LIPID PROFILES, COGNITIVE FUNCTION, AND THE ROLE OF PHYSICAL ACTIVITY IN MULTIPLE SCLEROSIS

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Abstract

Background: Delayed cognition is common among patients with Multiple Sclerosis (MS) affecting their quality of life. In MS, lipid biomarkers are associated with neurodegeneration, and the blood-brain barrier disruption. This study aimed to investigate the role of lipid components in MS and their association with cognition.

Methods: This case-control study included 71 patients with MS and 71 healthy control participants. The definitive diagnosis of MS was determined according to the revised McDonald criteria. Demographic and clinical data of patients were obtained. In addition, blood samples were collected from all participants. The lipid biomarkers panel included total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C). The physical disabilities were assessed using EDSS, progression index (PI), whereas the cognitive function was assessed utilizing BICAMS.

Results: The Symbol Digit Modalities Test (SDMT) was demonstrating negative correlation with TC, LDL-C, and TC/HDL-C in MS patients. Higher TG levels were associated with increased impairment and disease progression in MS patients, as TG exhibited a positive correlation with disease severity and progression.

Conclusions: Lipid biomarkers are associated with cognitive impairment in MS. The results suggest a potential association between lipid biomarkers and cognitive impairment.

Keywords: Multiple Sclerosis, triglycerides, low-density lipoprotein cholesterol

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Introduction

Multiple Sclerosis (MS) is an immune-mediated inflammatory neurodegenerative disorder that affects the central nervous system (CNS) (Mohamed Elshaer et al., 2018). Research has shown that MS frequently leads to cognitive impairment (Messinis et al., 2017), Cognitive impairment has been reported in up to 40–70% of MS. Therefore, early detection of cognitive impairment is crucial as the timely intervention may contribute to ameliorating, stabilizing, or compensating for cognitive impairment while addressing its emotional effects and improving the overall quality of life (Jackson et al., 2020). Lipids play an essential role in the formation of the myelin sheath, as well as supporting communication within the CNS (Pousinis et al., 2020). Moreover, lipids are potential targets for novel, efficient, and stage-specific therapeutic interventions. The derangements of lipid metabolism in MS remain inadequately investigated (Zahoor et al., 2021).

Previous studies indicate that approximately 30% of multiple sclerosis patients exhibit altered lipid profiles (Nori et al., 2019). However, it remains unclear whether there is a relationship between the lipid profile of MS patients and disability and cognitive function.

A Previous study suggested that atherosclerosis and abnormal systolic blood pressure may play a role in the progression and deterioration of cognitive function (Reia et al., 2021). Additionally, lipid biomarkers have been associated with cognitive outcomes in other neurodegenerative diseases, including Alzheimer's disease (Martin et al., 2014). These studies enhance our understanding that lipids may play a role in MS and could serve as potential biomarkers for disease progression.

This study aims to investigate the role of lipid in MS and their correlation with various disease characteristics.

Material and methods

Study population

Study Setting and Design: This case-control study was conducted at Neuropsychiatry Department in Kafrelsheikh University Hospital, With the IRB approval number (487)

This study was composed of two groups

- **Study group:** it consists of 71 patients diagnosed with MS according to revised McDonald criteria (Thompson et al., 2018).
- **Control group:** it includes 71 participants with no history of neurologic or psychiatric illnesses and did not receive any therapy. Participants in both groups were matched in terms of education, gender, and age.

MS patients were included in the study based on the following

Inclusion criteria

- MS diagnosis according to revised McDonald 2017 criteria
- Age >18 years

Exclusion criteria

- Presence of severe medical and psychiatric illness.
- MS clinical and/or neuroradiological relapse in the sex months prior to enrollment
- Treatment with steroids, psychoactive drugs
- Adherence to a special diet, such as vegetarian or weight loss regimen
- History of alcohol or drug abuse

Demographic and clinical features of the study population

Data regarding sex, age, BMI, marital status, years of education, and history of other medical conditions were collected through in-person interview.

History taking included age of onset, clinical type of first attack, disease duration, number of relapses, disease activity (Ontaneda, D et al., 2024), and disease progression (Comi, G et al., 2024) were retrieved from patients' clinical records.

The disability status of MS cases was evaluated as follows

The Expanded Disability Status Scale (EDSS): The EDSS assesses disability in eight Functional Systems (FS) by assigning a Functional System Score (FSS) in each of these functional systems (pyramidal, cerebellar, brain stem, sensory, visual, bowel /bladder, mental and ambulation).

The EDSS follows an ordinal rating system ranging from 0 (normal neurological status) to 10 (death due to MS) in 0.5-increments interval (Kurtzke JF., 1983).

Progression index (PI): The PI serves as an indicator of disease progression and is calculated by dividing an individual's EDSS score by their disease duration (Cendrowski WS et al., 1985). PI scores lower than 2 have good prognostic value (Pinto et al., 2020).

Cognitive assessment

The cognitive function was evaluated using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) (Artemiadis et al., 2021) , utilizing the Arabic version (Abualhasan A et al., 2023) (The BICAMS includes the following subtests:

- Symbol Digit Modalities Test (SDMT): The score is determined by counting the number of correct responses in matching an abstract symbol with its designated number.

- California Verbal Learning Test (CVLT): This test involves the oral presentation of a list of 16 words over five immediate-recall trials.
- Brief Visuospatial Memory Test-Revised (BVMT-R): This test consists of a visual display of six simple figures arranged in a 2 × 3 matrix over three consecutive 10-second trials.
- Higher scores in each subtest indicate better cognitive function (Benedict et al., 2002). For this study, cutoff scores were set at 34 for SDMT, 46 for CVLT, and 12 for BVMT-R (Arghaly, M et al., 2021).

Blood sampling

Lipids and apolipoproteins were analyzed on plasma samples obtained in the fasted state.

Plasma samples were stored at -80◦C until use. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured using an automated chemistry analyzer with diagnostic reagent kits. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation (Friedewald et al., 1972)

Data analysis

Descriptive statistics were performed and Spearman rank correlation coefficients were calculated. Independent sample t-test and Mann-Whitney U tests were performed to determine differences between groups. Statistical analysis was done using the Statistical Package for Social Science (SPSS v.22).

A categorical variable was created to classify participants into healthy controls (HC), relapsing-remitting multiple sclerosis (RR-MS), and progressive multiple sclerosis (P-MS).

Results

The demographic data indicated that approximately 76.1% of participants were females and 23.9% were males, with a mean age of 30.72 + 9.19. The age of onset ranged from 15 to 46 years, with a median of 25 years. The disease duration ranged from 1 to 33, with a median of 4. In terms of clinical data, approximately 85%, 75%, and 51% of patients exhibited sensory, motor, and sphincteric dysfunction, respectively. Visual acuity was impaired in 73.2% of patients, while the brainstem and cerebellum were affected in 63.4% and 43.7%, respectively. Neurophysiological function, Uthoff phenomenon and tonic spasm occurred in 46.5%, 18.3% and 9.9%, respectively. Among patients, 31% exhibited active disease and 22.5% experienced disease progression. Approximately 77.46% were diagnosed with RRMS, 12.7% with SPMS, and 9.86% with PPMS. The EDSS varied from 1 to 8.5, with a median of 2. The PI ranged from 0.12 to 3, with a median of 0.57. (Table 1).

There was a statistically significant difference between the studied groups for all BICAMS items (SDMT, CVLT, and BVST-R), with higher scores observed in the control group. (Table 2)

A statistically significant difference was observed between the studied groups regarding TG, LDL-C, HDL-C, and TC/HDL ratio. Specifically, LDL-C, TG, and TC/HDL ratio were significantly higher in the case group, while HDL-C levels were significantly lower. (Table 3).

There was a statistically significant positive correlation between total cholesterol and age, age of onset, and number of relapses in the past two years. Conversely, a statistically significant negative correlation was observed between total cholesterol and SDMT. (Table 4)

A statistically significant positive correlation was found between LDL-C and both age and age of onset, while a statistically significant negative correlation was observed between LDL-C and SDMT (Table 4).

HDL-C showed a statistically significant negative correlation with age and BMI. (Table 4)

TG demonstrated a statistically significant positive correlation with age, BMI, age of onset, and PI. (Table 4)

The TC/HDL-C ratio exhibited a statistically significant positive correlation with age, BMI, and PI, and a statistically significant negative correlation with SDMT. (Table 4)

(Table 5) summarizes the linear stepwise regression analysis of factors associated with SDMT. Factors independently and significantly associated with SDMT included LDL cholesterol (unstandardized β = -0.114, p = 0.005).

Discussion

Multiple Sclerosis (MS) is an immune-mediated inflammatory neurodegenerative disorder of the central nervous system that destroys myelinated axons. Cognitive impairment is a common consequence of multiple sclerosis and is defined as a reduction in intellectual abilities, such as memory, processing

Table 1. Distribution of patients according to demographic and disease-specific data.

	N=71	**%**
Sex		
female	54	76.10%
male	17	23.90%
Age	30.72 + 9.19	
	Median (IQR)	**Range**
Age of onset (year)	25(18 – 32)	15 – 46
Disease duration (year)	4(2.5 – 7)	1 – 33
Total number of relapses	3(2 – 5)	1 – 9
Number of relapses in the past 2 years	1(1 – 2)	0 – 5
	N= 71	%
System affection		
Sensory		84.50%
Motor		74.60%
Visual acuity		73.20%
Brainstem		63.40%
Sphincteric function		50.70%
Neurophysiological function		46.50%
Cerebellum		43.70%
Uthoff phenomenon		18.30%
Tonic spasm		9.90%
disease activity		
Inactive	49	69%
Active	22	31%
Progression		
Absent	55	77.50%
Present	16	22.50%
Type of MS		
RRMS	55	77.46%
SPMS	9	12.70%
PPMS	7	9.86%
	Median (IQR)	**Range**
EDSS	2(1.5 – 3.5)	1 – 8.5
PI	0.57(0.38 – 1.03)	0.12 – 3

Abbreviation: RRMS: relapsing-remitting multiple sclerosis, SPMS: secondary progressive multiple sclerosis, PPMS: primary progressive multiple sclerosis, EDSS: Expanded Disability Status Scale, PI: progressive index.

Table 2. Comparison between the studied groups regarding BICAMS.

	HC group	**All-MS group**	**Z**	**P**
	Median (IQR)	Median (IQR)		
SDMT	27(19 – 36)	43(39 – 50)	-7.874	<0.001
CVLT	63(49 – 71)	78(76 – 80)	-8.076	<0.001
BVST-R	28(20 – 32)	27(19.5 – 36)	-4.864	<0.001

The p-values for the differences between the HC and all-MS groups were based on the Mann-Whitney test for all items of BICAMS (SDMT, CVLT, and BVST-R).

Abbreviations: SDMT: Symbol Digit Modalities Test, CVLT: California Verbal Learning Test, BVST-R: Brief Visuospatial Memory Test-Revised.

Table 3. Comparison lipid profiles among the studied groups regarding.

	All-MS group	**HC group**	**T**	**P**
	Mean ± SD	Mean ± SD		
TC (mg/dl)	190.82 ± 36.96	181.63 ± 23.83	1.76	0.081
LDL -C (mg/dl)	122.56 ± 35.7	106.47 ± 16.7	3.44	0.001**
HDL -C (mg/dl)	49.38 ± 13.37	59.25 ± 22.45	-3.186	0.002*
	Median (IQR)	Median (IQR)	Z	P
Triglycerides (mg/dl)	92(62 – 111)	70(61 – 90)	-2.801	0.005*
TC/HDL ratio	3.89(3.21 – 4.61)	2.98(2.59 – 3.77)	-3.407	0.001**

The p-values for the differences between the HC and all-MS groups were based on independent samples t-test and Mann-hitney test for lipid pathway biomarkers.

Abbreviations: TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol.

Table 4. Correlation between lipid biomarkers components and the studied parameters of the studied patients.

	R			**P**	**R**		**P**	**R**	**P**	R	P	R	
	Total cholesterol				LDL cholesterol			HDL cholesterol		Triglycerides		TC/ HDL-C	
Age (year)	0.242		0.042		0.326	0.003		-0.267	0.024	0.347	0.001	0.323	
BMI	0.215		0.072		0.133	0.268		-0.236	0.048	0.46	<0.001	0.341	
Disease-specific data													
Age of onset (year)		0.338	0.004		0.266	0.025		-0.162	0.177	0.433	<0.001	0.226	0.058
Disease duration (year)		-0.106	0.385		-0.035	0.775		-0.218	0.071	-0.179	0.141	0.064	0.603
Total number of relapses		0.048	0.688		-0.035	0.774		-0.043	0.0723	-0.061	0.613	0.026	0.832
Number of relapses in the past 2 years		0.246	0.039		0.029	0.808		0.213	0.074	0.226	0.058	-0.038	0.751
EDSS		0.205	0.086		0.164	0.173		-0.149	0.215	0.204	0.088	0.147	0.223
PI		0.228	0.058		0.125	0.304		0.18	0.136	0.248	0.038	0.248	0.038
Vital data													
Systolic blood pressure (mmHg)		-0.055	0.651		-0.132	0.273		0.108	0.369	0.055	0.65	0.055	0.65
Diastolic blood pressure (mmHg)		-0.013	0.915		0.006	0.959		-0.026	0.833	0.046	0.705	0.046	0.705
Pulse (beat/minute)		0.005	0.966		-0.042	0.731		-0.043	0.721	0.046	0.663	0.063	0.663
BICAMS													
SDMT		-0.388	0.001		-0.358	0.002		0.175	0.144	-0.14	0.245	-0.322	0.006
CVLT		-0.201	0.092		-0.115	0.304		0.09	0.442	-0.182	0.128	-0.202	0.092
BVST-R		-0.231	0.053		-0.154	0.2		-0.047	0.694	-0.034	0.775	-0.079	0.514

Table 5. Linear stepwise regression analysis of factors associated with SDMT.

Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**p**	95.0% Confidence Interval	
		B	Std. Error	Beta			Lower	Upper
SDMT	(Constant)	70.864	5.366		13.206	<0.001**	60.253	81.474
	LDL Cholesterol	-0.114	0.04	-0.224	-2.876	0.005*	-0.193	-0.036
	Total cholesterol	-0.0015	0.036	-0.042	-0.042	0.967	-0.074	0.071
	TC/HDL-C ratio	-0.593	1.506	-0.394	-0.394	0.695	-3.599	2.413

In this work, MS patients had the range of EDSS scores from 1 to 8.5 with median 2, the range of Progression index from 0.12 to 3 with median 0.57.

The Brief International Cognitive Assessment for MS (BICAMS) includes tests of mental processing speed and memory that are assessed by the Symbol Digit Modalities Test (SDMT) , tests of learning and memory that are assessed by the California Verbal Learning Test (CVLT) and test of visual/spatial memory that is assessed by the revised Brief Visuospatial Memory Test (BVMT-R) (Benedict, R.H. et al., 2012). Greater score in each subtest means better cognitive function, the cutoff scores were 34 in SDMT, 46 in CVLT, and 12 in BVMT-R .in this work, we found that all items of BICAMs were higher among control groups than among MS groups.

The primary lipid component of neurons and myelin, cholesterol makes up around 25–30% of the brain's total content. It is essential for axonal growth and synaptic connection, and abnormalities in its metabolism may be the cause of neuroinflammation, ischemia, and brain atrophy (Hernández-Ledesma et al., 2020). In this work, we discovered that lipid components (TG, LDL-C, and TC/ HDL-C) were higher among MS groups than among control groups while HDL-C was lower this finding agreed with Meyers L et al., 2014 .

We discovered that PI and TG levels were correlated, with higher TG levels being linked to more impairment in MS patients; the age of patients and the age of onset were positively correlated with TC, TG and LDL-C. This result is in line with the previous study, which hypothesizes a link between elevated lesion load and hypercholesterolemia, therefore raising the likelihood of disability progression (Gafson et al., 2018). In contrast, Hesham B.M et al, 2023, who reported that no significant correlation was found between serum lipids and disease duration or disability.

We discovered that SDMT was negatively correlated with TC, LDL, and TC/ HDL-C. These findings are largely consistent with earlier studies on lipid pathway biomarkers and cognitive tests in MS (Andaloro et al., 2020), so underlining how this aspect is useful to consider for preventive patient monitoring. It has been discovered that elevated cholesterol levels in MS patients are linked to cognitive impairment. This discovery holds significance because it is a controllable factor, indicating that lowering cholesterol levels can avert future difficulties.

We discovered that disease duration and total number of relapses were not correlated with TC, TG, LDL-C, and HDL-C in similar to Hesham B.M et al, 2023.

Limitations of the study

The primary limitation of this study is the small sample. Further investigation is required to fully elucidate the relationships between cognitive functions and lipid distribution.

The lack of longitudinal data limits understanding of temporal relationship between lipid dysregulation and cognitive decline.

Future directions

Further studies with larger sample size and longitudinal designs are required to validate these findings. Investigating the effects of lipid-lowering interventions on cognitive outcomes in MS may yield valuable insights into potential therapeutic strategies.

Conclusion

Symbol Digit Modalities Test (SDMT) was used to assess mental processing speed and memory, demonstrating a negative correlation with TC, LDL-C, and TC/HDL-C ratio in MS patients. Higher TG levels were linked to increased impairment and disease progression in MS patients, as TG was positively correlated with disease severity and progression. Therefore, lipid pathway biomarkers are associated with cognitive function in MS patients. These findings highlight the association between lipid pathway biomarkers and cognitive function in MS patients. Hyperlipidaemia, as a modifiable risk factor, can be managed to improve lipid profiles in patients with MS, potentially mitigating cognitive impairment and enhancing overall disease outcomes.

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Declaration of Competing Interest

None

References

1. Abualhasan A, Naseer MA, Shalaby N, et al. 2023. Reliability and validity of the Arabic version of brief international cognitive assessment for multiple sclerosis in Egyptian pediatric multiple sclerosis patients. Mult Scler Relat Disord. .82:105374. http://doi.org/ 10.1016/j.msard.2023.105374. Epub 2023 Dec 14.
2. Andaloro, A., Russo, M., Pastura, C., et al., 2020. Is there a correlation between dyslipidemia and cognitive impairment in patients with multiple sclerosis? Int. J. Neurosci. 1–6. http://doi.org/ 10.1080/00207454.2020.1807980.
3. Arghaly, M., Langdon, D.W., Shalaby, N.M. et al., 2021. Reliability and validity of Arabic version of the brief international cognitive assessment for multiple sclerosis: Egyptian dialect. Egypt J Neurol Psychiatry Neurosurg 57, 51. https://doi.org/10.1186/s41983-021-00303-6.
4. Artemiadis A., Bakirtzis C., Chatzittofis A. et al., 2021. Brief international cognitive assessment for multiple sclerosis (BICAMS) cut-off scores for detecting cognitive impairment in multiple sclerosis. Multiple Sclerosis and Related Disorders.49:102751. http://doi.org/10.1016/j.msard.2021.102751.
5. Asadollahi, S., Fakhri, M., Heidari, K., Zandieh, A., Vafaee, R., & Mansouri, B. (2013). Cigarette smoking and associated risk of multiple sclerosis in the Iranian population. Journal of Clinical Neuroscience, 20(12), 1747-1750
6. Benedict, R.H., Amato, M.P., Boringa, J. et al., 2012. Brief International Cognitive Assessment for MS (BICAMS): international standards for validation. BMC Neurol 12, 55. https://doi.org/10.1186/1471-2377-12-55
7. Benedict, R.H., Fischer, J.S., Archibald, C.J., et al., 2002. Minimal neuropsychological assessment of Ms patients: a consensus approach. Clin. Neuropsychol. 16 (3), 381-397. http://doi.org/10.1076/clin.16.3.381.13859
8. Cendrowski WS.1985. Progression index and disability status in multiple sclerosis: a resurvey of 207 patients in central Poland. Schweiz Arch Neurol Psychiatr. 1986;137(4):5-13. PMID: 2428106.
9. Comi, G., Dalla Costa, G., Stankoff, B. et al., 2024. Assessing disease progression and treatment response in progressive multiple sclerosis. Nat Rev Neurol 20, 573–586. https://doi.org/10.1038/s41582-024-01006-1
10. Deleu D, Mir D, Al Tabouki A, et al., (2013). Prevalence, demographics and clinical characteristics of multiple sclerosis in Qatar. Mult Scler.; 19(6):816–819.
11. Donald W. Paty, Alexei N. Boiko, G.K. Vorobeychi.(2003). blue Books of Practical Neurology.Chapter 18 Multiple Sclerosis with Early and Late Disease Onset,Volume 27,2003,Pages 285-302,ISSN 1877-3419,ISBN 9780750673488,https://doi.org/10.1016/S1877-3419(09)70047-9.
12. Elshebawy, H., Fahmy, E. M., Elfayoumy, N. M., Abdelalim, A. M., & Ismail, R. S. (2021). Clinical predictors to cognitive impairment in multiple sclerosis patients. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery, 57, 1-6
13. Eshandarieh S., Allahabadi N.S., Sadeghi M. et al., 2018. Increasing prevalence of familial recurrence of multiple sclerosis in Iran: a population based study of Tehran registry 1999-2015. BMC Neurology. 18 (1), 15. https://doi.org/10.1186/s12883-018-1019-2.
14. Friedewald, W.T., Levy, R.I., Fredrickson, D.S., 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem. 18 (6), 499–502.
15. Gafson, A.R., Thorne, T., McKechnie, C.I.J. et al., 2018. Lipoprotein markers associated with disability from multiple sclerosis. Sci Rep. 8: 17026.http://doi.org/ 10.1038/s41598-018-35232-7.
16. Harbo HF, Gold R, Tintoré M. Sex and gender issues in multiple sclerosis. Ther Adv Neurol Disord. 2013 Jul;6(4):237-48. doi: 10.1177/1756285613488434. PMID: 23858327; PMCID: PMC3707353
17. Hernández-Ledesma A.L., Rodríguez-Méndez A.J., Gallardo-Vidal L.S. et al., 2020. Lipid profile: causal relationship on cognitive performance in multiple sclerosis?. Molecular Biology Reports. (47): 9667–9676 . https://doi.org/10.1007/s11033-020-06011-3.
18. Hesham B.M. , Mona H.T. , Ehab H.Y., et al., 2023. Dyslipidemia in patients with Multiple Sclerosis and its correlation with disease parameters. Egyptian Journal of Medical Research. Volume 4, Issue 3; Pages 53:64. http://doi.org/10.21608/EJMR.2022.113515.1177
19. Jackson D.A., Nicholson R., Bergmann C. et al., 2022. Cognitive impairment in people with multiple sclerosis: Perception vs. performance – factors that drive perception of impairment differ for patients and clincians. Multiple Sclerosis and Related Disorders. 69. http://doi.org/10.1016/j.msard.2022.104410.
20. Kurtzke JF. 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 33(11):1444-52. http://doi.org/ 10.1212/wnl.33.11.1444.
21. Martin, M.G., Pfrieger, F., Dotti, C.G. 2014. Cholesterol in brain disease: sometimes determinant and frequently implicated. EMBO Rep.15 (10), 1036–1052. https://doi. org/10.15252/embr.201439225 [published Online First: 2014/09/17].
22. Mssinis L., Naios G., Mary H. et al., 2017. Efficacy of a Computer-Assisted Cognitive Rehabilitation intervention in RRMS Patients: A Multicenter Randomized Controlled Trial. Behavioural Neurology. vol 2017: 17.http://doi.org/10.1155/2017/5919841.
23. Meyers L., Groover C.J., Douglas J., et al., 2014. A Role for Apolipoprotein A-I in the Pathogenesis of Multiple Sclerosis. J. Neuroimmunol. 277:176–185. http://doi.org/ 10.1016/j.jneuroim.2014.10.010.
24. Mohamed Elshaer A.R., Alqrinawi S.H., Hassan Kallab M.A. et al., 2018. Approach in Diagnosis and Management and Common Mistakes in Diagnosis of Multiple Sclerosis. The Egyptian Journal of Hospital Medicine .70(11) : page 2008-2015. http://doi.org/ 10.12816/0044859.
25. Nori H., Gheini M.R., Rezaeimanesh N. et al., 2019. The correlation between dyslipidemia and cognitive impairment in multiple sclerosis patients. Multiple Sclerosis and Related Disorders. 39. https://doi.org/10.1016/j.msard.2019.101415
26. Ontaneda, D., Chitnis, T., Rammohan, K. et al., 2024. Identification and management of subclinical disease activity in early multiple sclerosis: a review. J Neurol 271, 1497–1514. https://doi.org/10.1007/s00415-023-12021-5.
27. Pinto MF, Oliveira H, Batista S, et al., 2020. Prediction of disease progression and outcomes in multiple sclerosis with machine learning. Sci Rep. 3;10(1):21038. http://doi.org/ 10.1038/s41598-020-78212-6.
28. Pousinis P., Ramos I.R., Woodroofe M.N., et al., 2020. Lipidomic UPLC-MS/MS profiles of normal-appearing white matter differentiate primary and secondary progressive multiple sclerosis. Metabolites. 10(9):366. https://doi.org/10.3390/metabo10090366.
29. Reia A., Petruzzo M., Falco F. et al., 2021. A Retrospective Exploratory Analysis on Cardiovascular Risk and Cognitive Dysfunction in Multiple Sclerosis. Brain science.11:502. http://doi.org/10.3390/brainsci11040502
30. Siger, M. Magnetic Resonance Imaging in Primary Progressive Multiple Sclerosis Patients. Clin Neuroradiol 32, 625–641 (2022). https://doi.org/10.1007/s00062-022-01144-3
31. Thompson, A.J., Banwell, B.L., Barkhof, F., et al., 2018.Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neural. 17 (2), 162-173.
32. Zahoor I., Rui B., Khan J. et al. 2021. An emerging potential of metabolomics in multiple sclerosis: A comprehensive overview. Cellular and Molecular. Life Science. 78:3181–3203. https://doi.org/10.1007/s00018-020-03733-2.
33. El-Sayed, M. S., Kilany, A., & El Shemy, S. A. (2025). Efficacy of Task-Oriented Circuit Training on Gait Kinematics, Pelvic Symmetry and Trunk Endurance in Children with Hemiplegia: A Randomized Controlled Trial. Journal of musculoskeletal & neuronal interactions, 25(1), 36–46. https://doi.org/10.22540/JMNI-25-036