DOI: 10.7860/JCDR/2023/62607.18539

Original Article

Radiology Section

Association between Migraine Patterns and White Matter Hyperintensities in MRI Brain: A Cross-sectional Analytical Study

JIBIN ANTONY[1], ATHUL DAMODARAN NAMBOOTHIRI[2], LENYTHOMAS MATHEW[3]

ABSTRACT

Introduction: Migraine is a neurological condition characterised by recurrent episodes of headaches. The role of Magnetic Resonance Imaging (MRI) as a diagnostic tool in evaluating migraines is yet to be fully understood. Changes that occur in the blood vessels during a migraine attack lead to hypoperfusion in the brain, causing neurovascular dysfunction and cortical spreading depression. These events are manifested as White Matter Hyperintensities (WMHs) in brain MRI.

Aim: To determine the association between migraine patterns and WMHs in the MRI brain scans.

Materials and Methods: A cross-sectional analytical study was conducted at Department of Neurology, Mar Baselios Medical Mission Hospital, a tertiary care centre for Neurology and Movement disorders in South India, from June 2021 to June 2022. The study included 100 patients aged between 18 and 50 years who had been diagnosed with migraine. A questionnaire was prepared, which included various parameters such as the presence or absence of aura, duration, frequency, tolerability, disability, intensity of pain, nausea, and resistance to treatment. The severity of migraine in the patients was evaluated using the Migraine Intensity and Severity Evaluation (MIGSEV) scale, which considers parameters such as pain intensity, attack duration, nausea, disability, tolerability, treatment resistance, and attack frequency. Based on this assessment, patients were classified into Grade I, II, or III. After obtaining informed consent, MRI brain scans were performed on all patients. Patients exhibiting WMHs underwent Gadolinium IV contrast, and those with contrast-enhancing lesions underwent whole spine screening and CSF analysis testing. Statistical Package for the Social Sciences (SPSS) version 20.0 was used for data analysis. The statistical tests employed included the Mann-Whitney test, Kruskal-Wallis test and Spearman coefficient.

Results: The mean age of the participants was 28.60±7.0 years. WMHs were present in 47 out of 100 patients (47%). A significant association was observed between WMHs and aura (U=487.50) (p-value <0.001). Multivariate analysis revealed that migraine severity grade, pain intensity during the attack, nausea, disability, tolerability, migraine duration, and resistance to treatment were statistically significant with a p-value of <0.001.

Conclusion: WMHs in MRI were more significant in patients with Grade III MIGSEV scores. There was a statistically significant association between the number of WMHs, high intensity of pain, vomiting, severe disability, and tolerability during a migraine attack. Therefore, these parameters can be considered as risk factors for developing WMHs in the brain MRI of migraine patients.

Keywords: Cerebrospinal fluid, Migraine intensity and severity evaluation scale, Magnetic resonance imaging, Neuromyelitis optica spectrum disorder

INTRODUCTION

Migraine is a neurological disorder characterised by headache of varying intensity, duration, and frequency, often manifesting as unilateral pain. Migraine with aura, also known as classic migraine, is accompanied by sensory symptoms and is associated with underlying hereditary or acquired cerebrovascular disorders [1]. The pathophysiology involves alterations in blood vessels during the attack, resulting in hypoperfusion in the brain and subsequent neurovascular dysfunction, as well as the initiation of cortical spreading depression [1]. This phenomenon is widely considered to be the primary cause of aura symptoms, which are subsequently observed as WMHs in brain MRI scans of migraine patients [2,3]. The presence of WMHs in individuals with migraines provides valuable insights into their association with migraine type, headache duration, intensity, and attack frequency. Unlocking the mystery behind the higher presence of WMHs in migraines poses an intriguing puzzle. One captivating theory suggests that these WMHs may arise from disrupted blood flow in small, deep arteries during migraine attacks. This disruption leads to reduced blood supply to deeper regions of the brain, potentially causing the formation of WMHs [4]. This study sets out on a compelling mission: to uncover the intriguing connection between migraine patterns and the ethereal landscape of WMHs in MRI brain scans. The aim of the study was to determine the association between migraine patterns and WMHs in the MRI brain.

MATERIALS AND METHODS

A cross-sectional analytical study was conducted at Department of Neurology, Mar Baselios Medical Mission Hospital, a tertiary care centre for Neurology and Movement disorders in South India, from June 2021 to June 2022. Ethical approval for the study (No: 112/2021) was obtained from the appropriate committee. All participants provided informed consent before undergoing an MRI brain scan.

Inclusion criteria: Patients aged between 18 and 50 years with both migraine with and without aura were included in the study.

Exclusion criteria: Patients with known diabetes mellitus, hyperlipidaemia, hypertension, cardiac disease, oncological and haematological diseases were excluded from the study. Additionally, individuals who were reluctant to participate were also excluded from the study.

Sample size: During the study duration, 119 patients with migraines were referred from neurology for MRI evaluation. However, 19 individuals were excluded from the study due to co-existing systemic co-morbidities such as type 2 diabetes, hypertension, and

hyperlipidaemia. Therefore, the study included 100 patients who were diagnosed with migraines.

The severity of migraines in the patients was assessed using the MIGSEV scale, which included the following parameters [5,6]:

A. Intensity of pain: (1) mild; (2) moderate; (3) intense; (4) very intense.
B. Duration of attack (hours): (1) <4; (2) 4-12; (3) 12-24; (4) >24.
C. Nausea: (1) none; (2) mild; (3) intense; (4) vomiting.
D. Disability: (1) no; (2) mild; (3) marked; (4) confined to bed.
E. Tolerability: (1) tolerable; (2) barely tolerable; (3) intolerable.
F. Resistance to treatment: (1) no; (2) yes.
G. Frequency of attacks: (1) 1-4/month; (2) 5-10/month; (3) >10/month.

The severity was assessed using the MIGSEV scale, which takes into account four main factors: intensity of pain, disability, tolerability, and nausea. According to the scale, migraines were categorised into three grades based on the following criteria:

Low severity (Grade I): This category includes cases where atleast one of the four items had a minimum score, and none of them reached the maximum score.

High severity (Grade III): Migraines were classified if atleast one of the four items received the maximum score, and none of them received the minimum score. Alternatively, if atleast two items obtained the maximum score, they also fell into the high severity category.

Intermediate severity (Grade II): Cases that did not meet the low or high severity criteria were classified as intermediate severity (Grade II).

To determine the severity of migraines, a complete neurological examination and basic laboratory investigations were performed on each patient. All patients with migraines underwent MRI brain scans. Among them, those who showed WMH proceeded to receive intravenous contrast with Gadolinium. Patients with contrast-enhancing lesions underwent additional screenings, including whole spine evaluation and Cerebrospinal Fluid (CSF) analysis testing.

Imaging protocol: The MRI scans of all migraine patients included in the study were conducted at the Department of Radiodiagnosis, Mar Baselios Medical Mission Hospital in Kerala, India, using a 1.5 Tesla GE Signa Creator machine. The imaging protocol consisted of the following sequences:

- Diffusion-weighted (DW) images with a b value of 1000 s/mm^2
- Fluid Attenuation Inversion Recovery (FLAIR) sequence (TR/TE: 6000/120; inversion time "TI": 2000)
- T2-weighted turbo spin-echo sequence (TR/TE: 2455/110; echo train length "ETL": eight)
- T1-weighted (sagittal) spin-echo sequence (TR/TE: 450/15)
- T1 post-contrast images in axial, coronal and sagittal plane were acquired

Image analysis: All acquired images were analysed by a radiology consultant who was blinded to the clinical data of the patients. The study focused on analysing WMHs visible in the T2/FLAIR sequences, predominantly observed in the corona radiata, centrum semiovale, and frontal white matter. The study participants were divided into two groups: Group 1 (n=47) included patients with WMHs (T2/FLAIR hyperintense foci without T1 hypointense signal alteration and size greater than 3 mm), while Group 2 (n=53) comprised patients without any MRI signal changes.

STATISTICAL ANALYSIS

Data entry and analysis were performed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp) (Kirkpatrick and Feeney, 2013). Descriptive statistics were used to describe qualitative data in terms of numbers and percentages. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. Quantitative variables were presented as means with standard deviation. The statistical tests employed included the Mann-Whitney test (for abnormally distributed quantitative variables, to compare between two studied groups), the Kruskal-Wallis test (for abnormally distributed quantitative variables, to compare between more than two studied groups), and the Spearman coefficient (to correlate between two abnormally distributed quantitative variables). A p-value <0.05 was considered statistically significant, while a p-value <0.01 was considered highly significant.

RESULTS

A total of 100 patients with migraines were involved in this study, with a mean age of 28.60±7.0 years. White matter hyperintensities (WMH) were present in 47 patients (47%). Among the patients, 59% were females, and 41% were males.

Using the MIGSEV, patients were categorised as follows: 25% experienced mild pain, 21% moderate pain, 32% intense pain, and 22% very intense pain. Regarding attack duration, 25% had attacks lasting less than 4 hours, 31% had attacks lasting 4-12 hours, 29% had attacks lasting 12-24 hours, and 15% had attacks lasting more than 24 hours [Table/Fig-1].

Variables	n (%)
Intensity of pain	
Mild	25 (25.0)
Moderate	21 (21.0)
Intense	32 (32.0)
Very intense	22 (22.0)
Duration of attack (hours)	
<4	25 (25.0)
4-12	31 (31.0)
12-24	29 (29.0)
>24	15 (15.0)
Nausea	
Non	23 (23.0)
Mild	28 (28.0)
Intense	26 (26.0)
Vomiting	23 (23.0)
Disability during the attack	
No	24 (24.0)
Mild	35 (35.0)
Marked	25 (25.0)
Confined to bed	16 (16.0)
Tolerability of headache during attack	
Tolerable	35 (35.0)
Barely Tolerable	34 (34.0)
Intolerable	31 (31.0)
Resistance to treatment	
No	71 (71.0)
Yes	29 (29.0)
Frequency of attacks per month	
1-4	48 (48.0)
5-10	28 (28.0)
>10	24 (24.0)

[Table/Fig-1]: MIGSEV Scale in studied cases (n=100).

Based on the severity of migraines calculated by the MIGSEV Score, 41% of patients were Grade I, 13% were Grade II, and 46% were Grade III [Table/Fig-2].

WMH increased significantly with pain intensity during attacks: very intense pain (6.09±4.13), intense pain (3.47±2.70), moderate pain (0.14±0.66), and mild pain (0.40±1.80). Treatment resistance also showed a significant difference: resistance (4.59±3.96) and no resistance (1.76±2.94) [Table/Fig-3].

Variables		N	Number of WMH in MRI			Test of sig.	p-value
			Min.-Max	Mean±SD	Median		
Sex	Male	41	0-11	2.66±3.64	0	U=1193.50	0.903*
	Female	59	0-12	2.53±3.42	0		
Type of migraine	Migraine with aura	52	0-12	4.12±3.49	3.50	U=487.50	0.001*
	Migraine without aura	48	0-12	0.92±2.66	0		
Duration of symptoms (years)	1	22	0-9	0.50±1.95	0	H=40.04	0.001**
	2	35	0-9	1.20±2.37	0		
	3	27	0-12	4.22±3.72	4		
	4	15	0-11	5.33±3.39	6		
	5	1	11-11	-	11		
Migraine severity grade	Grade I	41	0-9	0.24±1.41	0	H=43.97	0.001**
	Grade II	13	0-9	3.46±3.09	2		
	Grade III	46	0-12	4.41±3.73	4		

[Table/Fig-2]: Relation between the number of white matter hyperintensities in MRI and sex, migraine type, duration of symptoms (years) and migraine severity grade.
*p-values for Kruskal Wallis test. U, **p values for Mann Whitney test.
statistically significant if p<0.001

Variables		N	Number of WMH in MRI			Test of sig.	p-value
			Min.-Max	Mean±SD	Median		
Intenisty of pain	Mild	25	0-9	0.40±1.80	0	H=52.84	0.001*
	Moderate	21	0-3	0.14±0.66	0		
	Intense	32	0-9	3.47±2.70	3		
	Very intense	22	0-12	6.09±4.13	6		
Duration of attack (hours)	<4	25	0-10	1.08±2.66	0	H=11.69	0.009*
	4-12	31	0-11	2.16±3.21	0		
	12-24	29	0-12	3.62±3.71	3		
	>24	15	0-11	3.93±4.08	4		
Duration of attack (years)	<5	24	0-9	0.39±1.79	0	H=51.77	0.001*
	5-10	36	0-3	0.14±0.65	0		
	10-20	33	0-9	3.47±2.70	3		
	>20	7	0-12	6.10±4.23	6.5		
Nausea	Non	23	0-2	0.13±0.46	0	H=21.53	0.001*
	Mild	28	0-11	2.61±3.51	0		
	Intense	26	0-11	3.27±3.61	2		
	Vomiting	23	0-12	4.22±3.92	3		
Disability during attack	No	24	0-9	0.38±1.83	0	H=38.76	0.001*
	Mild	35	0-9	1.6±2.7	0		
	Marked	25	0-11	3.8±3.0	3		
	Confined to bed	16	0-12	6.13±4.23	6.5		
Tolerability during attack	Tolerable	35	0-9	1.14±2.6	0	H=24.68	0.001*
	Barely tolerable	34	0-10	1.88±2.87	0		
	Intolerable	31	0-12	4.97±3.84	4		
Resistance to treatment	No	71	0-11	1.76±2.94	0	U=566.00	0.001**
	Yes	29	0-12	4.59±3.96	3		
		N	Number of WMH in MRI			Test of sig.	p-value
			Min.-Max	Mean±SD	Median		
AURA	Yes	52	0-12	4.12±3.49	3.5	U=487.50	0.001*
	No	48	0-12	0.92±2.66	0		
		N	Number of WMH in MRI			Test of sig.	p-value
			Min.-Max	Mean ± SD	Median		
Frequency of attack	1-4 attacks per month	48	0-9	0.71±2.04	0	H=39.88	0.001*
	5-10 attacks per month	28	0-12	3.21±3.54	2.5		
	>10 attacks per month	24	0-12	5.58±3.51	5		

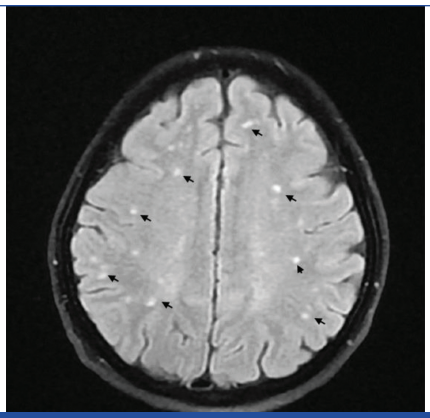
[Table/Fig-3]: Number of white matter hyperintensities and MIGSEV parameters.
*p-values for Kruskal Wallis test. U, **p values for Mann Whitney test. Statistically significant if p<0.001.
Relation between number of white matter hyperintensities in MRI and Freq. of Attack; *p-values for Kruskal Wallis test; Relation between the number of white matter hyperintensities in MRI and AURA; *p-values for Mann-Whitney test

According to multivariate analysis, neither gender, age, nor attack duration (in hours) had statistical significance, however, migraine severity grade, pain intensity during an attack, duration of symptom (in years), nausea, disability, tolerability, attack frequency, and treatment resistance showed statistical significance [Table/Fig-4].

Variables	Number of WMH in MRI	
	rs	p-value*
Age	-0.158	0.115
Sex	-0.012	0.904
Intensity of pain	0.685	0.001
Nausea	0.443	0.001
Disability	0.621	0.001
Tolerability	0.477	0.001
Resistance to Rx	0.384	0.001
MIGSEV score	0.639	0.001
Duration of attack (years)	0.338	0.001
Duration of symptoms	0.619	0.001

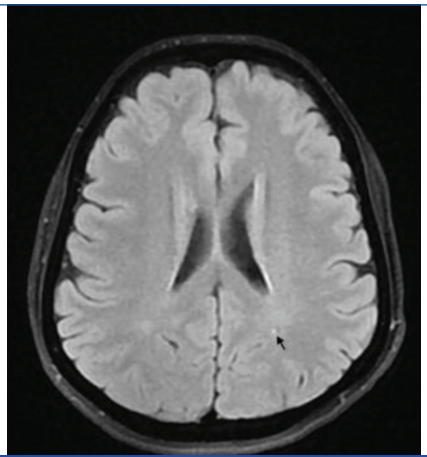
[Table/Fig-4]: Multivariate analysis of development of WMH among migraineurs.
*p-values for Spearman correlation coefficient rs
Statistically significant if p<0.001

Based on the MRI results, 47 patients (47%) exhibited WMH. The patient with the highest number of lesions had a total of 12 lesions, with a mean of 5.49±3.168 lesions [Table/Fig-5].



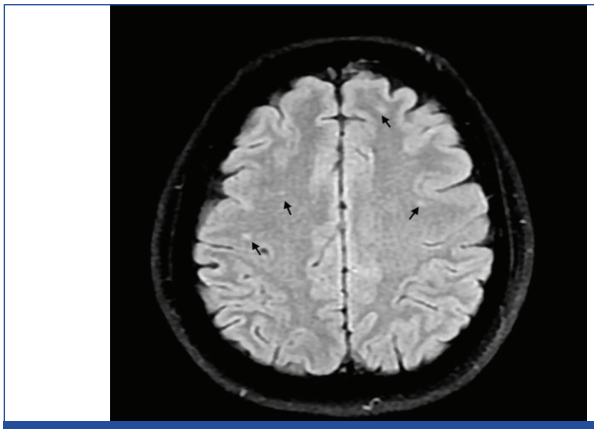
[Table/Fig-5]: A 45-year-old female with severe migraine with aura resistant to treatment for 14 years. Axial FLAIR image shows multiple white matter hyperintensities 12.

Among them, three patients (6.4%) had one lesion [Table/Fig-6], six patients (12.8%) had two lesions, seven patients (14.9%) had three lesions, six patients (12.8%) had four lesions, and the remaining 25 patients (53.1%) had more than four lesions [Table/Fig-7,8].

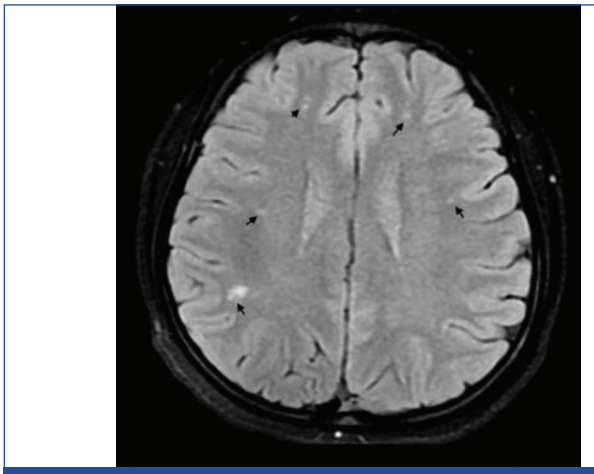


[Table/Fig-6]: A 27-year-old female with mild migraine headache without aura for 6 years. Axial FLAIR image shows a single white matter hyperintensities.

WMH were statistically significant and more frequent in migraines with aura, with a mean of 4.12±3.49 lesions [Table/Fig-2]. In migraines without aura, the mean was 0.92±2.66 lesions [Table/Fig-2], with a maximum number of 12 lesions.

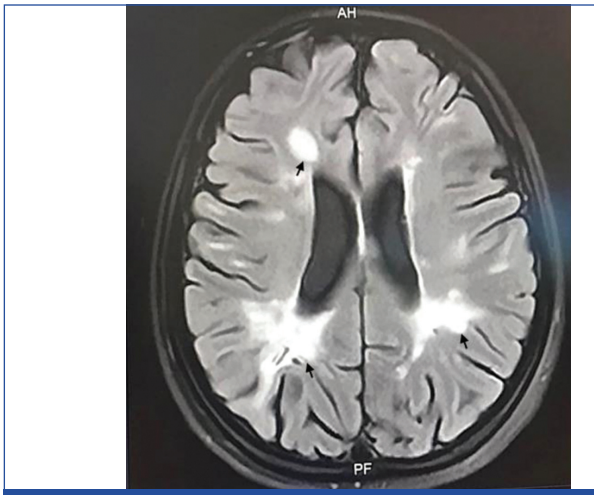


[Table/Fig-7]: A 32-year-old male with migraine headache with aura for 14 years. Axial FLAIR image shows a multiple white matter hyperintensities (6 in number).

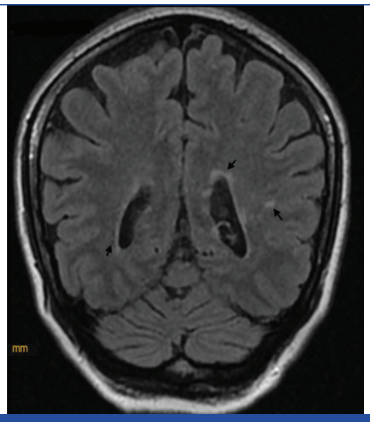


[Table/Fig-8]: A 29-year-old male with migraine headache with aura resistant to treatment for 5 years. Axial FLAIR image shows a multiple white matter hyperintensities (8 in number).

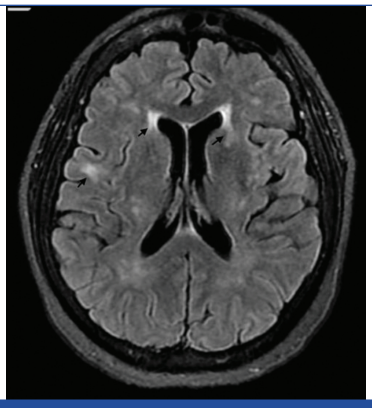
Patients diagnosed with WMH underwent intravenous contrast administration with Gadolinium. Among these patients, eight exhibited contrast-enhancing lesions, leading to further investigations including whole spine screening and CSF analysis. Among these eight patients, two tested positive for multiple sclerosis antibody [Table/Fig-9,10], two tested positive for anti-aquaporin 4 Neuromyelitis Optica Spectrum Disorder (NMOSD) [Table/Fig-11], one tested positive for Anti-Mog antibody, and three patients tested negative for antibody presence. Importantly, the obtained p-value (p>0.005) indicated non significance. Patients who tested negative were advised to undergo regular follow-up scans and seek neurology consultations.



[Table/Fig-9]: A 42-year-old female patient with headache, blurring of vision during attacks of headache. Axial FLAIR image showing white matter hyperintensities. CSF done- proven to be Multiple Sclerosis.



[Table/Fig-10]: A 29-year-old female patient with headache, blurring of vision during attacks of headache. Coronal FLAIR image showing white matter hyperintensities. CSF done- proven to be Multiple Sclerosis.



[Table/Fig-11]: A 25-year-old female patient with headache, blurring of vision during attacks of headache. Axial FLAIR image showing white matter hyperintensities. CSF done- proven to be Neuromyelitis optica spectrum disorder.

DISCUSSION

This study aimed to investigate the association between WMHs and migraines. The prevalence of WMHs in patients experiencing migraine attacks was found to be 47%, consistent with previous studies [3,5]. However, variations in prevalence rates can be attributed to factors such as the inclusion of patients with migraines with aura, ethnicity, lifestyle differences, and geographical factors. Present study findings revealed a statistically significant association between WMHs and various aspects of migraine severity, including the grade of migraine severity, pain intensity during an attack, nausea, disability, tolerability, migraine duration, and resistance to treatment, consistent with the study by Negm M et al., [5]. Age was not identified as a contributing factor to the development of WMHs in migraine patients, in line with previous studies [7,8]. Regarding gender and duration of attack (hours), present study did not find any statistical significance, which aligns with findings from Trauninger A et al., Kruit MC et al., and Toghae M et al., [9-11]. However, Trauninger A et al., reported an increase in WMHs with the duration of the disease, which contrasts with present study results [9].

Migraine with aura was associated with a higher number of WMHs compared to migraine without aura, supported by studies [1,8,12]. This association can be explained by the hypoperfusion of cerebral blood flow during migraine attacks, neurovascular dysfunction, and cortical spreading depression. However, Hamedani AG et al., found more WMHs in migraine without aura, potentially due to sample size and patient selection [13]. Furthermore, present study demonstrated that migraines with Grade III severity were associated with more WMHs than Grade I, consistent with findings by Toghae M et al., and Rothwell PM [11,14]. Additionally, a relevant meta-analysis by Zhang W et al., found concerning WMHs and migraines [15]. It is important to note that present study was conducted in South India, at a tertiary care centre, providing unique insights into this region.

Spearman's correlation coefficient indicated a highly significant positive correlation between WMHs and migraine severity grade according to the MIGSEV, as well as disability and tolerability during an attack. These factors were identified as important risk factors for the development of WMHs. By exploring the association between WMHs and migraines, this study contributes to the current understanding of this relationship and highlights the importance of controlling these risk factors in preventing the development of WMHs in migraine patients. Present study had a large sample size, which increased the strength of the study's outcomes. It is the first of its kind in South India and can guide the development of changes in the investigation of migraine patients in a large, diverse population like India.

Limitation(s)

This study was a single-centered, short-term study, so there can be variations in the outcomes from centre to centre. It would be better to conduct this as a large-scale, multicentre study with a five-year follow-up to obtain more details regarding the relationship between WMHs and migraines.

CONCLUSION(S)

Present study revealed that patients with migraines have an increased likelihood of developing WMHs in the frontal region of the brain. These WMHs differ from those associated with periventricular distribution, which are more indicative of neuro-demyelinating disorders. The presence of WMHs in migraines demonstrates a strong correlation with the parameters of the MIGSEV, suggesting their clinical relevance. Furthermore, the identification of WMHs in an MRI brain can serve as a differential diagnosis for migraines, providing valuable insights into the clinical significance of WMHs in this context. Further exploration into the demyelination spectrum is warranted to better understand the underlying mechanisms and implications of these findings.

Acknowledgement

The authors are grateful to all the patients for consenting to the publication of this study and accompanying MRI images. Authors also thank the entire radiology and neurology departments for their help and support.

REFERENCES

[1] Hadjikhani N, Sanchez del Rio M, Wu O, Schwartz D, Bakker D, Fischl B, et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. Proc Natl Acad Sci. 2001;98(8):4687-92. Available at: https://doi.org/10.1073/pnas.071582498.

[2] Palm-Meinders IH, Koppen H, Terwindt GM, Launer LJ, Konishi J, Moonen JME, et al. Structural brain changes in migraine. JAMA. 2012;308(18):1889. Available at: https://doi.org/10.1001/jama.2012.14276.

[3] Rossato G, Adami A, Thijs V, Cerini R, Pozzi-Mucelli R, Mazzucco S, et al; SAM study group. Cerebral distribution of white matter lesions in migraine with aura patients. Cephalalgia. 2010;30(7):855-59. Available at: https://doi.org/10.1177/0333102409355660.

[4] Ashina S, Bentivegna E, Martelletti P, Eikermann-Haerter K. Structural and functional brain changes in migraine. Pain Ther. 2021;10(1):211-23. Available at: https://doi.org/10.1007/s40122-021-00240-5.

[5] Negm M, Housseini AM, Abdelfatah M, Asran A. Relation between migraine pattern and white matter hyperintensities in brain magnetic resonance imaging. Egypt J Neurol Psychiatry Neurosurg. 2018;54(1):24. Available at: https://doi.org/10.1186/s41983-018-0027-x.

[6] El Hasnaoui A, Vray M, Blin P, Nachit-Ouinekh F, Boureau F, HEMISHERE Study Group. Assessment of migraine severity using the MIGSEV scale: Relationship to migraine features and quality of life. Cephalalgia. 2004;24(7):597-604.

[7] Gomez-Beldarrain M, Oroz I, Zapirain BG, Ruanova BF, Fernandez YG, Cabrera A, et al. Right fronto-insular white matter tracts link cognitive reserve and pain in migraine patients. J Headache Pain. 2016;17(1):4. Available at: https://doi.org/10.1186/s10194-016-0593-1.

[8] Bashir A, Lipton RB, Ashina S, Ashina M. Migraine and structural changes in the brain: A systematic review and meta-analysis. Neurology. 2013;81(14):1260-68. Available at: https://doi.org/10.1212/WNL.0b013e3182a6cb32.

[9] Trauninger A, Leél-Őssy E, Kamson DO, Pótó L, Aradi M, Kövér F, et al. Risk factors of migraine-related brain white matter hyperintensities: An investigation of 186 patients. J Headache Pain. 2011;12(1):97-103. Available at: https://doi.org/10.1007/s10194-011-0299-3.

[10] Kruit MC, van Buchem MA, Hofman PA, Bakkers JT, Terwindt GM, Ferrari MD, et al. Migraine as a risk factor for subclinical brain lesions. JAMA. 2004;291(4):427. Available at: https://doi.org/10.1001/jama.291.4.427.
[11] Toghae M, Rahimian E, Abdollahi M, Shoar S, Naderan M. The prevalence of magnetic resonance imaging hyperintensity in migraine patients and its association with migraine headache characteristics and cardiovascular risk factors. Oman Med J. 2015;30(3):203-07. Available at: https://doi.org/10.5001/omj.2015.42.
[12] Le Pira F, Reggio E, Quattrocchi G, Sanfilippo C, Maci T, Cavallaro T, et al. Executive dysfunctions in migraine with and without aura: What is the role of white matter lesions? Headache J Head Face Pain. 2014;54(1):125-30. Available at: https://doi.org/10.1111/head.12158.
[13] Hamedani AG, Rose KM, Peterlin BL, Mosley TH, Coker LH, Jack CR, et al. Migraine and white matter hyperintensities: The ARIC MRI study. Neurology. 2013;81(15):1308-13. Available at: https://doi.org/10.1212/WNL.0b013e3182a8235b.
[14] Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. The Lancet. 2010;375(9718):938-48. Available at: https://doi.org/10.1016/S0140-6736(10)60309-1.
[15] Zhang W, Cheng Z, Fu F, Zhan Z. Prevalence and clinical characteristics of white matter hyperintensities in migraine: A meta-analysis. Neuroimage Clin. 2023;37:103312. Available at: https://doi.org/10.1016/j.nicl.2023.103312.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Radiodiagnosis, Mar Baselios Medical Mission Hospital, Kothamangalam, Kerala, India.
2. Consultant, Department of Radiodiagnosis, Mar Baselios Medical Mission Hospital, Kothamangalam, Kerala, India.
3. Consultant, Department of Neurology, Mar Baselios Medical Mission Hospital, Kothamangalam, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Jibin Antony,
Chittete (H), Keezhpally P.O., Kannur-670704, Kerala, India.
E-mail: jibinantony222@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 11, 2023
- Manual Googling: Jul 18, 2023
- iThenticate Software: Jul 29, 2023 (14%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 11, 2023**
Date of Peer Review: **Jul 05, 2023**
Date of Acceptance: **Aug 01, 2023**
Date of Publishing: **Oct 01, 2023**