulting from the accumulation of stress. Cannabidiol (CBD) has been reported to reduce anxiety-like behaviors and improve recognition memory in mice. This has led to the hypothesis that hemp extract with a high concentration of CBD could potentially be developed to reduce anxiety and improve memory.

AIM

This study aimed to investigate the effects of CBD-enriched hemp extract (CHE) and CBD isolate (CBI) on anxiety and recognition memory in rats induced by chronic unpredictable mild stress (CUMS).

METHODS

Male Sprague-Dawley rats were orally administered either CHE or CBI. Anxiety-like behaviors were induced by CUMS, in which the rats were exposed to a variety of stressors daily for 14 days. Rats were divided into 6 groups (n=4 per group); control, CUMS, CUMS administered with CHE (2.5&5 mg/kg), and CBI (2.5&5 mg/kg). All rats were behaviorally tested on the final day of the stress induction period including open field test (OFT), elevated plus maze test (EPM) and novel objective recognition test (NOR).

RESULTS

The CUMS group showed an increase in the total number of entries into the border and corner areas in OFT, along with an increase in the percentage of time spent in closed arms and a decrease in the percentage of time spent in open arms in EPM compared to the control group, indicating anxiety-like behavior. Administration of CHE (2.5 mg/kg) and CBI (2.5&5 mg/kg) increased the total number of entries into the internal area compared to the CUMS group. Additionally, CUMS administered with CBI (5 mg/kg) decreased the total number of entries



into the corner area compared to the CUMS group, suggesting that both CHE and CBI demonstrate an anxiolytic effect. The discrimination index in the NOR also increased in the CUMS group administered with CBI (5 mg/kg) compared to the CUMS group.

CONCLUSION

This study provides evidence suggesting that CHE and CBI attenuate anxiety-like behaviors and improve recognition memory in rats subjected to CUMS.

KEYWORDS

Anxiety, Cannabidiol, Chronic unpredictable mild stress

NEUROTHERAPEUTIC EFFECTS OF CANNABIDIOL (CBD) ON COGNITION AND HIPPOCAMPAL SYNAPTIC CHANGES IN D-GALACTOSE (D-GAL) AND ALUMINIUM CHLORIDE (ALCL₃) INDUCED ALZHEIMER'S LIKE ANIMAL MODEL IN MALE WISTAR RATS

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BACKGROUND

Alzheimer's disease (AD) is a neurological condition and cause most common type of dementia, which is progressive and characterised by cognitive decline, memory loss, and difficulties with reasoning. The pathology of AD includes the accumulation of β -amyloid plaques and tau protein tangles in the brain, impairing neural transmission and leads to cell death. The cause of the pathological changes is yet to be identified, however, lifestyle, environmental, and genetic variables have been implicated. With 50 million dementia cases occurring globally, of which 60–70% are linked to AD, highlighting public health importance due to lack of a cure and the limited symptomatic therapy available.

CBD, a compound derived from the Cannabis plant, has received attention due to its possible therapeutic benefits in neurodegenerative diseases and its non-psychoactive property. Pharmacological benefits of CBD also include anti-inflammatory, antioxidant, and anxiolytic effects which are related to regulation of different signalling pathways, including the endocannabinoid system. CBD has been shown to have neurotherapeutic benefits in preclinical models of AD, indicating the potential for delaying disease development. Further research is needed to investigate the effects of CBD on cognitive functioning and pathological alterations in AD, as it is known to boost memory.

This study aims to evaluate the impact of CBD on cognitive deficits and hippocampus alterations in an animal model of AD like cognitive changes caused by D-gal and A β 13. The goal is to acquire a better understanding of CBD's potential therapeutic utility in the treatment of AD.

METHOD

Fourty-eight male Wistar rats were divided into six groups: Control group of rats received distilled water and normal saline, Model group administered with D-gal (60 mg/kg, intraperitoneal (i.p)) and A β 13 200 mg/kg (oral), while the treatment groups that are CBD groups received 20 mg, 40mg, and 80 mg of CBD (i.p), and Donepezil group rats were received 1mg/kg of Donepezil (oral). The model group rats were administered D-gal and A β 13 daily for 10 weeks to induce Alzheimer's-like pathology after which CBD and Donepezil treated groups received treatment daily for 3 weeks. At end of 13 weeks, cognitive function was assessed by Novel Object Recognition (NOR) Test which was statistically analysed and thereafter rats were euthanized and hippocampal tissue were collected to analyse for ultrastructural alterations in synaptic morphology via Transmission Electron Microscopy (TEM).

RESULTS

The AD model rats exhibited significant cognitive impairments compared to controls, as demonstrated by a reduced NOR test recognition index. rats co-administered with Donepezil or CBD spent most of their time exploring the novel object introduced. TEM analysis revealed marked reductions in synaptic vesicles, widened and blurred synaptic clefts in the AD model group. Remarkably, the administration of donepezil and CBD ameliorated some of the observed synaptic abnormalities.

CONCLUSION

In summary, the study suggests that CBD treatment holds promise for alleviating cognitive impairments and preserving synaptic integrity in an animal model of AD.

KEYWORDS

Alzheimer's disease, Cannabidiol, Donepezil, Cognitive impairments, Synaptic changes.

BEHAVIOURAL CHANGES DUE TO ROTENONE TOXICITY IN ZEBRAFISH LARVAE IMPLICATES DOPAMINERGIC NEURON DEGRADATIONTan Zing Hern¹, Suzita Mohd Noor¹, Kamariah Ibrahim¹, Anwar Norazit^{1*}¹ Department of Biomedical Science, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia

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INTRODUCTION

Rotenone, a polyphenolic and heteropentacyclic natural plant product, is often utilized to induce Parkinson's disease symptoms, including dopaminergic neuron death and motor deficits in animal models. The zebrafish (*Danio rerio*) serves as an effective model due to the conservation of dopaminergic neurons with mammals.

METHODOLOGY

Adult AB wildtype (WT) zebrafish were bred to obtain embryos which were raised in 0.0002% methylene blue in E3 media. At 3 days post-fertilization (dpf), WT larvae (n=48/group) were exposed to 125 nM rotenone for four consecutive days at 28°C. Vehicle controls were raised in 0.01% DMSO. All larvae were assessed daily under a SZX10 stereomicroscope (Olympus, Japan). Larvae exhibiting deformities were classified as abnormal but were not removed from the study. Behaviour was also assessed daily using the DanioVision observation chamber (Noldus, Netherlands), measuring total mean velocity, total distance travelled, and acceleration over a 5-minute period. Statistical analyses were performed using GraphPad Prism.

RESULTS

Odds ratio analysis indicated a higher incidence of phenotypic abnormalities in the rotenone-exposed larvae compared to vehicle controls, but the difference was not statistically significant. There was significant decrease in distance travelled and mean velocity at 1- and 4-days post-exposure (dpe) in rotenone-exposed larvae compared to vehicle control larvae. Acceleration showed significant reduction only at 1 and 2 dpe.

DISCUSSION AND CONCLUSION

Although not statistically significant, phenotypic defects in rotenone-exposed suggested a potentially disruptive association between rotenone and development. Rotenone clearly affected behaviour, as evidenced by changes in swimming distance, velocity, and acceleration which could be suggestive of impaired dopaminergic neurons, particularly those involved in locomotion. These findings underscore the robust impact of rotenone on larval development and behaviour, giving credence to the use of rotenone in generating zebrafish larval models of dopaminergic pathologies.

CAROTENE INDUCED FOXO-MODULATED CELL CYCLE ARREST *IN SILICO* ANDEXERTED *IN VITRO* CYTOTOXICITY AGAINST P53-WILDTYPE HUMAN GLIOBLASTOMA CELLS

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BACKGROUND

Glioblastoma multiforme (GBM) is a grade IV brain tumour that occurs in the central nervous system (CNS). The use of temozolomide (TMZ) as standard-of-care has resulted in the emergence of TMZ-resistant GBM tumours. Carotenoids, a class of antioxidants, have shown great potential for the management of GBM. However, a comprehensive review of the pathways modulated by carotenoids to exert their anticancer effects was lacking.

METHODS

A systematic scoping review was conducted to identify differentially expressed proteins modulated by carotenoids in cancer. A literature search on five databases namely Web of Science, PubMed, Ovid Medline, Ovid Embase and Scopus was carried out, and studies investigating the protein expression of carotenoids-treated cancer cell lines over the past ten years were included. The cytotoxicity of natural β -carotene, synthetic β -carotene and natural mixed carotenoids were tested on the p53-mutant T98G and p53-wildtype A172 human glioblastoma cell lines. RT-qPCR was then performed to compare the expression levels of FOXO3, PTEN, MDM2, MGMT, NF1, TP53, APNG, EGFR, TERT and VEGF in untreated and carotenoids-treated GBM cell lines.

RESULTS

Seventeen carotenoids were identified across 63 studies. Breast cancer, gastric cancer, and lung cancer cell lines were the primary cell lines investigated. Protein-protein interaction network analysis revealed the upregulation of pro-apoptotic cluster and FoxO signaling cluster. Together with the downregulation of PI3k/Akt, TNF and cell cycle regulation clusters, they exerted cytotoxic effects in cancer. All carotenoids did not induce cytotoxicity against T98G cells. Conversely, only natural mixed carotenoids exerted time- and dose- dependent cytotoxicity against A172 cells.

CONCLUSIONS

Our computational findings suggest the induction of cell cycle arrest may result from the direct activation of the FoxO signaling pathway by carotenoids. Our experimental findings suggest that the cytotoxicity of the natural mixed carotenoids in A172 cells may be due to the activation of p53-dependent cell cycle arrest.

CHARACTERIZING SOMATIC LINE1 INSERTIONS IN HUMAN NEURONS AND GLIA WITH DEEP-LEARNING METHODS

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INTRODUCTION

LINE1 is the only autonomous retrotransposons capable of independent movement in the human genome. Somatic LINE1 insertions are more likely to occur in early brain development, result in somatic mosaicism with development, and contribute to many brain disorders. Current detection methods are mainly based on DNA Whole Genome Sequencing (WGS). Among them, single-cell or third-generation DNA WGS are too expensive. Bulk DNA WGS methods need extensive supporting reads, except for our previously developed machine-learning-based pipeline *RetroSom*, which uses only two supporting reads. *RetroSom* still has the false positive issue, and a step called *RetroVis* is needed to graphic the candidate insertions for the time-consuming manual inspection.

METHODS

We use deep learning to improve performance and eliminate manual inspections. Encode two supporting reads into images suitable for human observation and model learning. Training set contains 600 trios from 1000 Genome, and 54 trios from Polaris dataset were used to compare convolutional neural network (CNN) and vision transformer (ViT) models. Benchmark the best model with *RetroSom* in the genome-mixing sequencing data. New pipeline was applied to detect candidate LINE1 insertions in neurons and glial cells derived from two schizophrenia-control pairs with 200X whole-genome coverage.

RESULTS

Two CNN models, ResNet18 and GoogleNet, performed better than ViT in the Polaris. The performance between ResNet18 and GoogleNet has no significant difference, but ResNet18 is more lightweight in computing scale. Also, ResNet18 outperformed *RetroSom* in all gradient mixing experiments, achieving higher sensitivity at equal precision. In the neuron and glial cells sequencing data, we found two LINE1 insertions validated before and identified more candidate insertions.

CONCLUSION

The new pipeline, *RetroNet*, performs better in detecting somatic LINE1 insertions and identifies more candidate LINE1 insertions in the schizophrenia brain. This method can extend to the other two non-autonomous retrotransposons in humans, Alu and SVA, which are still active.

EXTRACELLULAR SIGNAL-REGULATED PROTEIN KINASE (ERK) INHIBITION AMELIORATES ALLODYNIA AND HYPERALGESIA IN PAINFUL DIABETIC NEUROPATHY RAT MODEL

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INTRODUCTION

Painful diabetic neuropathy (PDN) is a common consequence of diabetic mellitus (DM). The major factor contributed to PDN is hyperglycemia which can induce neurotoxicity. Current drug only alleviates the pain symptoms but not the mechanism of PDN and also produce many side effects. This study investigates the role of extracellular signal-regulated protein kinase (ERK) in the mechanism of PDN through the effects of U0126 (ERK inhibitor) on pain behaviour responses, expression of phosphorylated ERK (pERK) protein and mRNA of ERK1 and ERK2 in the spinal cord of streptozotocin (STZ)-induced PDN rats.

METHODS

Forty-eight Sprague-Dawley male rats were assigned into 4 groups (n=12 per group) consisting of normal control group (C), PDN-diabetic control group (PDN), PDN+U0126 -treated groups: U5 (low dose, 5µg/day) and U10 (high dose; 10µg/day). After STZ injection, two-week period was allowed for all DM rats to develop early PDN conditions. Then, intrathecal injection of U0126 was given for seven days. The pain behavioural test was performed by Von Frey, hot plate and formalin test. The rats were then sacrificed, and the spinal cords were collected for immunohistochemistry (IHC) and quantitative PCR (qPCR) analyses.

RESULTS

Analysis of pain behavioural response test showed a significant effect of U0126 ($p<0.05$) as anti-allodynia and anti-hyperalgesia in Von Frey, hot plate and formalin test (tonic phase). The PDN group displayed a markedly significant increment in pERK positive cells at both ipsilateral and contralateral sides ($p<0.05$). Interestingly, the number of pERK positive cells was suppressed in U5 and U10 groups ($p<0.05$). Low mRNA expression levels of ERK1 and ERK2 were also detected in both U5 and U10 groups ($p<0.05$) by qPCR.

CONCLUSION

Our findings suggested that ERK inhibition can modulate the mechanism of PDN by STZ-injected rat model. Exploration of ERK pathway may provide a new therapy for pain control in PDN.

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MODULATION OF GLIAL CELLS BY ENDOCANNABINOID SYSTEMS LEADS TO COGNITIVE AMELIORATION: A SYSTEMATIC REVIEW AND META-ANALYSIS IN RODENTS

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INTRODUCTION

Alzheimer's disease (AD) is a neurological illness that affects millions of people worldwide. It is clinically defined by a progressive loss of cognitive function and increased memory loss. It is among the top 10 most burdensome conditions among older people worldwide. In contrast with other conditions, its impact comes mainly from years living with disability, rather than years of life lost from premature mortality. Several animal AD models demonstrated the direct and indirect influence of endocannabinoid system (ECS) on glial cells affecting cognition.

METHOD

It is shown in this systematic review and meta-analysis. The electronic databases Scopus and the EBSCOhost platform were searched up until Oct 2022. "Alzheimer's disease," "endocannabinoid," "glial cells," "cognition," and "animal" were the search phrases used. PRISMA-compliant systematic review protocols were applied. Using the PICO approach, the key concept of this study such as AD, cannabinoid, glial cells, and cognition were applied to search articles from six databases: Scopus, EBSCOHost, PubMed, CINAHL, Cochrane, and Web of Science. The SYRCLE risk of bias tool was used to assess each pre-clinical study's methodological quality.

RESULTS

Twenty-six original articles were included in this analysis describing (1050 rodents) with AD-like symptoms. Rodents treated with cannabinoid agonists showed significant ability to discriminate novel objects ($p < 0.00001$) compared to the control group. Neuroprotection effects were observed as represented by decreased levels of astrocyte markers ($p = 0.008$) and microglial markers ($p = 0.0002$). Significantly decreased levels of pro-inflammatory markers IL-1, TNF- α , and IL-6 were observed in the wild-type mice studies ($p = 0.00001$).

CONCLUSION

Modulation of glial cells via endocannabinoid stimulation led to cognitive improvement, decreasing proinflammatory markers in AD-like rodent models.

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ASSESSING THE NEUROPROTECTIVE ROLE OF CANNABINOID RECEPTOR AGONIST, WIN55,212-2 THROUGH HISTOMORPHOMETRY IN ALUMINIUM CHLORIDE AND D-GALACTOSE INDUCED COGNITIVE IMPAIRMENTS IN MALE WISTAR RATS

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INTRODUCTION

Cognitive impairment and disturbances in neurotransmission are commonly associated with Alzheimer's disease (AD). Aluminium possesses neurotoxic properties, while D-galactose (D-gal) is recognised as an inducer of senescence. WIN55,212-2 (WIN) is a cannabinoid receptor agonist that may help in restoring neurogenesis in aged rats. However, there is limited data on its therapeutic efficacy in rat models induced with Aluminium chloride (AlCl₃) and D-gal. This study aims to establish an AD-like rat model to investigate the therapeutic potential of WIN for treating AD-like symptoms in rats.

METHODS

200g-250g of healthy male albino Wistar rats were injected with D-gal (60 mg/kg; i.p), while AlCl₃ (200 mg/kg; p.o) was administered once daily for 10 consecutive weeks. Behavioural assessments were carried out via elevated plus maze, open field test, Morris water maze, Novel object recognition, and T-maze test. Histopathological examinations of hippocampi and prefrontal cortices were conducted, and brain acetylcholine (ACh) and amyloid beta (A β) were evaluated. Subsequently, commencing from week 8 of the experiment, rats were co-administered with WIN (0.5, 1 and 2 mg/kg) and donepezil 1 mg/kg until week 11. Behavioural assessments of the rats, brain morphological analyses, levels of A β and its synthetic proteins were analysed.

RESULTS

Rats treated with AlCl₃ 200 mg/kg/day and D-gal 60 mg/kg/day exhibited cognitive deficits in both spatial and non-spatial learning and memory tests, which were associated with neuronal loss ($p < 0.05$), and decreased ACh level ($p < 0.05$). However, administration of WIN (0.5 mg/kg/day, 1 mg/kg/day and 2 mg/kg/day) reversed the cognitive impairments, increased ACh level and decreased A β 42 levels. It also attenuated cytoarchitecture abnormalities in the hippocampus and prefrontal cortex.

CONCLUSION

In conclusion, WIN has therapeutic effects that prevent neurodegeneration and improve cognitive ability. Cannabinoid agonists such as WIN may be safe and effective compounds to treat Alzheimer's-related cognitive deficits.

DETERIORATION OF COGNITIVE PERFORMANCE IN AGEING SPONTANEOUSLY HYPERTENSIVE RATS: AN ANIMAL MODEL OF CEREBRAL SMALL VESSEL DISEASE

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BACKGROUND

Cerebral small vessel disease (CSVD) is a known pathological neurological process affecting cognitive impairment. This cognitive decline pattern comprises attention, processing speed and memory task in which prevalent in older age individuals with evidence of association with hypertension and neuroinflammation. Nevertheless, the involvement of hypertension and neuroinflammation in the progressiveness of CSVD remains uncertain. Therefore, an establishment of an in vivo model prepares a fundamental groundwork in exploring neuroinflammatory in hypertensive CSVD progression. This study was aimed to evaluate the cognitive function of spontaneously hypertensive rats at different ages as animal model of CSVD.

METHODS

A total of 27 male age-matched stroke prone spontaneously hypertensive rats (SHRSP) and 27 male normotensive Wistar Kyoto rats (WKY) were randomly assigned into three age groups; 8, 14 and 42 weeks. The rats' locomotion activity, anxiety behaviour and natural exploring novelty; discrimination capability and recognition memory were observed throughout Open Field test (OFT) and Novel Object Recognition test (NORT).

RESULTS

In an open field area, SHRSP demonstrated greater explorers and central area preference as compared with WKY in three age groups altogether, yet only data at the age of 14 weeks determined statistically significant. During acquisition phase, in all three age groups, SHRSP exhibited again higher exploratory behaviour but data have shown significant only at the age of 42 weeks. At the first two age of 8 and 14 weeks, SHRSP showed better novelty discrimination capability than WKY strain, however evidenced a deterioration trended down with ageing. Recognition memory was also observed higher at week 8 and week 14 and subsequently declined at 42 weeks.



CONCLUSION

As the SHRSP rats matured, they demonstrated greater exploratory behaviours with deterioration of learning and recognition memory of novel object. Further analyses on histopathological neurodegeneration combined with investigation of the localization and expression of neuroinflammatory markers may clarify these behavioral occurrences ultimately elucidating the hypertensive CSVD pathomechanism.

KEYWORDS

Cerebral small vessel disease, cognitive impairment, spontaneously hypertensive rats, open field test, novel object recognition test.

ELUCIDATING THE POTENTIAL OF TOCOTRIENOL-RICH FRACTION IN MITIGATING DIABETIC PERIPHERAL NEUROPATHY THROUGH UNTARGETED METABOLOMIC PROFILING

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INTRODUCTION

Persistent increased in blood glucose level in Type II diabetic mellitus (TIIDM) patient leads to the accumulation of reactive oxygen species (ROS) as well as increasing the oxidative stress. This condition contributes to the development of diabetic peripheral neuropathy (DPN), one of the microvascular complications in TIIDM. Tocotrienol-rich fraction (TRF) has been found to poses significant antioxidant properties and might have a potential role in halting or slowing the progression of DPN. This study aimed to determine the effect of TRF on the expression of metabolites and their metabolic pathways in the DPN rat's animal model.

METHODS

Sprague Dawley (SD) rats were divided into 2 groups, Normal control (NC) and Diabetic Mellitus (DM) where TIIDM was induced in the DM group. After 4 weeks of diabetic confirmation in the DM group, the rats were further divided into 4 groups (DM Control, DM Metformin, DM TRF and DM Metformin TRF) and were given treatment accordingly for 12weeks. Blood was collected at week 0 and week 12 and plasma was used to performed metabolomic analysis using liquid chromatography-tandem mass spectrometry (LCMS/MS).

RESULTS

DM group show a significant increase on the level of phenyllactic acid and indole with reduction in tryptophan and catechol which important for synthesis of catecholamine and serotonin. TRF in the other hand cause a significant reduction on the level of both phenyllactic acid and indole as well as increase the level of tryptophan, acetylcholine, and catechol. TRF also cause a significant decrease in the metabolite involve in histamine synthesis and prostaglandin A2 metabolism either alone or in combination with metformin.

CONCLUSION

TRF significantly improve the catecholamine, acetylcholine, and serotonin synthesis, as well as lipid metabolism. TRF also reduce the histidine and prostaglandin metabolism in DPN rat's animal model thus suggesting potential therapeutic effect in hyperalgesia.

ELUCIDATING THE ANTIOXIDANT PROPERTIES OF NATURAL EXTRACTS IN RAT'S MODEL OF DIABETIC PERIPHERAL NEUROPATHY: A SYSTEMATIC REVIEW

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INTRODUCTION

Oxidative stress is a known factor contributing to the progression of diabetic peripheral neuropathy (DPN), affecting about 50% of the patient with Type II diabetic mellitus (TIIDM). To date, most of the treatment for DPN only focusing on treating the symptoms without improving the conditions. Thus, there is urgent need for an early intervention where natural extract with antioxidants properties have been proposed as potential therapeutic agents. This systematic review aims to evaluate the existing evidence on the antioxidant capacity of these natural extract as well as to provide insight on the role of antioxidants in the progression of DPN in rat's animal model.

METHODS

A literature search was conducted in Scopus, Web of Science, and EbscoHOST to determine the antioxidant properties of selected natural extract and their potential in mitigating DPN. Studies were included if they treated the rat's animal model for DPN with natural extract, had antioxidant parameters, performed behavioural parameters related to DPN and reported the relevant outcomes. Data extraction was performed, and this systematic review was written following the PRISMA 2020 statements.

RESULTS

From the literature search, 1178 articles were screened and a total of 95 full text articles were further screened before 25 were analyzed. Data on behavioural parameters, biochemical parameters as well as histopathological parameters were tabulated and illustrated. Type of animal model used, concentration of the compound or extract as well as the intervention duration were also summarized in this review.

CONCLUSION

The systematic review provides a comprehensive understanding on the effects of the natural extract with antioxidants properties on various parameters related to the pathogenesis of DPN.

EFFECTS OF LITHIUM ON ANXIETY, LOCOMOTOR ACTIVITY, AND LEARNING AND MEMORY IN MICE: A NEUROBEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDY

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INTRODUCTION

Lithium is a well-established medication for treating psychiatric disorders, especially bipolar disorder. It is known for its mood-stabilizing properties and is commonly used to manage manic depressive episodes. Lithium has anti-manic, antidepressant, and anti-suicidal effects. Additionally, it improves memory, cognitive function and protects against memory impairments from various causes. This study aims to investigate the effect of lithium on anxiety, locomotor activity, and learning and memory in normal mice prior to its administration on other disease mouse models.

METHODS

Adult wild type C57BL/6 mice (2-3 months old) were randomly divided into two groups: a control group ($n=10$) and a treated group ($n=11$). Via oral gavage, these mice were fed either saline or lithium chloride (16 mg/kg) daily for 30 days in the control and treated groups, respectively. Neurobehavioral functions were evaluated through various tests including hanging wire, rotarod, open field, novel object recognition, and Morris water maze experiments. *In vivo* electrophysiological properties and synaptic plasticity of dorsal hippocampal CA3-CA1 synapse were evaluated.

RESULTS

Lithium treatment did not impact balance or forelimb strength in the rotarod and hanging wire tests ($P>0.05$). However, the lithium-treated group showed reduced anxiety as they spent more time in the central zone during the open field test ($P<0.05$). Further investigation using novel object recognition and Morris water maze tests revealed that lithium treatment on wildtype mice did not improve their short-term or long-term spatial learning and memory ($P>0.05$). However, the input/output curves at the CA3-CA1 synapse showed increasing sigmoid-like curves in *in vivo* field excitatory postsynaptic potentials (fEPSPs) for both groups (control: $n=5$; treated: $n=6$, $P=0.000$). The group treated with lithium exhibited a significant increase in fEPSP changes compared to the control group ($P=0.048$). No significant differences were found between groups at any of the selected intervals (10-500ms) in the evaluation of the paired-pulse paradigm (control: $n=5$; treated: $n=6$, $P>0.05$). *In vivo* high-frequency stimulation (HFS) at CA3 Schaffer collaterals significantly increased the induction and maintenance of long-term synaptic plasticity in the stratum radiatum of dorsal CA1 for 90 minutes after HFS (control: $n=5$, $P=0.02$; treated: $n=6$, $P=0.01$). There were no significant differences between groups in



the mean fEPSP amplitude (control: $131 \pm 8\%$ of baseline; treated: $165.5 \pm 19\%$ of baseline) during the 90 minutes following HFS ($P > 0.05$).

CONCLUSION

Treatment with lithium chloride at a dose of 16 mg/kg/day for 30 days resulted in a significant anxiolytic effect, enhanced electrophysiological properties and synaptic plasticity of the dorsal hippocampal CA3-CA1 synapse. It did not affect locomotor activity, muscle strength, short- or long-term learning and memory.

KEYWORDS

Lithium chloride, learning and memory, anxiety, locomotor activity, local field potential, CA1

IN VITRO AND IN VIVO SCREENING OF *Coccoloba uvifera*, *Mimusops elengi* AND *Syzygium aqueum* EXTRACTS ON COGNITIVE FUNCTION OF VASCULAR DEMENTIA RATS MODELKesevan Rajah Kumaran,^{1,2,3} Habibah Abdul Wahab,² Zurina Hassan,¹¹ Centre for Drug Research, Universiti Sains Malaysia, Gelugor, Penang, Malaysia.² School of Pharmaceutical Sciences, Universiti Sains Malaysia, Gelugor, Penang, Malaysia.³ Department of Pharmacology and Toxicology, Faculty of Pharmacy and Biomedical Sciences, MAHSA University, Bandar Saujana Putra, Selangor, Malaysia.**INTRODUCTION**

Vascular dementia (VaD), is one of the most common types of dementia in the ageing population, initiated by chronic cerebral hypoperfusion (CCH). At present, effective therapeutic approaches to cure VaD are still missing. Cholinergic system dysfunction in the central nervous system (CNS) has been recognised as one of the main reasons for learning and memory impairment in VaD patients. Therefore, medications that restore the level of acetylcholine (ACh) neurotransmitter by inhibiting cholinesterase activity were proposed as a potential candidate to treat VaD patients. The present study evaluated the anti-cholinesterase activity of three Malaysian plant methanol leaf extracts *in vitro* and further validated its cognitive-enhancing effects *in vivo* using vascular dementia rats model.

METHODS

The selected plant extracts were *Coccoloba uvifera* (stems), *Mimusops elengi* (leaves) and *Syzygium aqueum* (leaves). All the plant extract was prepared by soaking the respective plant parts in methanol using maceration method and subjected to freeze drying to lyophilised the extract. The *in vitro* anti-cholinesterase activities of these plants were determined using Ellman's method. Permanent occlusion of bilateral common carotid arteries (POBCCA) surgery method was performed to develop CCH in rats. The effects of selected plant extracts (100 and 200 mg/kg, p.o.) on cognitive functions were evaluated using novel object recognition test and morris water maze test.

RESULTS

All the selected plant extracts exhibited good anti-acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) activities *in vitro*, with IC₅₀ ranging from 3.67 to 16.04 and 5.6 to 13.95 µg/mL, respectively. Extracts of *S. aqueum* (200 mg/kg) improve both short-and long-term recognition memories, whereas *M. elengi* and *S. aqueum* (200 mg/kg) extracts improve spatial learning.

CONCLUSION

Methanol extracts of *C. uvifera*, *M. elengi* and *S. aqueum* showed good anti-cholinesterase activity *in vitro*. However, only *M. elengi* and *S. aqueum* improve learning and memory function in vascular dementia rats model.

INTRACRANIAL HEMORRHAGE FOLLOWING INTRAVENOUS THROMBOLYSIS IN OLD ACUTE ISCHEMIC STROKE PATIENTS: SINGLE STROKE CENTER

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BACKGROUND

The majority of strokes occur in older adults, with more than 75% occurring in people over the age of 65. However, there is no consistent recommendation of intravenous thrombolysis for older patients. Thrombolysis is not considered in old stroke patients due to concern of increased risk of intracranial hemorrhage and poor stroke outcome.

We aimed to study the incidence and factors associated with intracranial hemorrhage following intravenous thrombolysis and in-patient mortality.

METHODOLOGY

We performed a retrospective cross-sectional study on all old acute ischemic stroke patients aged 60 years and above who received intravenous thrombolysis during the period from January 1st, 2011 to December 31st, 2023. Data was collected from the local stroke registry in Hospital Seberang Jaya, a regional stroke center.

RESULTS

A total of 191 patients were included within these 12 years, with a mean age of 68 ± 6 years. 47 patients (24.6%) developed thrombolysis-associated intracranial hemorrhage, and 18 (38.3%) were symptomatic. Post-thrombolysis in-patient mortality rate was 26.2% ($n = 50$). The most common cause of death was acute ischemic stroke (11.0%), followed by intracranial hemorrhage (10.5%), and non-cerebral deaths (4.7%). The severity of National Institute of Health Stroke Scale (NIHSS) score increased the risk of thrombolysis-associated intracranial hemorrhage (hazard ratio, 1.08; 95% confidence interval 1.02 – 1.15). Although age, NIHSS score and intracranial hemorrhage were found associated with in-patient mortality ($p < 0.05$), NIHSS score was the single factor influencing in-patient mortality after binary logistic regression (hazard ratio, 1.15; 95% confidence interval 1.08-1.24).

CONCLUSION

NIHSS score is an important factor in intracranial hemorrhage following intravenous thrombolysis and mortality in old acute ischemic stroke patients. Although thrombolysis-associated intracranial hemorrhage is common but majority is asymptomatic and it is not independently affecting mortality in this group of patients. Our center in-patient mortality was recorded higher than previous studies, in which 10% of deaths occurred. The reason may be multifactorial because our stroke center lacks a well-established post-stroke rehabilitation program for older patients.

AN UNEXPECTED TURN OF STROKE CODE ACTIVATION

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INTRODUCTION

Forty percent of cerebral venous thrombosis (CVT) cases present with stroke mimic symptoms such as hemiparesis, triggering an unusual stroke code activation¹. However, the treatment approach for CVT may vary from arterial ischemic stroke due to differences in structural composition².

METHODS

A stroke code was activated for a 55-year-old woman, presented with sudden right-sided body weakness with right limbs power 0/5 and NIHSS 14. Initial Computed Tomography (CT) brain showed ASPECT score 10. She was treated as left subcortical stroke with thrombolysis (IV Alteplase 0.9mg/kg) within 30 minutes door-to-needle time. NIHSS 1 hour post-thrombolysis showed minimal improvement to 13. However, repeated CT brain 24 hours post-thrombolysis revealed atypical subarachnoid hemorrhage (SAH) at parasagittal area. Subsequently, the patient developed seizures. Magnetic resonance imaging (MRI) brain displayed hyperintense signal on T2/FLAIR and hypointense signal on T1 at right frontoparietal region indicating infarct, which did not correlate with her neurological deficit. MR Angiography for anterior circulations were patent. MR Venography confirmed extensive CVT at superior sagittal sinus, right transverse sinus, right sigmoid sinus and up to right internal jugular vein. Antiepileptics and low-molecular-weight heparin were started 48 hours post-thrombolysis. Consequently, her seizures were controlled and right limbs power returned to 5/5. Thrombophilia testing, autoimmune screening, tumor markers, infective markers and history of hormonal pills all yielded negative results. Patient was discharged two weeks later with NIHSS 0 and scheduled to repeat CTV in six months time.

DISCUSSION

This case highlights the persistence of extensive CVT despite intravenous thrombolysis (IVT), contrasting with studies that demonstrate better recanalization with local thrombolysis³. Evaluation of IVT effectiveness in CVT remains inconclusive due to limited sample size⁴.

CONCLUSION

To date, there is no evidence of superior outcomes with endovascular therapy for CVT patients⁵, thus heparin remains the first-line treatment due to its proven efficacy, safety, and practicality.

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NAVIGATING THE UNKNOWN: REHABILITATION JOURNEY OF PEOPLE WITH POST-STROKE APHASIA IN MALAYSIA

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INTRODUCTION

Aphasia affects up to one-third of stroke survivors, yet aphasia rehabilitation services in Malaysia remain limited. Recent studies highlighted challenges and resource constraints faced by Malaysian speech-language therapists in delivering aphasia rehabilitation. This study aims to explore the rehabilitation experiences and needs from the perspective of people with post-stroke aphasia.

METHODS

This mixed-method study combined a survey and a semi-structured interview. Twenty-seven adults with post-stroke aphasia were recruited from various rehabilitation settings using maximum variation sampling. Diagnosis of aphasia was confirmed by a speech-language therapist before recruitment. The participants completed an aphasia-friendly survey and were interviewed in their preferred language (English, Malay or Mandarin). The survey was analysed descriptively while the interview responses were analysed using Qualitative Content Analysis.

RESULTS

The participants (n=27), predominantly male (74%) and aged between 31-40 years old (33%, Range: 27 -74 years old), primarily resided in urban areas (52%) and possessed tertiary education (44%). The majority of the participants were unfamiliar with the term "aphasia" (63%), and had not received information about aphasia (60%). Despite this, a significant percentage underwent language screening (56%), aphasia assessment (62%), and aphasia treatment (96%). Additionally, two-thirds (64%) sought complementary and alternative treatments, including traditional massage and acupuncture. Qualitative analysis revealed key themes regarding rehabilitation needs, barriers, and facilitators.

CONCLUSION

The rehabilitation journey for individuals with post-stroke aphasia in Malaysia is influenced by factors such as aphasia awareness, resource availability, and socioeconomic status. Addressing unmet needs and providing guidance throughout this journey is essential for optimising rehabilitation outcomes.

CONVULSIVE BASILAR ARTERY OCCLUSION – AN UNDERREPORTED MALIGNANT ENTITY: CASE SERIES AND LITERATURE REVIEW

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INTRODUCTION

Basilar artery occlusion (BAO) carries poor prognosis with high mortality rate of 30-40% despite endovascular thrombectomy (EVT). Early recognition of symptoms of BAO can significantly improve the outcome. However, diagnosing BAO can be challenging if convulsion was the presenting symptom.

REPORT

We present a cohort of seven patients with BAO who manifested convulsions early in the disease. In all 7 cases, their ages ranged between 28 to 69 years, all but one patient were chronic smokers or had hypertension. All of the patients do not have past medical history of epilepsy. The overall outcomes for our patients were unfavourable, with four succumbed to brainstem strokes. The other 3 surviving patients had a modified Rankin Scale of 2-3. 5 out of the 7 patients received either intravenous thrombolysis or EVT, whilst the other 2 missed time window for intervention. There was significant delay from onset of symptoms to diagnosis and treatment in most of patients, as a results of either failure to promptly recognise symptoms or delayed imaging of the arterial system. Only one patient underwent EEG, which was unremarkable.

CONCLUSIONS

It's crucial for early recognition of BAO in patients presenting with sudden convulsive movements. Awareness of this entity is required to recognise this potentially treatable, but otherwise devastating seizure mimic. Prompt diagnosis and reperfusion therapy may significantly improve prognosis.

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**STROKE AWARENESS AND EDUCATION AMONG CHILDREN IN MALAYSIA:
FAST HEROES PROGRAM**

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INTRODUCTION

Recognition of stroke symptoms among children is often underestimated, yet they serve as crucial first responders in saving the lives of their grandparents, who are more susceptible to strokes. The FAST (Face, Arm, Speech, Time) Heroes program educates children about stroke symptoms, improving their ability to recognize strokes and understand the importance of seeking timely medical attention.

METHODS

We implemented the FAST Heroes program in three English-speaking kindergarten around Klang Valley, Malaysia from December 2023 until March 2024. Over the course of five weeks, this program sought to teach recognition of stroke symptoms and timely respond to stroke in children aged five to six. Week zero introduced the program, while weeks one to four focused on illustrating the FAST acronym in association with stroke symptoms with four heroes in weekly hourly sessions. A pictorial questionnaire with verbal explanations assessed participants at week zero (pre-program) and one week post program. The variables used were increment of stroke symptoms recognition in the FAST acronym pre and post program, and appropriate course of action (calling emergency number, 999).

RESULTS

A total of 83 children participated, 40 boys (48.2%) and 43 girls (51.8%) with a mean age of 5.5 years. Malay ethnicity constituted of 72.3% while Chinese were 27.7%. Before programme implementation, 54.2% of children could recognize stroke symptoms which increased to 97.5% post fast hero program implementation ($p=0.00$). Children awareness of the emergency number 999 before programme implementation was relatively poor (31.3%) but improved to 87.9% post program ($p<0.05$).

CONCLUSION

This program is effective in enhancing stroke symptom recognition among children, offering a potential avenue to improve stroke prognosis through early detection and prompt emergency response to stroke. Larger and diverse samples are necessary to validate the effectiveness of this program in future studies.

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PERSISTENCE OF NON- VITAMIN K ANTAGONIST ORAL ANTICOAGULANT TREATMENT FOR STROKE PREVENTION AMONG OLDER ADULTS WITH ATRIAL FIBRILLATIONVictoria Wei Fang Boey¹, Kit Mun Tan², Sheron Sir Loon Goh², Zheng Yang Lee³, Wan Chian Cheah³, Nicole Kumari Kunaseelan⁴¹*Masters in Internal Medicine Program, Department of Medicine, Faculty of Medicine, Universiti Malaya*²*Division of Geriatric Medicine, Department of Medicine, Faculty of Medicine, Universiti Malaya*³*Universiti Malaya Medical Program, Faculty of Medicine, Universiti Malaya*⁴*Department of Pharmacy, Universiti Malaya Medical Centre***INTRODUCTION**

Non-vitamin K antagonist oral anticoagulant (NOAC) is the preferred treatment for stroke prevention in atrial fibrillation (AF). Older adults are complex and are commonly associated with frailty and polypharmacy. Medication persistence of NOAC among patients with AF is important for the success of the anticoagulation in stroke prevention. The aim of this study was to investigate NOAC persistence among older adults with AF along with its clinical characteristics and outcomes.

METHODS

This was a retrospective observational study involving older adults age 65 years and above with AF who were started on NOAC treatment for stroke prevention at Universiti Malaya Medical Centre from 2016-2018.

RESULTS

A total of 337 patients were included in this study. 73.6% (n=248) were frail with clinical frailty scale of 4 or more. The patients were followed-up for a median of 898 days (IQR 1653). NOAC persistence was observed in 72.7% (n=245). Non-persistence of NOAC was observed in 27.3% (n= 92) of our cohort. Several reasons for discontinuation of NOAC include: bleeding (32.6%), worsening renal impairment (17.4%), sepsis (7.6%), patients' decision (6.5%), cost (5.4%), reducing haemoglobin levels (5.4%), worsening frailty (4.3%) and others (20.8%). Median time till NOAC discontinuation was 344 days (IQR 627). In the study, the non-persistent group exhibited higher death rates and bleeding rates in comparison to the persistent group. Specifically, the death rate was 48.9% for non-persistent versus 14.3% for persistent patients. Similarly, the bleeding rates were 52.2% for non-persistent compared to 20.4% for those who were persistent.

CONCLUSION

Older adults with atrial fibrillation show low persistence in taking NOACs, leading to poorer clinical outcomes. There is a critical need for further studies to explore the underlying causes of this low persistence. Enhancing patient education and strengthening monitoring protocols are recommended to improve adherence to NOAC therapy among older adults.

EVALUATING THE RISK OF SYMPTOMATIC INTRACRANIAL HEMORRHAGE IN ACUTE STROKE PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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INTRODUCTION

While acute stroke treatment has achieved many advancements, there is still ongoing debate regarding the safety of administering intravenous thrombolysis (iv-RTPA) among patients eligible for mechanical thrombectomy (MT) who arrive within iv-RTPA treatment window. There is concern regarding bleeding risk in this group of patients which will preclude them from undergoing MT. Caution has to be made in treating those eligible patients while not causing more harm to them. Furthermore, there is still limited data on safety outcome of iv-RTPA in the South East Asian population. Hence in this study, we evaluate the bleeding risk of acute ischemic stroke (AIS) patients given iv-RTPA according to different stroke etiologies and severity.

METHODS

This study employed an 8-year retrospective cross-sectional study using record review from Hospital Information System involving registered AIS patients given iv-RTPA for the period of Jan 2014 -Dec 2022 under Neurology Clinic Hospital Sultanah Nur Zahirah follow up. Descriptive statistics, crosstabulation, rank-biserial correlation and logistic regression were employed for data analysis using SPSS 26.

RESULTS

A total of 235 AIS patients were examined with age ranging from 15 to 90 years old, and a gender distribution consisting of 60.4% male and 39.6% female. The result obtained shows that 36 patients developed symptomatic intracranial hemorrhage (SICH) (Mean=2.65, SD=0.58) and 199 patients didn't (Mean=2.43, SD=0.73). A rank-biserial correlation analysis indicated a significant positive correlation between cardioembolic stroke with SICH ($R=0.21$, $p=0.001$) and a negative relationship between small vessel stroke with SICH ($R=-0.198$, $p=0.002$). Other stroke etiologies showed no significant relationship with the occurrence of SICH. We also found a strong correlation between severe stroke (NIHSS 21-42) with SICH ($R=0.177$, $p=0.007$).

CONCLUSION

This study suggests that among AIS patients given iv-RTPA, acute stroke due to cardioembolism and severe strokes have higher tendency to cause SICH compared to other types of strokes.

A LARGE INTRACRANIAL VESSEL OCCLUSION TREATED BY INTRAVENOUS THROMBOLYSIS WITHOUT MECHANICAL THROMBECTOMY: A CASE REPORT

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INTRODUCTION

In some occasions, when equipment and human resources needed to perform mechanical thrombectomy (MT) are not readily available, intravenous thrombolysis (IVT) can be the only choice of treatment for large intracranial vessel occlusion (LVO). This case report describes how IVT has contributed in saving a LVO patient in Indonesia.

REPORT

A 35-year-old male with a history of 6-year controlled hypertension was admitted with sudden difficulty of speaking and weakness of right extremities started an hour before admission. The computed tomography (CT) brain imaging showed left insular ribbon sign and medial cerebral artery (MCA) hyperdense sign. Angiography confirmed clot in M2 of left MCA. The patient underwent 2 times of generalized seizure 14 hours after receiving thrombolysis of 50 mg alteplase, had anisocoria, and became comatose. A decision to do decompressive hemicraniectomy was made after the latest brain CT imaging showed massive edema of left hemisphere and midline shifting to the right. The patient survived the comatose state and variably infection and septic complications. After a year of treatment, albeit regaining consciousness, the right hemiparesis and fluent aphasia persisted (mRS 4).

CONCLUSION

Candel et al in a trial in Germany showed that while recanalization through IVT alone achieves lower rate of reperfusion, IVT treatment is not inferior in clinical outcomes and survival rate compared to MT. A meta-analysis by Waqas et al did not demonstrate a significant difference between MT and IVT for distal LVO patients with regard to favorable outcome, occurrence of intracranial hemorrhage, or 90-day mortality. In minor strokes with LVO patients, a study from the German registry also suggested similar effectiveness of IVT alone compared to MT with or without IVT. Contrarily, Kastrup et al showed in dependent patients with LVO, MT avoids poor outcome and leads to smaller infarcts compared to IVT alone. The case report does not justify treatment with IVT alone; however, LVO patients may benefit from IVT alone especially in distal LVO and minor stroke cases.

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CORRELATION BETWEEN DE RITIS RATIO WITH COGNITIVE IMPAIRMENT IN ACUTE STROKE PATIENTS: A CROSS-SECTIONAL STUDY IN SARDJITO GENERAL HOSPITAL, YOGYAKARTA

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BACKGROUND

The aspartate transaminase/alanine transaminase ratio (AST/ALT or De Ritis ratio, AAR) is a biomarker for liver damage that has been reported to have associations with the risks and prognosis of diseases such as cancer and infection. Cognitive impairment is a common clinical consequence and manifestation of stroke with direct implications for post-stroke functioning and quality of life. This study aimed to analyze the association between De Ritis ratio on acute stroke admission with cognitive impairment.

METHODS

This is a cross-sectional study conducted at Stoke Unit of Dr. Sardjito General Hospital Yogyakarta within the period of July 2021 to May 2023. All hospitalized patients with acute stroke were included in the study. Inclusion criteria in this study were : consciousness, able to communicate, accessible Moca-Ina test, and received AST and ALT laboratory tests. Patient's with unconsciousness and aphasia are automatically included in the exclusion criteria. The cognitive function status assessments with Moca-Ina, clinical and laboratory data were examined within 24 hours of patient's admission and collected from the patients' medical records.

RESULTS

There were 236 acute stroke patients who were included in the study. Clinical characteristics showed the average of age 59 ± 11.43 years old, 56.4% male. NIHSS score 5.07 ± 4.81 . Laboratory characteristics showed the average of AST 30.01 ± 35.40 μ /l (micro per liter), ALT 25.29 ± 24.75 μ /l (micro per liter) and De Ritis ratio 1.36 ± 0.69 . The average Moca-Ina score was 20.00 ± 9.34 . The Pearson's correlation test showed significant inverse correlation between De Ritis ratio and Moca-Ina on acute stroke patients ($p = 0.002$, pearson correlation = -0.205). The results suggested the higher De Ritis score, the lower Moca-Ina score, and vice versa.

CONCLUSION

There was a significant inverse correlation between De Ritis ratio and Moca-Ina score in acute stroke patients. This results suggested that increased De Ritis ratio was correlated with cognitive impairment in acute stroke patients.

KEYWORDS

acute stroke; cognitive impairment; De Ritis ratio

THE ASSOCIATION BETWEEN IMMUNONUTRITIONAL BIOMARKER HALP AND IN-HOSPITAL MORTALITY IN NON-GERIATRIC HEMORRHAGIC STROKE PATIENT

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INTRODUCTION

Hemorrhagic stroke has been determined to have higher mortality risks compared to ischemic stroke. Prognostic factors for survival and mortality in hemorrhagic stroke patients are essential, particularly to those who are suffered from the disease in the productive age. HALP (Hemoglobin, Albumin, Lymphocyte, and Platelet) score is considered to be an easily calculated marker of systemic inflammation and nutritional status. This study aimed to investigate the association between HALP score and in-hospital mortality in non-geriatric hemorrhagic stroke patients.

METHODS

This was a retrospective cohort study. Data were obtained from Stroke Registry of the Dr. Sardjito General Hospital in Yogyakarta from January 2020 to December 2023. Exclusion criteria were patients with infection disease; neoplastic disorders; major trauma or surgery within 3 months; liver and kidney dysfunction; and adults who were >60 years of age. HALP score was obtained from the multiplication of hemoglobin, albumin, and lymphocytes divided by the platelet count, on admission.

RESULT

A total of 76 patients were included in this study. The study population was divided into two groups based on HALP score, HALP score ≥ 29.9 is considered high score ($n = 43$, 56.6%) while HALP score < 29.9 is considered low score ($n = 33$, 43.4%). There were 10.5% of patients who were deceased. The results of the analysis showed no statistical significance was found between the HALP score and in-hospital mortality in non-geriatric hemorrhagic stroke patients ($p = 0.250$, CI = 95%).

CONCLUSION

HALP score, as an immunonutritional biomarker, was not associated with in-hospital mortality in non-geriatric hemorrhagic stroke patients.

KEYWORD

hemorrhagic stroke, HALP score, mortality

**BLOOD PRESSURE AND DIFFERENT TYPES OF STROKE: A STUDY IN
SEBERANG JAYA HOSPITAL, PENANG, MALAYSIA**Tang, A.S.N.¹, Chin C.J.², Azlam, M.¹ Looi, I.¹¹ Department of Internal Medicine, Seberang Jaya Hospital, Penang, Malaysia² Clinical Research Center, Seberang Jaya Hospital, Penang, Malaysia**INTRODUCTION**

High blood pressure (BP) is a common presentation during acute stroke, and it is presumably related to underlying hypertension, cerebral ischemia or cerebral autoregulation. The previous studies that look into the relationship of high or low BP and stroke severity produced mixed results. High BP is a risk factor for stroke, but low BP during acute stroke is associated with a worse outcome. This study aims to look into the relationship between admission systolic and diastolic BP, with different types of stroke.

METHODS

This is a retrospective cross-sectional study involving patients who received hyperacute stroke treatment (either thrombolysis, mechanical thrombectomy or both) in Seberang Jaya Hospital from the year 2012 to 2023. Data were extracted from the medical records and analysed with SPSS IBM version 26.

RESULTS

A total of 423 stroke cases data were collected. Patients were classified into LACI (n=89), PACI (n=149), TACI (n=139) and POCI (n=423). The mean age was 58.6 (SD 12.7), 68.4% were male, and 31.6% were female.

The mean systolic and diastolic BP for LACI was 170.7mmHg (SD 35.3) and 92.4mmHg (SD 19.1). The mean systolic and diastolic BP for PACI was 165.2mmHg (SD 32.0) and 95.0mmHg (SD 18.8). The mean systolic and diastolic BP for TACI was 156.2mmHg (SD 30.9) and 91.7mmHg (SD 23.3). The mean systolic and diastolic BP for POCI was 164.1mmHg (SD 33.1) and 117.3mmHg (SD 43.7).

Further data analysis showed that there were statistical significance observed in systolic BP among the different stroke groups ($p=0.003$), and diastolic BP among the different stroke groups ($p=0.005$).

CONCLUSION

Patients who had TACI were found to have a lower mean systolic BP and diastolic BP compared to others. Further studies on the significance of low BP in more severe stroke types are encouraged.

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ATRIAL FIBRILLATION AND ISCHEMIC STROKE: A STUDY IN SEBERANG JAYA HOSPITAL, PENANG, MALAYSIA

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INTRODUCTION

Atrial fibrillation (AF) increases the ischemic stroke risk by 4-5 folds, and the incidence of AF increases with age. AF is estimated to account for 20-25% of all ischemic strokes worldwide. This study aims to look into the relationship of AF, and stroke severity upon admission and discharge.

METHODS

This is a retrospective cross-sectional study involving patients who received hyperacute stroke treatment (either thrombolysis, mechanical thrombectomy or both) in Seberang Jaya Hospital from the year 2012 to 2023. Data were extracted from the medical records and analysed with SPSS IBM version 26.

RESULTS

A total of 440 stroke cases data were collected. 16.4% of the stroke patients had AF. The mean age was 58.6 (SD 12.7), 68.4% were male, and 31.6% were female.

The mean admission NIHSS for the AF group was 14.6 (SD 5.1), and 13.5 (SD 6.2) for the non AF group. The mean admission MRS for the AF group was 4.6 (SD 0.5), and 4.3 (SD 0.7) for the non AF group.

The mean discharge NIHSS for the AF group was 10.1 (SD 7.3), and the non AF group was 7.2 (SD 5.5). The mean discharge MRS for the AF group was 4.1 (SD 1.4), and the non AF group was 3.7 (SD 1.56).

Further data analysis showed that there were statistical differences for AF and discharge NIHSS (p value=0.003), and AF and admission MRS (p value=0.007). However, there was no statistical association between AF and admission NIHSS (p value=0.205), AF and discharge MRS (p value= 0.298).

CONCLUSION

Patients who had AF are shown to have higher NIHSS and MRS, upon both admission and discharge. Ischemic stroke patients with AF had more severe stroke and morbidity compared to those without AF.

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CASE SERIES OF NEW STROKE ONSET POST STOPPING OF ANTICOAGULANT IN PATIENTS WITH ATRIAL FIBRILLATION

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INTRODUCTION

Atrial fibrillation(AF) increases the stroke risk by 3-5 times, and accounted for 15% of all strokes worldwide. This paper aims to describe the cases of patients with AF and develop acute stroke after stopping anticoagulant for various reasons. This is a case series of patients who had received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from the medical records of the patients.

REPORT

Case 1

A 77 year old lady developed a severe lower gastrointestinal bleeding 2 weeks post dabigatran for ischemic stroke with AF. Colonoscopy and CT scan revealed a stage 4 rectosigmoid tumor. She developed a right middle cerebral artery(MCA) infarct, with left hemiparesis of NIHSS 21, 2 weeks post stopping of anticoagulant. Her disease was complicated with an obstructing tumor 2 months later, and scar epilepsy 4 months later.

Case 2

A 80 year old man with diabetes mellitus, hypertension, AF on warfarin had ascending colon adenocarcinoma. Hemicolectomy was planned and warfarin was withheld. He suffered a left posterior circulation stroke on day 4 post stopping of warfarin. He had a left lower homonymous quadrantanopia, with NIHSS 3. Emergency ileostomy was carried out for the bleeding tumor. Post op he was complicated with ileus, fast AF, delirium and required ICU care.

Case 3

A 64 year old man with hypertension, dyslipidemia and AF, had haematuria with right ureteric calculus and obstructive uropathy. His dabigatran was withheld. He developed left hemiparesis, with NIHSS of 3 on day 4 of stopping anticoagulant. Lithotripsy for ureteral stone removal was done on day 3 of stroke and anticoagulant was restarted on day 5 of stroke.

CONCLUSION

Patients who discontinued oral anticoagulants are at greater risk of developing a new stroke. The practice shall be discontinued unless risk of devastating hazards is identified.



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ASSOCIATION OF ADMISSION BLOOD PRESSURE AND SEVERITY OF STROKE AMONG PATIENTS WHO RECEIVED TREATMENT IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Hypertension affected 30% of the Malaysian population, as reported in the National Health and Morbidity Survey (NHMS) 2019. Previous studies showed that persistent high blood pressure post stroke is associated with subsequent death and dependency. However, Lin (2015) pointed out that low to normal blood pressure was associated with poorer mortality post stroke. This study aims to study the association between admission blood pressure and the severity of stroke according to NIHSS among patients who received acute stroke treatment in Kek Lok Si Charitable Hospital (KLSCH).

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in KLSCH from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 patients had received stroke treatment in the mentioned period. The descriptive study revealed that 72.6% (n=69) were known to have hypertension. The mean systolic BP upon admission was 156.6 mmHg (SD : 27.6) and mean diastolic BP upon admission was 84.74 mmHg (SD 9.4).

The stroke severity was categorized according to NIHSS into mild (0-4), moderate (5-15) and severe (≥ 16). The mean admission systolic and diastolic BP for mild stroke was Systolic 156.2 mmHg (SD:26.3), Diastolic 83.0 mmHg (SD :19.1), moderate stroke Systolic 161.9 mmHg (SD: 24.1), Diastolic 89.1 mmHg (SD :17.6), and severe stroke Systolic 150.3 mmHg (SD:14.3), Diastolic 90.7 mmHg (SD :23.9).

Further data analysis showed that admission systolic blood pressure (p value= 0.589) and diastolic blood pressure (p value = 0.329) were not significantly associated with severity of stroke.

CONCLUSION

Our study in this cohort revealed that admission systolic and diastolic blood pressure were not associated with the severity of stroke upon admission. Further study on long term blood pressure control target post stroke is encouraged.

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	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Systolic BP	MILD	70 156.19	26.261	3.139	149.92	162.45	107	233
	MODERATE	16 161.94	24.057	6.014	149.12	174.66	122	219
	SEVERE	93 150.33	42.808	14.269	117.43	183.44	104	236
	Total	95 156.60	27.627	2.834	150.97	162.33	104	236
Diastolic BP	MILD	70 82.97	19.144	2.288	78.41	87.54	9	140
	MODERATE	16 89.13	17.561	4.390	79.77	98.48	58	128
	SEVERE	97 90.67	23.917	7.972	72.28	109.05	62	121
	Total	95 84.74	19.388	1.989	80.79	88.69	9	140

		Sum of Squares	df	Mean Square	F	Sig.
Systolic BP	Between Groups	821.277	2	410.638	.533	.589
	Within Groups	70925.523	92	770.930		
	Total	71746.800	94			
Daistolic BP	Between Groups	842.728	2	421.364	1.124	.329
	Within Groups	34489.693	92	374.888		
	Total	35332.421	94			

Statistics

		Systolic BP	Daistolic BP
N	Valid	95	95
	Missing	0	0
Mean		156.60	84.74
Median		156.00	82.00
Std. Deviation		27.627	19.388

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	26	27.4	27.4	27.4
	YES	69	72.6	72.6	100.0
	Total	95	100.0	100.0	

ASSOCIATION OF ATRIAL FIBRILLATION AND SEVERITY OF STROKE AMONG PATIENTS WHO RECEIVED TREATMENT IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice and affecting around 0.54% of the Malaysian population and it is one of the potentially modifiable risk factors associated with acute stroke. This study aims to determine the association between presence of AF and severity of stroke (NIHSS) among patients who received treatment of acute stroke in Kek Lok Si Charitable Hospital (KLSCH).

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in KLSCH from October 2022 to February 2024. Data were extracted from the medical records and analysed with SPSS IBM version 26.

RESULTS

A total of 95 patients received stroke treatment from October 2022 to February 2024. Among them, 14 patients (14.7%) were detected to have AF upon admission.

The mean age of the stroke patients with AF was 74.2 years old (SD : 8.1), and non-AF was 73.6 years old (SD : 12.86) (p-value of 0.235). The proportion of male and female patients with AF were 17.5% and 17.0% respectively (p-value : 0.597).

The severity of stroke was categorized according to NIHSS into mild (0-4), moderate (5-15) and severe (≥ 16). Among the patients with AF, 50% (n=7) developed mild stroke, 14.3% (n=2) developed moderate stroke and 35.7% (n=5) developed severe stroke. The frequency of mild, moderate and severe stroke among patients without AF are 77.8% (n=63), 17.3% (n=14) and 4.9% (n=4) respectively.

Further data analysis showed that presence of AF is statistically significant associated with moderate to severe stroke (p=0.001).

CONCLUSION

The presence of AF is significantly associated with stroke of more severity, namely moderate to severe stroke. The study findings are similar to Vinding's (2022) where AF is associated with more severe strokes, and leads to higher mortality.



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ASSOCIATION BETWEEN ADMISSION BLOOD GLUCOSE LEVELS AND SEVERITY OF STROKE (NIHSS) AMONG PATIENTS WHO RECEIVED ACUTE STROKE TREATMENT IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Stroke is a leading cause of morbidity and mortality globally, necessitating comprehensive investigations into factors influencing its severity and outcomes. Among the potential contributors, blood glucose levels have garnered attention due to their intricate relationship with neurological impairments. Elevated blood glucose has been implicated in exacerbating the severity of strokes. This study aims to determine the association between admission blood glucose and severity of stroke according to The National Institute of Health Stroke Scale (NIHSS) at both admission and discharge in hospital settings among patients who received treatment of acute stroke in Kek Lok Si Charitable Hospital.

METHODS

This retrospective cross-sectional study involved patients who received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 patients received acute stroke treatment from October 2022 to February 2024. The NIHSS severity scores were categorized into mild (0-4), moderate (5-15), and severe (16-42). For mild NIHSS, the mean blood glucose was 7.97 (SD = 3.21), for moderate NIHSS it was 9.26 (SD = 4.71), and for severe NIHSS it was 7.54 (SD = 3.75). At discharge, the mean blood glucose for mild, moderate, and severe NIHSS remained consistent with values of 7.93 (SD = 3.20), 9.48 (SD = 4.57), and 7.53 (SD = 4.00), respectively.

The 1-way ANOVA analysis indicated no significant differences in blood glucose levels among the NIHSS severity groups at both admission ($p = 0.426$) and discharge ($p = 0.309$).

CONCLUSION

Our study revealed that blood glucose level is not statistically associated with the severity of neurological impairment in stroke patients. The limitation of this study is small sample size, and the studied stroke patients have a low NIHSS score upon admission.

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ASSOCIATION BETWEEN ADMISSION BLOOD GLUCOSE LEVELS AND STROKE SEVERITY(MRS) AMONG ACUTE STROKE PATIENTS IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Stroke stands as a prominent contributor to both illness and death on a global scale, prompting in-depth inquiries into the determinants of its severity and consequences. One factor that has attracted significant scrutiny is blood glucose levels, given their complex connection to neurological impairments. Hyperglycaemia, commonly linked with diabetes, have been implicated in intensifying the severity of strokes. This study aims to determine the association between admission blood glucose and severity of stroke (MRS) at both admission and discharge in hospital settings among patients who received treatment of acute stroke in Kek Lok Si Charitable Hospital (KLSCH).

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in KLSCH from October 2022 to February 2024. Data were extracted from medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 patients received acute stroke treatment in the above mentioned period. The MRS severity scores were categorized into good (0-2) and poor (3-6).

Descriptive analyses at admission revealed that for patients with good MRS scores, the mean blood glucose was 8.14 (SD = 3.19), while for those with poor MRS scores, it was 8.11 (SD = 3.78).

At discharge, the mean blood glucose for good MRS scores was 8.01 (SD = 3.19), and for poor MRS scores, it was 8.21 (SD = 3.79).

There is no significant difference in blood glucose levels between good and poor MRS groups upon admission (p value = 0.970) and discharge (p = 0.792).

CONCLUSION

Our study in this cohort did not reveal any statistical association between admission blood glucose level and MRS stroke severity, possible due to small sample size and mild stroke severity upon admission. Further study on the correlation of past sugar control (HbA1c), and post admission sugar control, with post stroke outcome is encouraged.

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ASSOCIATION OF PRE-ADMISSION USE OF ANTIPLATELET/ANTICOAGULANT AND SEVERITY OF STROKE: EXPERIENCE IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Pharmacological agents, mainly antiplatelets and anticoagulants play a pivotal role in the management of stroke. Antiplatelets act by inhibiting the activation pathways of platelets and are commonly used in non-cardioembolic stroke prevention. Anticoagulants act by blocking the coagulation cascade and are commonly used in cardioembolic stroke. This study aims to determine the relationship between pre-admission use of antiplatelets and anticoagulants, with severity of stroke.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 patients received stroke treatment in KLSCH from October 2022 to February 2024. The severity of stroke was categorized according to NIHSS into mild (NIHSS 0-4), moderate (NIHSS 5-15) and severe (NIHSS ≥ 16). Post-stroke clinical outcomes were categorized using mRS measures (0-6).

Descriptive study revealed that among the stroke patients, 20% were taking aspirin, 9% with novel oral anticoagulants, 7% with clopidogrel, 3% with dual antiplatelets, and 1% with warfarin.

14.7% of patients had AF upon admission. 50% of the AF patients were on NOAC, 7% were on warfarin, and the remaining not on antiplatelet or anticoagulant.

Data analysis showed that there is no significant difference in stroke severity in patients taking any antiplatelet, anticoagulant or none (p value :0.532). There is no statistical association between admission MRS and the type of antiplatelet or anticoagulant patients were taking (p value: 0.243)

CONCLUSION

Our study did not find any significant association between pre-admission antiplatelet/anticoagulant with severity of stroke (NIHSS and MRS). More future studies are warranted to further explore and investigate the comparative roles of pre-admission antiplatelets and anticoagulants in reducing severity of stroke symptoms and functional impact on post-stroke lives.

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**ASSOCIATION OF PRE-ADMISSION ANTIPLATELETS/ANTICOAGULANTS,
AND STROKE TYPES AND DURATION OF HOSPITAL STAY: A STUDY IN
KEK LOK SI CHARITABLE HOSPITAL**Tan S.S.Y.¹, Toh C.H.¹, Tan M.K.C.¹, Teoh S.K.¹, Lee S.L.¹, Kee K.L.¹, Neoh K.K.¹, Thor Looi, I.²¹ *Kek Lok Si Charitable Hospital, Penang, Malaysia*² *Clinical Research Center, Seberang Jaya Hospital, Penang, Malaysia***INTRODUCTION**

Stroke poses a significant public health burden on the global population. Key pharmacotherapies, mainly antiplatelets and anticoagulants, underpin the treatment modalities of stroke. The types of antiplatelets and anticoagulant agents have often been the key research focus to further shed light on the postulated roles of these pharmacotherapy agents in the management of different types of cerebral infarction. This study aims to study the relationship between pre-admission antiplatelets and anticoagulants, and the types of stroke, and duration of hospital stay.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 patients received stroke treatment in KLSCH from October 2022 to February 2024. In this study, we compared the pre-admission use of antiplatelet and anticoagulants in stroke patients categorized with OSCP classification system.

Among the 14 patients (14.7%) who had AF upon admission, 8 of them were taking Novel oral anticoagulants (dabigatran and apixaban), and 1 of them was on warfarin treatment. In our non-AF cohort, 18.9% patients (n=18) were taking aspirin, 7.4% patients (n=7) were on clopidogrel, and 3.2% patients (n=3) were on dual antiplatelets regimen.

Further analysis showed that there is no statistical association between pre-admission antiplatelets and anticoagulants with stroke type (p value=0.096), and duration of hospital stay (p=0.932).

CONCLUSION

There is no significant association between pre-admission use of antiplatelet and anticoagulant, with admission stroke type and duration of hospital stay. The limitation of this is small sample size, hence more studies are required to establish the relationship between these factors.



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A STUDY ON GENDER DIFFERENCE WITH STROKE SEVERITY AMONG PATIENT WHO RECEIVED TREATMENT IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Stroke remains a leading cause of disability and mortality worldwide, with variations noted in its severity and outcomes across different demographic groups. Gender disparities in stroke incidence, severity, and outcomes have been a subject of interest in stroke research. This study aims to study the gender differences in stroke severity and functional outcomes in Kek Lok Si Charitable Hospital (KLSCH).

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in KLSCH from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

The total number of stroke patients admitted during the mentioned period was 95, in which 50.5% were female. The mean NIHSS score for female patients was 4.35 (SD = 6.28), and 4.11 (SD = 6.24) for male patients.

The stroke classification for male versus female patients were TIA (1 vs 3), LACI (38 vs 34), PACI (1 vs 4), TACI (1 vs 4), POCS (2 vs 0) and ICB (4 vs 3).

The stroke severity for male versus female patients were mild stroke of NIHSS 0-4 (35 vs 35), moderate stroke of NIHSS 5-15 (8 vs 8), and severe stroke of NIHSS 16-42 (4 vs 5).

The admission MRS for male versus female patients were divided into good MRS of 0-2 (22 vs 21), and poor MRS of 3-5 (25 vs 27).

Further statistical analysis revealed that there were no significant differences in stroke type (p value = 0.224), NIHSS scores (p value = 0.951), and MRS at admission (p value = 0.765) between the gender of patients.

CONCLUSION

This study revealed that there was no statistically significance between the stroke severity and functional status with gender of patients.

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STROKE CARE EFFICIENCY: A STUDY IN KEK LOK SI CHARITABLE HOSPITAL

Teoh S.K.¹, Tan S.S.Y.¹, Toh C.H.¹, Tan M.K.C.¹, Lee S.L.¹, Kee K.L.¹, Neoh K.K.¹, Thor T.G.¹ Looi, I.²

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INTRODUCTION

Kek Lok Si Charitable Hospital (KLSCH) has initiated its stroke services since October 2022. Over the past 16 months, a total of 95 patients were admitted for stroke care. This study aims to study the efficiency of stroke care, in terms of duration of onset to hospital and door to imaging, NIHSS, and hospital stay length.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

In the first 8 months (October 2022 to May 2023), 38 stroke cases were admitted. The mean duration of onset to hospital was 21.13 hours (SD : 25.26), the mean NIHSS was 5.66 (SD: 7.75), the mean door to imaging was 35.22 mins (SD 38.05) and the mean hospital stay length was 2.26 days (SD 1.78).

In the second 8 months (June 2023 to February 2024), 57 stroke cases were admitted. The mean duration of onset to hospital was 43.59 hours (SD: 60.06), the mean NIHSS was 3.28 (SD: 5.18), the mean door to imaging was 40.04 mins (SD 36.01) and the mean hospital stay length was 2.25 days (SD 1.79).

Further data analysis revealed a significant statistical difference in the duration of onset to hospital (p value=0.041), between the first and second 8 months of stroke service.

There was no statistical significance seen in NIHSS (p value=0.076), door to imaging time (p value : 0.538) and hospital stay length (p=0.963), between the first and second 8 months of stroke service.

CONCLUSION

The findings of the study showed that although the number of stroke cases increased and patients took a longer time from the onset of stroke to hospital, stroke care efficiency remained the same.

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ASSOCIATION OF AMBULANCE CALL AND THE SEVERITY OF STROKE AMONG PATIENTS WHO RECEIVED STROKE TREATMENT IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Stroke remains a significant health concern worldwide, with profound implications for morbidity and mortality. Timely access to appropriate medical care is important in mitigating the adverse effects of stroke and optimizing patient outcomes. Ambulance plays an integral role in stroke care, in terms of providing rapid transportation of patients to stroke designated centers. Despite the recognized importance of ambulance services in stroke management, the specific impact of ambulance calls on stroke severity and patient outcomes warrants further study. This study aims to look into the association between ambulance calls and stroke severity (NIHSS) among patients who received acute stroke treatment in Kek Lok Si Charitable Hospital.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

A total of 95 acute stroke cases data were extracted, and 25.3% of them had utilized ambulance service. The study findings reveal several key associations between ambulance calls and stroke severity. While no statistically significant association is observed between ambulance calls and specific stroke types (p-value: 0.347), a significant correlation is identified between ambulance calls and stroke severity upon admission (p-value: 0.00) and discharge (p-value: 0.00). Patients transported by ambulance exhibited a higher prevalence to moderate to severe strokes, as reflected by NIHSS scores.

CONCLUSION

In conclusion, this study highlights the association between ambulance calls and a more severe stroke severity upon admission and discharge. These findings underscore the critical role of timely emergency response in identifying and managing stroke cases. Further research is warranted to explore additional factors influencing ambulance utilization and stroke outcomes, with the ultimate goal of optimizing stroke care delivery and enhancing patient outcomes.

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DETERMINANTS OF AMBULANCE UTILIZATION AMONG STROKE PATIENTS WHO RECEIVED STROKE TREATMENTS IN KEK LOK SI CHARITABLE HOSPITALKee K.L.¹, Toh C.H.¹, Tan M.K.C.¹, Teoh S.K.¹, Lee S.L.¹, Tan S.S.Y.¹, Neoh K.K.¹, Thor T.G.¹ Looi, I.²¹ *Kek Lok Si Charitable Hospital, Penang, Malaysia*² *Clinical Research Center, Seberang Jaya Hospital, Penang, Malaysia***INTRODUCTION**

Stroke management encompasses a complex interplay of factors, with timely access to medical care serving as a cornerstone for better stroke outcomes. Among the critical components of stroke care delivery is the utilization of ambulance services, facilitating rapid transportation of patients to appropriate medical facilities. This study aims to look into the factors influencing the utilization of ambulance services by stroke patients, with a specific focus on exploring the relationship between house distance, time of onset to hospital, and ambulance usage.

METHODS

This retrospective cross-sectional study involved patients who received acute stroke treatment in Kek Lok Si Charitable Hospital (KLSCH) from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 25.

RESULTS

The mean distance from the house to KLSCH was 11.92km (SD : 22.06). 25.3% of the 95 stroke cases patients had utilized the ambulance service. The analysis reveals no significant association between house distance and the time of stroke onset to hospital (p-value: 0.076). House distance is also not found to be statistically associated with the utilization of ambulance services to the hospital (p-value: 0.032). However, a statistically significant association is observed between ambulance usage and poorer MRS upon both admission (p-value: 0.001) and discharge (p-value: 0.002), indicating a poorer functional outcome among patients who required ambulance services upon admission.

CONCLUSION

In conclusion, while factors such as house distance and time of onset to hospital did not significantly impact the decision to use ambulance services among stroke patients, ambulance usage was associated with poorer functional outcomes upon admission and discharge. These findings underscore the importance of optimizing stroke care pathways and emergency response systems to improve patient outcomes and enhance the efficiency of stroke care delivery.

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A DESCRIPTIVE STUDY OF STROKE PATIENTS IN KEK LOK SI CHARITABLE HOSPITAL

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INTRODUCTION

Stroke remains a significant global health concern, necessitating a thorough understanding of its associated risk factors for effective prevention and management. This descriptive study aims to look into the demographic and clinical profile of stroke patients, with a focus on reversible stroke risk factors.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital (KLSCH) from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

Over a 16-month period, a cohort of 95 stroke patients was admitted to KLSCH for acute stroke. The mean age of the patients was 73.7 years (SD: 12.2), with a gender distribution of 48 females and 47 males. Hypertension emerged as the most prevalent risk factor, affecting 72.6% of the cohort. Dyslipidemia and diabetes were also notably prevalent at 48.4% and 43.2%, respectively. A considerable proportion of patients exhibited a past history of stroke (23.2%), atrial fibrillation (14.7%), and smoking (13.7%). Chronic cardiac failure and a history of myocardial infarction were observed in 5.3% and 4.2% of the patients respectively.

The mean admission systolic blood pressure was 156 mmHg (SD 27.6), diastolic blood pressure of 84 mmHg (SD: 19.38), and mean blood sugar level of 8.1 (SD 5.1). The stroke classification was TIA (4.2%), LACI (75.8%), PACI (5.3%), TACI (5.3%), POCI (2.1%) and ICB (7.4%). The mean NIHSS was 4.23 (SD: 6.4), and 73.7% were mild strokes (NIHSS 0- 4), 16.8% were moderate strokes (NIHSS 5-15), and 9.5% were severe strokes (NIHSS 16-42).

CONCLUSION

This descriptive study offers a comprehensive overview of the risk factors associated with stroke in a diverse patient population. The findings underscore the importance of addressing multiple risk factors concurrently in stroke prevention and management strategies.

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IMPACT OF AGE ON STROKE SEVERITY AND FUNCTIONAL OUTCOMESLee S.L.¹, Kee K.L.¹, Toh C.H.¹, Tan M.K.C.¹, Teoh S.K.¹, Tan S.S.Y.¹, Neoh K.K.¹, Thor T.G.¹ Looi, I.²¹ *Kek Lok Si Charitable Hospital, Penang, Malaysia*² *Clinical Research Center, Seberang Jaya Hospital, Penang, Malaysia***INTRODUCTION**

Stroke is a devastating brain injury resulting in high mortality and morbidity. Age has a complex and interactive effect on stroke type and post stroke care. Previous study showed that aged patients have a higher mortality and poorer quality of life post stroke. This study aims to look into the relationship between age and stroke severity (NIHSS) and functional outcomes (MRS), upon admission and discharge.

METHODS

This is a retrospective cross-sectional study involving patients who received acute stroke treatment in Kek Lok Si Charitable Hospital (KLSCH) from October 2022 to February 2024. Data were extracted from the medical records and analyzed with SPSS IBM version 26.

RESULTS

A cohort of 91 patients were admitted for acute stroke during the mentioned period and their data were analyzed. The patients were grouped as follows: 4.3% were quinquagenarian (age of 50-59), 18.9% were sexagenarian (age of 60-69), 32.6% were septuagenarian (age of 70-79), 33.7% were octogenarian (age of 80-89), and 6.3% were nonagenarian (age of 90-99).

The mean admission NIHSS (SD) and MRS(SD) for quinquagenarian [NIHSS 3.5(SD 3.6), MRS 2.5(SD 1.29)], sexagenarian [NIHSS 4.0(SD 6.3), MRS 2.0(SD 1.4)], septuagenarian [NIHSS 5.3(SD 7.8), MRS 3.5(SD 1.6)], octogenarian [NIHSS 3.8(SD 6.0), MRS 3.1(SD 1.4)] and nonagenarian [NIHSS 1.5(SD 1.7), MRS 2.5(SD 1.2)]

There were no statistical differences observed between different age groups, and admission NIHSS (p value : 0.709), admission MRS (p value : 0.162), discharge NIHSS (p value : 0.843) and discharge MRS (p value : 0.158).

CONCLUSION

Our findings in this cohort showed that age alone is not a decisive factor in predicting stroke severity and functional outcomes. The limitation of this study is small in sample size and the majority of studied patients were of lower NIHSS score upon admission.

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ASSOCIATION BETWEEN MALNUTRITION AND LENGTH OF STAY OF ACUTE INTRACEREBRAL HEMORRHAGE PATIENTS

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INTRODUCTION

Malnutrition is associated with poor outcome in patients with both acute ischemic and hemorrhagic stroke. Acute intracerebral hemorrhage (ICH) is reported to be more severe clinically with longer hospital length of stay (LoS). Malnutrition increases LoS, mortality, disease complications and treatment costs in patients with stroke. The prognostic nutritional index (PNI) is a simple index that reflects nutritional and inflammatory status. This study aims to investigate the association between malnutrition as determined by the PNI score and length of hospital stay in patients with acute intracerebral hemorrhage.

METHODS

This study is a retrospective cohort study using stroke registry of Stroke Unit of Dr. Sardjito Hospital Yogyakarta within the period of 2022 – 2023. The inclusion criteria were patients with acute intracerebral hemorrhage without surgery, complete blood and biochemical indexes and no history of malignancy, autoimmune or chronic disease. PNI was calculated using the indicated formula with the components of serum albumin concentration and total peripheral blood lymphocyte count.

RESULTS

A total of 116 patients with acute ICH were included in the study. The patients were divided into two groups according to the cut-off value of PNI. The cut-off value of PNI was determined using Receiver Operating Characteristic (ROC) with the value of 40.6 to divide the patients into low PNI group ($PNI \leq 40.6$) and high PNI group ($PNI > 40.6$). Seventy-eight patients (67.2%) were categorized into high PNI group. The mean of LoS was 10.10 ± 4.905 days. The LoS was > 14 days in 13.8% patients (4.31% in low PNI group and 9.48% in high PNI group). There was no significant correlation between PNI categorization and longer hospital LoS ($p > 0.05$).

CONCLUSION

This study showed that malnutrition, as determined by the PNI score, is not associated with hospital LoS in acute intracerebral hemorrhage patients.

KEYWORDS

acute intracerebral hemorrhage, malnutrition, prognostic nutritional index, length of stay

ACUTE ANTERIOR CEREBRAL ARTERY INFARCTION WITH ACUTE DYSTONIA

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INTRODUCTION

Involuntary movement post-stroke can present acutely or delayed in manifestation. It accounts for 1-4% of stroke patients.

REPORT

49-year-old lady with hypothyroidism and hypertension, presented with sudden onset of left sided body weakness with lower limb weaker than the upper limb. Upon assessment, she was conscious. She appeared to be apathetic with cervical and left upper limb dystonia. Her face appeared to be in slight right sided torticollis. Her left shoulder was in adduction while her left elbow was in flexion position. Tone over left upper limb was increased but left lower limb tone was reduced. Her power of left upper limb was 4, and 1 for left lower limb. Left Babinski sign was upgoing. Sensation for all four limbs were normal. She was occasionally crying during history taking but mostly appeared to be abulia. CT brain shows old infarct at left lentiform nucleus. CTA shows distal right anterior cerebral artery (ACA) occlusion which was thought to be hypoplastic right A1 initially. MRI brain shows acute right ACA infarct. Her NIHSS score was 4 which consist of 1 for left upper limb and 3 for left lower limb. She received intravenous alteplase approximately 5 hours after the onset of stroke. Her NIHSS score remained the same post-intravenous alteplase. The dystonia of cervical and left upper limb resolved after few days in the ward.

The stroke area in this patient involved supplementary motor area (SMA), premotor cortex (PMC), cingulate gyrus and medial frontal. Lesion of SMA area causes weakness of upper and lower limbs. Cingulate gyrus functions similarly like SMA. Anterior medial frontal damages cause apathy. The SMA and PMC are connected to striatum and thalamus. Acute infarction at SMA and PMC disrupts the compensatory mechanism between SMA/PMC and thalamocortical circuit causing acute dystonia.

CONCLUSION

Acute ischemic stroke presenting with acute dystonia should be suspected in patients presenting with apathy, hemiparesis with movement disorders.

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DOES SMOKING HISTORY INCREASED RISK OF STROKE-ASSOCIATED PNEUMONIA?

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BACKGROUND

Stroke-associated pneumonia (SAP) is attributed as the most common complication in acute stroke. Some risk factor such as gender, history of smoking, National Institutes of Health Stroke Scale (NIHSS), and dysphagia have been proposed to contribute in this complication. This study aimed to analyse the association of smoking history and the others risk factor with stroke-associated pneumonia at RSUP Dr. Sardjito, Yogyakarta.

METHODS

This is a case control study using data from registry of Stroke Unit of RSUP Dr. Sardjito within July 2023 to March 2024. Patients who diagnosed with acute stroke infarct were included in this study. Gender classified as male or female, while history of smoking, dysphagia and SAP were classified as Yes or No, and NIHSS were divided into 0-18 dan >18 with the interpretation of non-severe and severe respectively. The data analysed using SPSS v22.

RESULTS

A total of 216 acute infarct stroke were included in this study. The average age of subject is 60.04 ± 13.97 years old, 53.2% male. On bivariate analysis, SAP was significantly associated with dysphagia ($p=0.000$), and history of smoking ($p=0.047$) while gender ($p=0.132$) and NIHSS score ($p=0.120$) were not significant. Then we do multivariate analysis with result only dysphagia independently associated with SAP (aOR=2.25, IK95% 2.33–39.12, $p=0.002$).

CONCLUSION

History of smoking and dysphagia increase risk of SAP, but only dysphagia that independently associated with SAP.

KEYWORDS

Pneumonia; smoking; stroke

A CASE REPORT OF CLAUDE SYNDROME

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INTRODUCTION

Claude syndrome is a rare ventromedial midbrain syndrome characterized by ipsilateral oculomotor nerve palsy with contralateral ataxia, mainly caused by vascular insult. It was first described by Henri Claude in 1912 and only few cases have been reported since then.

REPORT

A 46-year-old man, chronic active smoker with underlying hypertension, presented with acute onset of dizziness, right eyelid drooping and diplopia on left gaze for 1 day. On examination, he had right eyelid complete ptosis, dilated right pupil with downward and outward positioned eye, left past pointing and dysdiadochokinesia, positive left heel shin test and a tendency to fall towards his left during gait examination. There was no posterior communicating aneurysm seen on computed tomography angiography (CTA) of cerebral vessels. The brain magnetic resonance imaging (MRI) showed right medial midbrain and right thalamus DWI and T2-FLAIR hyperintensities with restricted diffusion. He was given oral antiplatelet, and commenced on physiotherapy and occupational therapy. He was discharged home 1 week later with improvement in signs and symptoms.

DISCUSSION

Claude syndrome is mainly a midbrain stroke syndrome secondary to occlusion of the small perforating branches of the posterior cerebral artery supplying the dorsomedial aspect of the midbrain. Claude syndrome has simultaneous involvement of: 1) oculomotor nerve fascicles causing oculomotor nerve palsy, complete ptosis and fixed, dilated pupil, and 2) red nucleus, brachium conjunctivum, or fibers of the superior cerebellar peduncle resulting in incoordination and cerebellar hemiataxia. Our case has the typical clinical presentation of Claude syndrome confirmed by brain MRI that showed midbrain infarction.

CONCLUSION

Clinicians must have a high degree of suspicion of Claude syndrome in cases which presented with acute ipsilateral oculomotor palsy and contralateral ataxia. MRI imaging is warranted in cases with normal CT brain imaging to facilitate proper management in this case.

PROSPECTIVE OBSERVATIONAL STUDY ON ACUTE ISCHEMIC STROKE RECOGNITION ACCURACY BY MEDICAL EMERGENCY COORDINATION CENTRE (MECC) - AN EMERGENCY DEPARTMENT QUALITY MEASURES IMPROVEMENT

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BACKGROUND

Hyperacute management for acute stroke results in timely intervention with improved outcome in stroke patients. Prehospital activation by Medical Emergency Coordination Centre (MECC) is crucial in recognising stroke as early and accurately possible. Various Prehospital Stroke Scale have been developed to enhance paramedics' ability to recognise stroke symptoms. Continuous medical education (CME) and training on Prehospital Stroke Scale have been shown to improve acute stroke recognition accuracy among MECC and Emergency Medical Services (EMS). We sought to measure MECC online stroke recognition accuracy with compliance to Medical Priority Dispatch System (MPDS) Prehospital Stroke Scale and EMS on-field stroke recognition accuracy using Balance, Eyes, Face, Arms, Speech and Time (BEFAST) Prehospital Stroke Scale. Effect of training on both Prehospital Stroke Scale documentation and implementation was also measured.

METHODS

Using MECC and hospital records, we identified a cohort of MECC-transported acute stroke activation cases. Sensitivity and positive predictive value (PPV) for MECC and EMS stroke recognition were calculated with Neuromedical Department diagnosis as the gold standard in comparison to MPDS and BEFAST documentation. Chi-squared test and z-test were used to determine significant differences between pre-training phase and post-training phase in relation to both Prehospital Stroke Scale documentation and implementation.

RESULTS

During a 12-month period, 192 acute stroke activation patients transported by MECC were enrolled. 130 cases (67.7%) were confirmed as acute ischemic stroke ($n=130$); of which, 59 (45.4%) were MECC-suspected stroke from MPDS and 101 (77.7%) EMS-suspected strokes with positive BEFAST. The overall sensitivity of MECC online stroke recognition was 45.38% (95% confidence interval, 36.6-54.3), and PPV was 85.51% (95% confidence interval, 78.4-90.6). Sensitivity of EMS stroke recognition was 91.82% (95% confidence interval, 85-96.2), and PPV was 89.38% (95% confidence interval, 86.3-91.8). Sensitivity (91.82% versus 10%; $P=0.0033$) and accuracy (83.33% versus 28%; $P=0.0033$) of stroke recognition were higher among cases with Prehospital Stroke Scale documentation; BEFAST performed compared to no BEFAST performed. Continuous medical education and training on Prehospital Stroke Scale leads to increase in MPDS online stroke recognition documented (49.5% versus

44.8%; $P = 0.5157$) and results in higher implementation and usage of BEFAST Prehospital Stroke Scale on-field (96.2% versus 72.4%; $P < 0.00001$).

CONCLUSION

MECC and EMS providers recognised 77.7% of the patients with acute ischemic stroke and recorded higher recognition sensitivity, positive predictive value and accuracy with Prehospital Stroke Scale application. Implementation of BEFAST Prehospital Stroke Scale on-field was associated with higher EMS stroke recognition sensitivity and accuracy. CME and training on Prehospital Stroke Scale results in improved documentation and implementation among MECC and EMS providers, ultimately improving Emergency Department services in delivering hyperacute stroke management.

KEYWORDS

Emergency medical services, acute stroke, continuous medical education

EVALUATION OF THROMBOLYSIS SERVICE QUALITY IN HYPERACUTE ISCHEMIC STROKE PATIENTS: A ONE-YEAR REVIEW IN A DISTRICT HOSPITAL

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INTRODUCTION

Thrombolysis stands as an evidence-based treatment for hyperacute ischemic stroke. This abstract offers a comprehensive review spanning one year of recently implemented thrombolysis services at Sri Aman Hospital, focusing on quality measures and patient outcomes.

METHODS

A retrospective analysis was conducted on all ischemic stroke patients who received thrombolysis at Sri Aman Hospital from December 2022 to December 2023. Data was collected from the health records and analyzed using descriptive analysis of patient's demographics, risk factors, NIHSS score, and modified Rankin scale (mRS). Quality measures assessed include onset-to-door time, door-to-CT scan, door-to-needle time, and onset-to-needle time.

RESULTS

Nine ischemic stroke patients underwent thrombolysis during the study period, comprising of 6 males and 3 females, with 4 of them aged over 65 years. Smoking was the most prevalent risk factor (77.8%) for stroke followed by hypertension, diabetes mellitus, and alcohol intake (66.7%). The mean onset-to-door time is 137 minutes with a mean initial NIHSS of 11.3. Eight patients showed neurological improvement within 24 hours. Three patients had favorable functional outcomes (mRS 0-2) upon discharge, increasing to five after 90 days. The average door-to-CT scan time was 21.9 minutes while door-to-needle time was 81.2 minutes. 4 patients received thrombolysis within 60 minutes of hospital arrival. The mean onset to thrombolysis time was 218.2 minutes, with 22.2% of patients receiving treatment within 180 minutes.

CONCLUSION

This study provides essential baseline information to enhance stroke thrombolysis service in Sri Aman Hospital. Continued monitoring and optimization of processes are essential for further improving stroke service delivery and patient outcomes.

POST HAEMODIALYSIS THROMBOLYSIS, TO GIVE OR NOT TO GIVE?

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INTRODUCTION

End stage renal failure (ESRF) patients have a higher incidence of stroke. With every increment of glomerular filtration rate (GFR) by 10%, there is an elevated risk of stroke by 7% . Stroke death is also 9 times higher in ESRF patients as compared to the general population . Furthermore, one third of acute ischaemic stroke (AIS) occurs during or soon after haemodialysis (HD), hence patients will usually present within the recommended window of intravenous thrombolysis (IVT). Certain studies have described that IVT in ESRF patients with AIS has no added benefit with increased risk of bleeding complications while some still recommend IVT as it improves neurological outcome .

We describe two cases of acute ischaemic stroke at 0 hours post HD and 3.5 hours post HD.

Case 1

62-year-old gentleman with underlying hypertension and ESRF on regular HD. Patient completed HD at 7.30pm and 3.5 hours later, presented with a left sided body weakness and slurring of speech. NIHSS on arrival was 9 then 7 prior to IVT. CTA showed a right distal M1 non occlusive thrombus. Patient was subsequently given IV Alteplase 40mg (4mg bolus and 36mg over 1 hour) using his dry weight of 50kg (0.65mg/kg). NIHSS post IVT at 6hours showed improvement to 3 and 0 upon discharge. Current mRS is 0.

Case 2

66-year-old gentleman with underlying Hepatitis C and ESRF, on regular HD at HSJ Haemodialysis Unit. Patient was undergoing regular HD until at 3hours of ongoing dialysis, became unresponsive. NIHSS upon arrival to Emergency Department 15minits later was 10. CTA showed left M2 occlusion. IV Alteplase 50mg was given (4.5mg bolus and 44.5mg over 1 hour) using his dry weight 74kg (0.67mg/kg). NIHSS 6hours post IVT is 7 and 4 upon discharge. Patient, however had oozing over his left BCF after 30minutes of Alteplase administration which resolved with compression bandage and a minimal sulcal SAH which did not worsen on serial CT brain post IVT. He was then discharged home at Day 4 post stroke with anticoagulant for a newly diagnosed atrial flutter. Current mRS is 1.

CONCLUSION

Post dialysis patients who suffer from an acute stroke, may be given intravenous thrombolysis as to improve their clinical outcome. However, parameters such coagulation profile and premorbid condition are important factors that will contribute to a sound decision to be made. In this study, both patients were given a lower dose of Alteplase (0.6mg/kg) and had favourable outcomes.

KEYWORDS

stroke, post haemodialysis, intravenous thrombolysis, end stage renal failure

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UNRAVELING THE COMPLEXITY: A CASE OF THROMBOEMBOLIC EVENT IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY/DYSPLASIA (ARVC/D) LEADING TO TOP OF BASILAR ARTERY OCCLUSION TREATED WITH INTRAVENOUS THROMBOLYSIS AND MECHANICAL THROMBECTOMY

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INTRODUCTION

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC/D) is a rare hereditary disorder characterized by the replacement of myocardial tissue in the right ventricle with fibrous and fatty tissue. This condition often leads to right ventricular dilatation, wall motion abnormalities, and an increased risk of congestive heart failure. While the association between ARVC/D and thromboembolic events like stroke is not extensively documented due to the rarity of the disease, several factors, such as atrial fibrillation and intracardiac thrombi formation, are believed to contribute to this elevated risk. In this study, our aim is to elucidate the intricacies of arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC/D) and its associated thromboembolic complications, particularly strokes, while also delving into the management strategies employed in such cases.

CASE PRESENTATION

A 37-year-old male with a history of hypertension and arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC/D), who had previously experienced strokes, presented with acute onset dizziness, imbalance, and vomiting. Physical examination revealed neurological deficits consistent with posterior circulation stroke, prompting imaging studies that confirmed a top-of-the-basilar artery occlusion. The patient underwent successful intravenous thrombolysis (IVT) followed by endovascular thrombectomy (EVT), achieving complete recanalization. Subsequent cardiac evaluations revealed significant ventricular dysfunction, but no intracardiac thrombus was observed. Long-term secondary prevention strategies, including initiation of anticoagulant therapy with a direct oral anticoagulant (DOAC), were recommended. Follow-up at three months showed no recurrence of stroke.

CONCLUSION

In conclusion, this case highlights the critical importance of promptly recognizing and managing acute posterior circulation stroke syndromes, especially in younger patients with multiple stroke risk factors. The utilization of multimodal imaging techniques, such as CT angiography and MRI, is essential for confirming the diagnosis and guiding appropriate therapeutic interventions like endovascular thrombectomy and intravenous thrombolysis. Furthermore, comprehensive cardiac evaluation is crucial for identifying underlying structural

heart disease and potential sources of cardioembolism. Long-term secondary stroke prevention strategies should be tailored to each individual based on their specific etiology and comorbidities. In this case, the decision to initiate anticoagulation therapy with direct oral anticoagulants (DOACs) reflects a careful balance between reducing the risk of recurrent stroke and minimizing the potential for hemorrhagic complications. Overall, this case underscores the intricate interplay between cardiovascular and cerebrovascular pathology and emphasizes the necessity of a multidisciplinary approach to optimize patient outcomes in acute stroke care.

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THREE-MONTH OUTCOMES OF ACUTE ISCHEMIC STROKE AND PREDICTIVE FACTORS IN PENANG: INSIGHTS FROM HOSPITAL SEBERANG JAYA STROKE REGISTRY DATA

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INTRODUCTION

Acute ischemic stroke (AIS) is a significant cause of morbidity and mortality worldwide. Understanding the factors influencing post-stroke outcomes is crucial for optimizing patient care and improving prognostic strategies. This study aims to investigate the three-month outcomes of AIS patients in Penang, Malaysia, and identify associated predictors of clinical prognosis.

METHODS

Patient data were retrieved from the National Neurology Registry at Hospital Seberang Jaya, spanning from January 2022 to December 2022. Among 319 patients initially identified, those with missing data were excluded from the analysis. Univariate and logistic regression analyses were conducted to determine predictors of clinical outcomes. An unfavorable outcome was defined as a Modified Rankin Scale (mRS) score > 2 at 90 days, while 90-day mortality was characterized by an mRS score of 6.

RESULTS

Of the 319 patients included, 290 survived upon discharge, while 29 experienced mortality within 90 days post-stroke. At the 90-day follow-up, 60.0% of patients exhibited a favorable outcome, while 4.8% succumbed. Post-discharge recovery was evident in 41% of cases, whereas 15.2% demonstrated worsened mRS scores. Multivariate analysis revealed age, hypertension, length of stay, and initial NIHSS (National Institutes of Health Stroke Scale) as significant predictors of unfavorable outcomes, with age and initial NIHSS emerging as significant predictors of 90-day mortality post-AIS.

CONCLUSIONS

Age and initial stroke severity are key determinants of long-term outcomes following AIS in Penang. These findings underscore the importance of early intervention and personalized management strategies to improve patient prognosis and enhance stroke care delivery. Further research is warranted to explore additional factors influencing post-stroke outcomes and develop targeted interventions to mitigate adverse effects.

FACTORS ASSOCIATED WITH INPATIENT MORTALITY AMONG THE HOSPITALIZED STROKE PATIENTS

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INTRODUCTION

Stroke was the third leading cause of death in Malaysia in 2019 after ischemic heart disease and lower respiratory infections. Malaysia showed a rising trend in stroke cases with incidence 47, 911 (UI 43,757–52,839); deaths 19,928 (95% UI: 15,909–25,000); prevalence 443,995 (95% UI: 414,703–476,838); Disability-adjusted life years (DALYs) 512,726 (95% UI: 420,450–629,695) in 2019. The objective of this study is to determine the significant factors associated with inpatient stroke mortality.

METHODS

This is an observational cross sectional study. A total of 2412 stroke patients data were extracted from the National Stroke Registry Hospital Seberang Jaya from 2021 to 2023. 798 cases were excluded due to stroke type other than ischaemic and haemorrhagic stroke based on WHO stroke classification and incomplete data. 1614 cases were included for analysis on stroke patient's demographics, clinical features, comorbidities, stroke complications, length of hospital stay and association with stroke mortality.

RESULTS

Out of 1614 hospitalized stroke patients, 126 patients died in the same admission. The stroke mortality was 7.8%. The factors associated with stroke mortality were haemorrhagic stroke type (adjusted OR 2.44, 95% CI 1.42,4.20, $p=0.001$), moderate Glasgow Coma Scale (GCS) impairment (adjusted OR 3.31, 95% CI 1.94,5.63, $p<0.001$), severe GCS impairment (adjusted OR 13.70, 95% CI 7.11,26.37, $p<0.001$), uncontrolled random blood sugar at presentation (adjusted OR 2.01, 95% CI 1.24,3.28, $p=0.005$), comorbidity of ischaemic heart disease (adjusted OR 2.08, 95% CI 1.15,3.76, $p=0.016$), complications of aspiration pneumonia (adjusted OR 4.96, 95% CI 2.93,8.39, $p<0.001$), acute kidney injury (adjusted OR 5.20, 95% CI 2.98,9.07, $p<0.001$) and increased intracranial pressure (adjusted OR 5.01, 95% CI 1.46,17.18, $p=0.010$).

CONCLUSION

A comprehensive post stroke care need to be implemented among the hospitalized stroke patients to reduce the medical complications that lead to inpatient mortality.

CHARACTERISTICS, PRESENTATION, RISK FACTORS AND OUTCOME OF OLD AND YOUNG STROKE PATIENTS: A COMPARATIVE STUDY

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BACKGROUND

Stroke presentation and risk factors in older adults can differ in comparison to younger adults. They might present with an atypical presentation like a fall or headache, triage to a non-urgent zone (i.e., the green zone), and miss the golden period for stroke thrombolysis, resulting in a poorer stroke outcome. We aimed to study to compare and associate the characteristics and risk factors with the outcomes of stroke in young and older stroke adults.

METHODOLOGY

We performed a retrospective cross-sectional study on all acute ischemic stroke patients from January 1st, 2023, to December 31st, 2023. Data was collected from the local stroke registry at Hospital Seberang Jaya, a regional stroke center. We categorised younger stroke adults as age <60 years and older stroke adults as age ≥ 60 years.

RESULTS

A total of 648 acute ischemic stroke patients were included. Older adults constitute about 56% (n = 364). In both stroke groups, we have more male patients. Chinese stroke patients were higher in the older adult (32% versus 17%). Motor symptoms with other neurological manifestations were the most common clinical presentation in both groups. 31% of older stroke adults have no motor symptoms. Our study revealed that there is a significant association between absent motor in the older adults ($p < 0.05$). Moreover, we found a significant association between hypertension and atrial fibrillation in older adults ($p < 0.05$). There is a significant association between TACI (Total Anterior Circulation Infarct) and POCI (Posterior Circulation Infarct) in older adults. Our study also revealed a significant association between unfavorable outcomes (MRS 3-6) and higher inpatient mortality in older adults ($p < 0.005$).

CONCLUSION

Our study revealed that older strokes adults presented atypically and higher proportion of TACI in older stroke adults. This might contribute to an unfavorable outcome and a higher risk of mortality in our study.

A CLINICAL AUDIT ON THE USE OF ALTEPLASE FOR THROMBOLYSIS IN A MALAYSIAN HOSPITAL

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INTRODUCTION

Thrombolysis is a critical intervention in the management of acute ischaemic stroke. Alteplase, a tissue plasminogen activator, is widely used for thrombolysis in many healthcare settings. The efficacy and safety of Alteplase administration are of paramount importance in optimising patient outcomes. This clinical audit aims to evaluate adherence to thrombolysis guidelines in the administration of Alteplase at Seberang Jaya Hospital in Penang, Malaysia.

METHODS

This clinical audit employed a retrospective observational study design. Relevant data including the time of stroke onset, time of the Alteplase injection, body weight, and dosage of Alteplase were obtained from the Seberang Jaya Hospital stroke patient database for the period from September 2022 to September 2023. Audit criteria include both the onset-to-needle time and the dose of Alteplase injected.

RESULTS

A total of 101 cases were evaluated. The first parameter considered was the time from onset of stroke to thrombolysis. Twelve (11.9%) cases were thrombolysed more than 4.5 hours from the onset of stroke, i.e. seven (6.9%) with unknown onset strokes; three (3.0%) within 9 hours from the time of onset but agreed to be thrombolysed by the stroke neurologist; and two (2.0%) with evidence of penumbra-core mismatch. The second parameter considered was the dosage of Alteplase. Six (5.9%) of the 101 cases were out of range. There were three (3.0%) overdoses (1.0mg/kg) and three (3.0%) underdoses. Two of the underdoses (2.0%) were administered with 0.7mg/kg and one (1%) was administered with 0.6mg/kg.

CONCLUSION

While the administration of Alteplase by injection mostly adhered to the Clinical Practice Guideline on the management of ischaemic stroke, 3rd Edition, Ministry of Health Malaysia, 2020, there are always opportunities to further optimise compliance with the guideline.

AM I TOO YOUNG?

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INTRODUCTION

Anterior spinal artery infarction or refer as anterior spinal artery syndrome (ASAS) one type of stroke resulting from direct occlusion of the anterior spinal artery, artery of Adamkiewicz or generalized hypoperfusion. Spinal cord infarction accounts for 1.2% of all strokes. Spinal cord infarct has an incidence in the USA of 3.1 per 100,000 persons

CASE PRESENTATION

A 20-year old lady with no known medical illness presented with unresponsive. Prior to that patient complain of severe headache and left sided shoulder pain.

On arrival to Emergency and Trauma Department (ETD), patient GCS was E2V1M1. Pupil unequal reactive, cyanosed, poor pv. Vital signs were stable. Neurological examinations appear to be power left upper limb 1/5 while lower limb 2/5. Had hyperaesthesia over left lower limb. Reduced sensation glove distribution over left hand. Reflexes normal and babiniski downgoing. However, patient was intubated for airway protection subsequently was sent to tertiary hospital for further investigations and treatment.

Computed tomography (CT) brain done showed no abnormality and proceed with Magnetic Resonance Image (MRI) Brain. It showed acute tentorial infarction of anterior spinal artery, involving part of anteromedial medulla oblongata and upper cervical anterior spinal cord. Suggestive of short thrombus signal in left distal Vertebral artery. Proceed with Digital subtraction angiography (DSA) Cerebral and spine with no significant arteries dissection and arteriovenous fistula. Blood investigation that has been done for this patient are normal.

DISCUSSION

ASAS is associated with an acute presentation after the time of insult. Usually, the first presenting symptom is acute back pain, whose location most of the time corresponds with the level of the injury in the spinal cord. Studies with small groups have described a median age of presentation between 50-70 years old. ASAS is the most common of all spinal cord infarctions described in some studies in up to 87.2% of the cases.

TAKE HOME MESSAGE

Anterior spinal artery infarction may be considered as a differential diagnosis for young patients that present with first onset of abnormal neurological disorder. Normal CT brain does not exclude other neurological abnormalities and further imaging is recommended especially in less suspicious age group.

ALBATROSS AROUND ONE'S NECK: STROKE POST MOTOR VEHICLE ACCIDENT

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INTRODUCTION

Carotid arterial dissection is one of the common causes of stroke in young patients. Dissection occurs when the structure of the arterial wall is compromised, allowing blood to collect between layers as an intramural hematoma.¹ Carotid arterial dissections are classified as extracranial and intracranial. Both can lead to secondary arterial thrombosis and cerebral ischemia, or compressive local symptoms.² Trauma remains one of the etiologies for carotid dissection.

METHODS

We present the case of a 39 years old gentleman who alleged motor vehicle accident. He skidded his motorbike and sustained deep laceration wound over his right clavicular area and multiple abrasion wound. Patient was still able to move his limbs after the accident. On day 2 of ward admission, he developed left upper and lower limbs paralysis. Upon assessment, there was right gaze preference, loss of nasolabial fold over his left face, and his left limbs power were 0/5. His initial CT brain showed deep and superficial watershed infarct over right middle cerebral artery territory. In the same time, CTA of the brain and carotid was done and showed features of right ICA dissection shortly after the carotid artery bifurcation with long segment total non-opacification of at the level of C2 up to the clinoid portion of the ICA. He was then transferred to tertiary center for close monitoring to watch out for full blown infarct which might need decompressive craniectomy. In view of the timing of presentation to tertiary center already exceeded more than 48 hours with some area of brain infarcted, thrombolysis and thrombectomy were not performed. He was instructed to be fully rested on bed for the next 24 hours in a supine position. IV drip was started to maintain hydration and to avoid hypotension. All these were done so that the remaining brain tissue can receive adequate collateral perfusion to prevent further progression of infarct. Single antiplatelet- aspirin was started to prevent further embolic event from the ICA occlusion. He was closely monitored for the next 72 hours and fortunately there was no worsening of his neurological status. He was then discharged home after 1 week of stay with MRS of 4 (wheelchair ambulation) without significant cortical sign.

DISCUSSION

This case highlights the management of Traumatic Internal Carotid Artery Dissection (TICAD). There is classical dilemma of whether antiplatelets or anticoagulants are more appropriate for symptomatic dissections. TREAT-CAD, a trial that did not find aspirin to be noninferior to vitamin K antagonists using a combination of imaging and clinical outcomes, was included for the first time in guideline.³ As in our case, single antiplatelet was initiated as we worried about the dissection might have extended intracranially, which increased risk of

intracranial bleed. Furthermore, the mechanism of stroke in our patient is likely due to hypoperfusion as a result of right internal carotid artery occlusion. Thus, few measures have been taken to ascertain adequate perfusion to brain by maintaining collateral flow.

CONCLUSION

TICAD is a rare condition largely described in correlation with traffic accidents. Stroke after trauma warrants further investigation including carotid CTA to look for any carotid or vertebral dissection.⁴ Understanding the mechanism of stroke caused by carotid dissection is crucial to plan for appropriate management in this group of patients.

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BILATERAL MIDDLE CEREBELLAR PEDUNCLE INFARCTION: A RARE STROKE PRESENTATION

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INTRODUCTION

Bilateral middle cerebellar peduncle infarction is a rare form, which accounts for 0.26% of acute ischemic stroke. It is usually associated with vertebrobasilar artery occlusion. It can lead to a severe and debilitating neurological dysfunction. We report a case of middle-aged man presented with severe presentation of acute vertigo, ataxia and hearing loss due to be bilateral middle cerebellar peduncle infarction.

CASE PRESENTATION

45-year-old male, with history of hypertension, presented with sudden onset of headache and giddiness associated with severe gait imbalance and left ear hearing impairment. He was initially treated as peripheral vertigo due to hypertensive urgency. He was discharged home, but the symptoms worsened. He had dysphagia and minimal oral intake with worsening gait imbalance and fall.

Neurological examination revealed impaired swallowing, mild dysarthria and left upper limb dysmetria. The hearing was impaired, and he could not sit or stand up still due to severe ataxia despite a normal muscle strength of MRC grade 5/5.

MRI brain reported as a well-defined T2- hyperintense lesion at the bilateral middle cerebellar peduncle with restricted diffusion on DWI and ADC indicating acute infarction. The posterior circulation arteries were not well demonstrated on brain MRA. Cardiac evaluation to look for atrial fibrillation, thrombus and LV function were within normal. He was given antiplatelet agent, statin, BP control and adequate hydration. After 1 month of rehabilitation, his motor function was still limited due to severe ataxia.

DISCUSSION

The middle cerebellar peduncles are in the watershed area between anterior inferior cerebellar artery (AICA) and superior cerebellar artery (SCA) (1). A study by Chan et al reported that 12 from 14 cases of bilateral cerebellar peduncle infarction had stenosis or occlusion of the vertebrobasilar arteries and the main cause of infarction are caused by hypoperfusion (2). The prognosis of patient with bilateral cerebellar peduncle is poor due to no collateral potency of posterior communicating artery.

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PREVALENCE OF BRANCH ATHEROMATOUS DISEASE (BAD) IN ACUTE ISCHEMIC STROKE (AIS) IN HOSPITAL SULTAN ABDUL AZIZ SHAH

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INTRODUCTION

Branch atheromatous disease (BAD) is an emerging subtype of acute ischemic stroke (AIS) caused by perforating arteries occlusion due to proximal atherosclerosis of the arteries which usually causes early neurological deterioration and recurrent stereotyped transient ischemic attacks. The prevalence of BAD in Malaysia, like in many other countries, is of growing concern especially due to its detrimental early neurological deterioration. This abstract aims to summarise the available data on the prevalence of BAD in Malaysia particularly in Hospital Sultan Abdul Aziz Shah.

METHOD

This is a single-centre study in which a retrospective study was conducted on patients diagnosed with AIS who underwent magnetic resonance imaging and angiography (MRI/MRA) in Hospital Sultan Abdul Aziz Shah. Data on demography, stroke risk factors, imaging findings and stroke outcomes was collected and analysed from HSAAS Acute Stroke Census 2022 and 2023.

RESULTS

A total of 631 cases of acute ischemic stroke (AIS) were included in the analysis. Among these cases, a total 28 (4.8%) were found to have Branch Atheromatous Disease (BAD). A total of 19 (69%) of them are male while the rest of them are female. The mean age of patients with BAD-related strokes was 62 years indicating that BAD affects individuals predominantly in their third quarter of life.

Further breakdown of the data revealed that out of total 28 BAD affected patients around 17 (60%) of them has Type 2 Diabetes Mellitus and Hyperlipidemia while around 21 (75%) of them has Hypertension.

CONCLUSION

Understanding the prevalence of BAD in Malaysia is crucial for developing effective strategies for prevention, early detection, and management of this condition. Further population-based studies with standardised diagnostic criteria are needed to provide more accurate estimates of the burden of BAD and its impact on public health in Malaysia.

BASILAR ARTERY THROMBOSIS SECONDARY TO ATRIAL SEPTAL DEFECT WITH SUCCESSFUL ENDOVASCULAR THROMBECTOMY: A CASE REPORT

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INTRODUCTION

Basilar artery thrombosis is a devastating form of stroke with high morbidity and mortality. It accounts for approximately 1% of strokes.^[1] Common causes are emboli from cardiac origin or large artery (36%) and atherosclerosis (35%). [2][3] We report a case of basilar artery thrombosis in a healthy 34-year-old who underwent successful endovascular thrombectomy and made a significant recovery. Transoesophageal echocardiography (TEE) showed atrial septal defect and later she underwent atrial septal defect closure.

REPORT

Madam N a healthy 34-year-old woman presented to emergency department with acute onset of giddiness, vomiting and slurring of speech eleven hours prior to presentation. There were no risk factors for thromboembolic diseases or family history of young stroke. Vital signs and electrocardiogram were normal upon presentation. Clinical examination showed bilateral horizontal nystagmus with left upper limb dysmetria and dysidiadochokinesia.

Cerebral CT angiography and perfusion showed distal basilar artery thrombosis causing posterior circulation ischemia with penumbra area involving posterior circulation territory with core infarct in bilateral cerebellar region.

She underwent a successful endovascular thrombectomy within 12 hours of symptoms onset. Symptoms improved remarkably and no complications post thrombectomy.

Transcranial doppler (TCD) bubble study was positive with multiple microembolic showers of grade 4 to 5. Rest of the young Stroke workup were unremarkable. Further assessment with outpatient TEE following a positive TCD revealed atrial septal defect (14mm) and ruled out PFO which was our main suspicion.

Patient was discharged home well on day 6 of stroke. She then had a successful atrial septal defect closure (ASD)

CONCLUSION

A case of successful reperfusion of distal basilar artery occlusion likely due to paradoxical embolism via ASD. Importance of an urgent TCD bubble study in young strokes patients or Embolic Stroke of Undetermined Source (ESUS)/Cryptogenic Stroke is highlighted.



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STROKE AND ATRIAL FIBRILLATION: A DESCRIPTIVE STUDY ON CHARACTERISTICS AND OUTCOMES OF PATIENTS WHO RECEIVED INTRAVENOUS THROMBOLYSIS FROM THE HSNZ STROKE REGISTRY

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INTRODUCTION

Stroke is a major complication of atrial fibrillation (AF). Previous epidemiological studies showed that about 15% of ischaemic stroke are caused by AF. This study describes the patients with ischemic stroke and AF who received intravenous thrombolysis in Hospital Sultanah Nur Zahirah (HSNZ) from 2014 to 2023 based on the HSNZ stroke registry.

METHODOLOGY

Patients diagnosed with AF who presented with acute stroke and received intravenous thrombolysis in HSNZ between 2014 to 2023 are identified. Demographic data and types of strokes are reviewed. Outcomes are quantified based on the Early Neurological Improvement (ENI) - defined as drop of 4 or more NIHSS score within 24 hours and Modified Rankin Score 3 months post discharge. The complications encountered were recorded respectively.

RESULTS

Among 230 stroke patients who received intravenous thrombolysis in HSNZ between 2014 to 2023, 37 or 16% had AF. 5 patients were excluded as their outcomes at 3 months were unknown. 20 patients (63%) aged more than 65 and 8 patients were less than 60 years old. Female were predominant compared to male (19 patients, 60% vs 13 patients, 40%). As for stroke subtypes, 14 patients (44%) had TACI, 12 (38%) had PACI, 5 patients (15%) had POCI and only 1 (3%) had LACI. In terms of complications, 11 patients developed intracranial bleeding causing 3 mortalities, 2 patients had gum bleeding while 1 patient had acute pulmonary oedema. Only 13 patients had ENI, at 3 months post discharge, 16 patients (50%) showed favourable mRS score between 0-2, 13 (41%) patients had mRS between 3-6, while 3 patients died due to the intracranial bleed.

CONCLUSION

The prevalence of AF in patients with ischemic stroke in HSNZ is comparable with previous studies. This suggested increasing age associated with AF and development of large stroke. More studies are needed to identify the factors influencing outcome and complications among stroke patients with AF in our population.

EXPLORING THE THERAPEUTIC POTENTIAL OF STINGLESS BEE HONEY AS A NOVEL THERAPEUTIC APPROACH FOR MIDDLE CEREBRAL ARTERY OCCLUSION STROKE MODELS

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INTRODUCTION

Stroke has been the leading cause of death and disability worldwide and approximately 87% of cases are attributed to ischemia. A worrying trend towards a rise in cases of stroke in an ageing population is seen and strokes have become more prevalent in Malaysia. In fact, it is predicted that Malaysia will become an ageing country by 2030 which warrants attention.

METHODS

In the present study, new insights on the potential neuroprotective influences of stingless bee honey (SBH) in treating middle cerebral artery occlusion (MCAO) stroke model was tested. After occluding rats with stroke via MCAO, the rats were treated with SBH for a period of 14 days.

RESULTS

The 2,3,5-triphenyltetrazolium chloride (TTC) staining for ischemic stroke model showed a distinct presence of infarction confirming the reliability of MCAO method. Following confirmation, modified neurological severity score (mNSS) scoring was used to assess neurological deficits exhibiting a significant improvement after 14 days. Behavioural analysis encompassing cognitive and sensorimotor performance was conducted using several tests exhibiting significant positive changes. Furthermore, histological studies exhibit improved neuronal morphology, reduced neuronal loss and decreased inflammation.

CONCLUSION

These studies provide encouraging results in the improvement of neurological impairments and brain tissue, highlighting the potential neuroprotective benefits of SBH in the setting of ischemic stroke.

SUCCESSFUL THROMBOLYSIS OF BASILAR ARTERY STROKE BEYOND THE 4.5-HOUR GUIDELINE: A CASE REPORT

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INTRODUCTION

Intravenous Thrombolysis within 4.5 hours of symptom onset is a standard treatment in the guideline for acute ischemic strokes, aimed at restoring blood flow and improving clinical outcomes. However, patients presenting outside this conventional time window pose challenges in acute management due to limited treatment options and a higher risk of adverse outcomes. Basilar artery strokes, in particular, present unique challenges given their potential for devastating consequences and high mortality.

CASE PRESENTATION AND OUTCOME

A 62-year-old female pensioner with no known medical illnesses presented to our institution with left-sided weakness, facial drooping, aphasia, vomiting, and dizziness at 8 hours post-symptom onset. Initial NIH Stroke Scale (NIHSS) assessment yielded a score of 15. Urgent neuroimaging was done, and CT angiogram of the brain revealed thrombosis at the tip of the basilar artery. Despite presenting outside the conventional 4.5-hour thrombolysis window, given the patient's disabling symptoms and the significance of recanalization therapy in basilar artery occlusion (BAO), the multidisciplinary team decided to proceed with intravenous thrombolysis using rTPA. This resulted in significant improvement within 24 hours (NIHSS score reduced from 15 to 1). The patient was then discharged with a comprehensive post-stroke management plan.

CONCLUSION

This case underscores the potential for successful thrombolysis beyond the conventional 4.5-hour window, emphasizing the importance of individualized treatment decisions and further exploration of optimal management strategies for acute ischemic strokes, particularly vertebrobasilar stroke presenting outside the standard thrombolysis window.

A CASE REPORT: TUBERCULOUS MENINGITIS PRESENTING AS A STROKE MIMIC. A DIAGNOSTIC DILEMMA

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INTRODUCTION

Tuberculosis meningitis is a severe infection of the membranes covering the brain and spinal cord, causing inflammation and potentially life-threatening complications, often requiring prompt diagnosis and treatment. Complications of TB meningitis can extend beyond the central nervous system, occasionally presenting with cerebrovascular events, such as stroke. However, the incidence, clinical characteristics, and outcomes of TB meningitis presenting as stroke in Malaysia remain poorly understood (1)

CASE REPORT

A 73-year-old Sarawakian woman, previously in good health but with underlying conditions including hypertension, diabetes mellitus, dyslipidaemia, and aortic stenosis, presented with sudden drowsiness and difficulty walking. Although she could still swallow, she experienced slurred speech the following day, requiring a nasogastric tube, and developed weakness on her right side. Her NIH Stroke Scale score was 12.

Three months earlier, she had experienced a dry cough and coughed up blood. A CT brain during her admission revealed multiple old infarcts and some cerebral atrophy. A lumbar puncture was performed, revealing slightly cloudy cerebrospinal fluid with an opening pressure of 20 cmH₂O, a protein level of 3.37, and a lymphocyte count of 90. Subsequent testing using TB GeneXpert returned a positive result for tuberculosis.

CONCLUSION

TB meningitis presenting as stroke poses diagnostic challenges due to its atypical presentation and overlapping symptoms with other neurological conditions. Early recognition, prompt diagnosis, and initiation of appropriate treatment are crucial for optimizing patient outcomes. Further research is warranted to better understand the pathophysiology and improve management strategies for this uncommon but potentially life-threatening presentation of TB meningitis.

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NEUROPROTECTIVE EFFECTS OF STINGLESS-BEE HONEY (*Trigona spp*) ON THE LEVEL OF ANTIOXIDANT ENZYMES IN PATIENTS WITH POST-STROKE COGNITIVE IMPAIRMENT

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INTRODUCTION

Cognitive impairment occurs typically following stroke onset and is associated with significant morbidity and poor functional outcome. Several preclinical studies have reported the neuroprotective potential of stingless bee honey (SBH), yet the evidence is still minimal. This study aimed to investigate the effects of SBH supplementation on halting the progression of post-stroke cognitive impairment three months after stroke onset.

METHODS

Seventy-two stroke patients were randomly assigned into two groups: the SBH-supplemented group (n=36), supplemented with 20g of SBH daily for three months, and the control group (n=36). Demographic data of the study participants were recorded. The subjects were assessed for cognitive impairment, severity of stroke, and the functional ability by using the Montreal Cognitive Assessment MoCA, NIH Stroke Scale (NIHSS) and Modified Ranking Scale (MRS) respectively during the acute stroke phase and after three months post-stroke. The concentration of serum Catalase (CAT), Superoxide dismutase (SOD) and Glutathione peroxidase (GPx) were measured by using enzyme-linked immunosorbent assay (ELISA). Split-plot ANOVA was employed to determine the significance between the SBH-supplemented and the control group at pre- and post-intervention.

RESULTS

The concentration of GPx was significantly higher in the post-SBH supplemented group than the control group. No significant differences were observed for CAT and SOD.

CONCLUSION

This study suggests that SBH supplementation may hold a promising value as a therapeutic intervention in mitigating post-stroke cognitive impairment, though further research with larger sample sizes and longer intervention periods may be warranted to fully elucidate its efficacy.

DEMOGRAPHICS, CLINICAL MANIFESTATIONS AND OUTCOMES OF POSTERIOR CIRCULATION INFARCT (POCI) IN HOSPITAL SULTAN ABDUL AZIZ SHAH (UPM): A TWO-YEAR RETROSPECTIVE STUDY.

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INTRODUCTION

Posterior circulation infarcts (POCI) represents 20-25% of ischemic strokes, but are frequently missed due to their non-specific symptoms. We aim to show that using MRI enhances detection accuracy and timely treatment in POCI.

METHOD

This is a retrospective study involving patients who were diagnosed with POCI, receiving hyperacute stroke treatment in Hospital Sultan Abdul Aziz Shah (HSAAS) from January 2022 to December 2023. Data were retrieved from the digital medical records by trained medical personnel and analyzed with SPSS IBM version 26.

RESULTS

A total of 111 patient were included in this study, constituting 15% of total ischemic strokes in HSAAS. The median age is 60.5 years and are predominantly males (81.5%). Majority of them had hypertension (78%) followed by dyslipidaemia (54%) and diabetes mellitus (53%). Almost 20% of the patients had a history of previous stroke. Utilizing MRI, reperfusion therapy was administered in approximately 18% of patients, with 14.8% receiving intravenous thrombolysis (IVT-only), 2% undergoing mechanical thrombectomy (MT) and 1 patient receiving both IVT and MT.

Overall patients receiving reperfusion therapy had positive outcomes at day 90. In IVT-only group, the median NIHSS at admission was 2.5 and improved to 0 at day 90. In the MT group the median NIHSS at admission was 11 and improved to 1 at day 90 while in the IVT and MT group the NIHSS at admission was 7 and improved to 0 at day 90.

There were three intracranial bleeds (ICB) requiring decompressive craniectomy (2.8%) which is comparable to international data. Overall there were four mortalities (3.7%) in which the cause of death were stroke-related in three patients.

CONCLUSION

Using MRI facilitated in diagnosing POCI and expedited timely delivery of reperfusion therapy resulting in overall improvement of NIHSS at day 90 with no added risk of bleeding or mortality.

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ENDOVASCULAR THROMBECTOMY VERSUS MEDICAL MANAGEMENT IN LARGE VESSEL OCCLUSION (LVO) WITH LOW NIHSS

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INTRODUCTION

The potential benefits of Endovascular Thrombectomy (EVT) for cases with mild Acute Ischemic stroke (AIS) and LVO (NIHSS <6) remain uncertain. Our study sought to evaluate both the effectiveness and safety of EVT versus medical management (MM) in mild stroke cases with LVO.

METHOD

From a retrospective analysis of the HSAAS UPM stroke registry between 2022 and 2023, we included all acute ischemic stroke (AIS) patients with LVO and a baseline National Institutes of Health Stroke Scale (NIHSS) score of <6, presenting within 24 hours from the time last known well (LKW). Patients were divided into two groups: those who received endovascular thrombectomy (EVT) and those who received medical management (MM). The primary outcome was a 90-day modified Rankin Scale (mRS) score of 0 to 1. Safety outcomes included Early Neurological Deterioration (END) and symptomatic intracerebral hemorrhage (sICH).

RESULTS

A total of 29 patients were included in the study, with 8 (27.6%) received EVT and 21 (72.4%) received MM. The mean NIHSS score was 2 (SD = 1.85). There was no significant difference in the proportion of patients achieving a mRS score of 0-1 at 90 days between the EVT and MM groups (14% versus 41%; $P=0.294$). END in EVT and MM group was (7% vs 3%; $P=0.09$) respectively. The rate of recurrence stroke rate at 3 months did not significantly differ between the two groups (EVT 3% vs MM14%; $P=0.247$). No sICH or mortality were reported in either group.

CONCLUSION

EVT appears equivalent to MM for patients with large-vessel occlusion who present with low NIHSS in acute ischemic stroke (AIS). This data also shows patients treated with EVT may have a lower incidence of recurrent stroke at 3 months compared to those with MM. Further research and prospective studies are needed to validate these findings.

ISOLATED MIDDLE CEREBRAL ARTERY DISSECTION IN A YOUNG PATIENT: A CASE REPORT ON TREATMENT AND OUTCOME

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INTRODUCTION

Isolated middle cerebral artery (MCA) dissection (MCAD) is a rarely reported cause of stroke (1,2). Although the first case was reported in 1915, isolated MCAD remains poorly understood compared to dissections of the intracranial internal carotid artery (ICA) with extension into the MCA. A combination of low clinical suspicion and inadequate understanding of the etiology, presentation, imaging findings, and treatment strategies may contribute to the low reported incidence of isolated MCA. Here we report a case of a healthy 24-year-old man with acute ischaemic stroke due to MCAD.

CASE PRESENTATION

A 24-year-old previously healthy male presented with acute-onset right-sided hemiparesis and dysarthria, with a National Institutes of Health Stroke Scale (NIHSS) score of 5. MRI revealed a left lentiform infarct, and MRA showed irregularity and small calibre of the left MCA M1 segment, raising concerns for vasculitis or atherosclerotic disease. Cerebral angiogram done confirmed dissection of the mid MCA M1 segment. Further workup showed patient had young hypertension and hyperhomocysteinaemia. No evidence of connective tissue disease or other causes of young stroke was identified in this patient. The patient was treated with dual antiplatelet therapy for 3 months, antihypertensive medications for blood pressure control, and a high-dose statin. He showed clinical improvement and was discharged with an NIHSS score of 3. At 2 months post-stroke, he achieved a modified Rankin Score (mRS) of 1, indicating minimal disability.

CONCLUSION

MCA dissection in young patients, though rare, should be considered in cases of acute stroke symptoms. The condition requires a high index of suspicion for timely diagnosis. Management strategies vary, ranging from conservative medical treatment to surgical intervention. In this case, conservative management with dual antiplatelet therapy and blood pressure control proved effective. This case also highlights the importance of considering MCA dissection in young and early diagnosis and appropriate treatment are essential for positive outcomes. Further research is needed to establish standardized treatment guidelines for MCA dissection.

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FIGURES

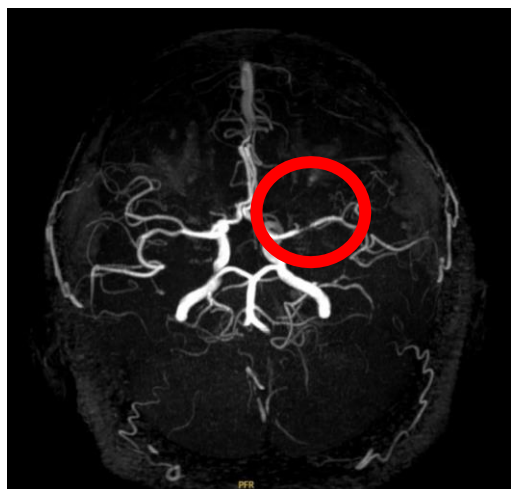


Figure 1: The MRA shows irregularity and small calibre of the left middle cerebral artery (MCA) M1 indicates possible atherosclerosis or vasculitis

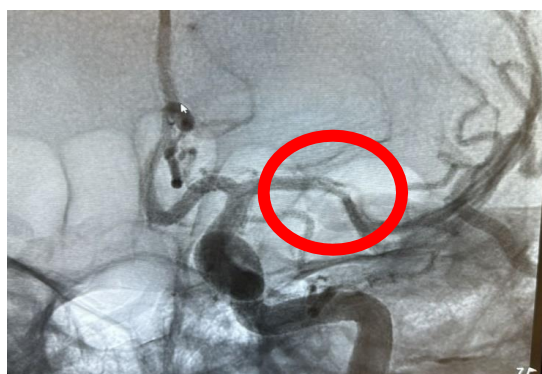


Figure 2: The cerebral angiogram demonstrated a double lumen or intimal flap within the left MCA M1 segment, suggesting the presence of dissection.

JAK2V617F MUTATION AND ISCHAEMIC STROKES: A CASE SERIES

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INTRODUCTION

Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by excessive production of red blood cells, often underdiagnosed and accidentally detected during the workup for stroke. This case series report aims to highlight the association between PV and ischemic stroke through the presentation of three case reports.

METHODS

Three cases of patients with acute ischemic stroke were described, including their clinical presentations, investigations, and management. Relevant neuroimaging findings, such as brain MRI and MRA, were included. Hematological investigations, including the presence of the JAK2V617F mutation and serum erythropoietin levels, were used to confirm the diagnosis of PV.

RESULTS

In the first case, a 62-year-old female with no known underlying medical illness presented with acute left basal ganglia and occipital infarction. Screening for traditional risk factors for stroke were unremarkable however further investigations revealed a positive JAK2V617F mutation suggesting the presence of newly diagnosed PV. The second case involved a 42-year-old male with a right middle cerebral artery infarct. His initial full blood count revealed marked evidence of erythrocytosis, leukocytosis, and thrombocytosis, ultimately diagnosed with PV which confirmed by detection of JAK2V617F mutation. The third case described a 67-year-old male with a chronic left posterior temporal and occipital lobe infarct, accompanied by polycythemia and a positive JAK2V617F mutation. All patients received treatment with hydroxyurea, periodic venesection and antiplatelet therapy. All patients received multidisciplinary post-stroke therapies and co-managed by both neurologists and hematologists. During subsequent follow ups all patients achieved good stroke recovery and stroke recurrence were not observed.

CONCLUSION

The presence of the JAK2V617F mutation and low serum erythropoietin levels are crucial in diagnosing PV, which can initially present with ischemic stroke. Early recognition and multidisciplinary management involving venesection, cytoreductive therapy, and antiplatelet agents are essential to prevent further thrombotic complications. Increased awareness of the association between PV and ischemic stroke is vital for timely diagnosis and appropriate management.

THROMBECTOMY OUTCOMES IN ACUTE ISCHEMIC STROKE: A MALAYSIAN PERSPECTIVE

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INTRODUCTION

Thrombectomy has revolutionised the management of acute ischemic stroke (AIS), offering a potential for significant improvement in patient outcomes. However, the efficacy and safety of thrombectomy in the Malaysian population remain understudied. This study aims to address this gap by providing insights into the real-world outcomes of thrombectomy in AIS patients in Malaysia.

METHOD

A retrospective analysis was conducted on AIS patients who underwent mechanical thrombectomy between 2020 and 2023 at Hospital Sultan Abdul Aziz Shah. Data on patient demographics, clinical outcomes were collected and analysed.

RESULTS

A total of 109 patients who underwent MT were included (67 men [61.5%]; median age 65; median NIHSS upon admission of 13.50). At 30 days, 37 (median NIHSS of 5) of the 109 patients (33.9%) patients showed good outcomes (mRS 0-2). At 3 months, 36 patients (33%) showed good outcomes; mortality was 15.6%. Other than that, 11 patients (10%) ended up with a decompressive craniectomy.

CONCLUSION

Thrombectomy demonstrates promising outcomes in AIS patients in Malaysia, with high rates of procedural success and favourable clinical outcomes. Further research is warranted to explore long-term outcomes and refine patient selection criteria for thrombectomy in the Malaysian population.

AN ANALYSIS of BLEEDING PATTERNS and OUTCOMES ASSOCIATED WITH DIRECT ORAL ANTICOAGULANTS (DOACS) IN MALAYSIAN CLINICAL PRACTICE

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INTRODUCTION

Direct Oral Anticoagulants (DOACs) have emerged as promising alternatives to warfarin for managing thromboembolic disorders and atrial fibrillation, with reduced intracranial bleeding risk. However, concerns persist regarding major bleeding events associated with DOAC utilization, necessitating a deeper understanding of real-world data in Malaysia. This retrospective study aimed to analyse bleeding adverse events related to DOACs (Apixaban, Rivaroxaban, and Dabigatran) utilization within the Malaysian clinical setting.

MATERIALS & METHODS

Data from 852 adverse drug reaction (ADR) reports submitted to the National Pharmaceutical Regulatory Agency (NPRa) database between 2019 and 2023 were analysed. Information included patient demographics, adverse event details, active ingredients, dosages, and outcomes. Causality was assessed using the Naranjo algorithm. Primary endpoints encompassed the distribution of bleeding events, associated risks with specific DOACs, and mortality rates.

RESULTS

Out of 852 adverse drug reactions (ADRs) reported to the NPRa, 527 (61.9%) were from Dabigatran, 167 (19.6%) from Apixaban, and 158 (18.5%) from Rivaroxaban. A total of 300 bleeding events were reported. Gastrointestinal bleeds made up 42%, while intracranial bleeds were 16.3%. Dabigatran had the highest number of bleeding events (192), followed by Apixaban (60) and Rivaroxaban (48). There were 22 deaths, with varying numbers for each DOAC. Additionally, 126 events had unknown outcomes across all three DOACs.

CONCLUSION

This study underscores the impact of DOAC-related bleeding in Malaysian clinical practice, stressing vigilant monitoring and risk assessment. Mortality rates highlight the need to mitigate bleeding risks, especially with specific DOACs. The high number of unknown outcomes emphasizes improving ADR reporting. Enhancing reporting practices can improve pharmacovigilance. Standardized protocols and education for healthcare providers can optimize DOAC therapy and inform guidelines. Further research is needed to reduce DOAC-associated bleeding risks and enhance patient safety.

CYP2C19 METABOLIZER STATUS: TEST AND TREAT OR TREAT THEN TEST?

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INTRODUCTION

In intracranial atherosclerotic disease (ICAD), the most effective treatment to prevent recurrent stroke is with double antiplatelet (DAPT). Among Asians, nearly half possess at least one allele with reduced enzyme function. This reduced function arises from the variability in hepatic CYP450 enzyme activity, particularly the loss of function CYP2C19, which hinders the conversion of Clopidogrel into its active metabolite. Hence, the effectiveness of our standard DAPT with Cardiprin and Clopidogrel comes in doubt. On the other hand, Ticagrelor, a non-reversible antagonist of P2Y receptors, emerges as a potential alternative to heightened the platelet inhibition. However, it is associated with an increased risk of bleeding and cost. Therefore, testing the CYP2C19 metabolizer status is deemed important in the management of ICAD to prevent recurrence of stroke. The long turn-around-time for CYP2C19 metabolizer status when tested in a central lab, instead of point of care testing, leads to a delay in initiating the optimal DAPT.

OBJECTIVE

Our study aimed to assess the feasibility of pharmacogenomics guided dual antiplatelet treatment protocol among patients with ICAD and to determine the prevalence of Clopidogrel resistance in our population with ICAD.

METHODOLOGY

This is a single centre, investigator initiated, randomized control trial which will be conducted in Hospital Canselor Tuanku Muhriz. Patients admitted for acute ischemic stroke with ICAD will be recruited. They will then be randomised into two groups; precision medicine which is treat with Cardiprin and Ticagrelor upon diagnosis and then test for the metabolizer status, or standard of care group which is to be treated with Cardiprin and Clopidogrel and only switched to Ticagrelor if there is presence of intermediate or poor CYP2C19 metabolizer.

CONCLUSION

We hope that this study would be able to change the paradigm of ICAD treatment in our population.