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ORIGINAL ARTICLE

Frequency of White Matter Hyperintensities on MRI in Patients with Migraine

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ABSTRACT

Background: Migraine is a common neurological disorder characterized by recurrent headaches that significantly affect quality of life and daily functioning. Brain magnetic resonance imaging (MRI) often demonstrates white matter hyperintensities (WMHs), but their clinical significance remains uncertain. Therefore, this study was conducted to determine the frequency and radiological characteristics of WMHs on MRI in patients with migraine.

Methods: This descriptive cross-sectional study was conducted at Pak Emirates Military Hospital, Rawalpindi. A total of 400 patients aged 18–60 years with migraine diagnosed according to the International Classification of Headache Disorders, 3rd edition (ICHD-3), were included through non-probability consecutive sampling. Brain MRI was performed using T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences. Associations were evaluated using the Chi-square test, and multivariable binary logistic regression analysis was performed to identify independent predictors of WMHs. Data were analyzed using SPSS version 28.

Results: WMHs were significantly more frequent in patients aged >40 years ($p<0.001$), those with chronic migraine ($p=0.01$), and those with a migraine duration >5 years ($p=0.003$). Binary logistic regression demonstrated that age >40 years, chronic migraine, and migraine duration >5 years were independent predictors of WMHs, whereas gender, migraine aura, hypertension, and diabetes mellitus were not independently associated.

Conclusion: WMHs are common MRI findings in patients with migraine, particularly in older patients and those with chronic or long-standing disease. Most lesions are small, mild, and predominantly involve the frontal and deep white matter. These findings may improve the interpretation of MRI findings and contribute to a better understanding of migraine-related brain changes.

Keywords: Fazekas Scale, Magnetic Resonance Imaging, Migraine Disorders, White Matter Hyperintensities

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Introduction

Migraine is a common neurological disorder characterized by recurrent headaches that significantly affect quality of life and daily functioning. It affects approximately 15 out of every 100 people worldwide and is one of the leading causes of disability among young and middle-aged adults (1).

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The diagnosis of migraine is based on the International Classification of Headache Disorders, 3rd edition (ICHD-3), which provides standardized diagnostic criteria for clinical practice and research (2). Migraine causes repeated headaches that can be moderate or very painful. The pain is often on one side of the head. Many people also feel sick, may vomit, and become sensitive to light and sound. Some patients experience warning signs before the headache starts, known as aura, which may include visual disturbances, numbness, or difficulty speaking.

In recent years, MRI has been used to study the brain in people with migraine. MRI allows clinicians to evaluate structural brain changes and see changes. One common finding is white matter hyperintensities (WMHs). These appear as hyperintense lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) MRI sequences. They may represent subtle abnormalities caused by reduced blood flow, endothelial dysfunction, repeated neuro-vascular inflammation, or small-vessel ischemic changes (3,4).

Studies have found that these lesions are more common in people who have migraine than in those who do not. One study found that about 63.9% of migraine patients had WMHs on MRI. These lesions were mostly found in the frontal and deep white matter regions (5). The research also showed that older individuals and those with a long history of migraine were more likely to have these lesions.

The exact mechanism responsible for the development of WMHs is still not fully understood. One possible explanation is cortical spreading depression, which produces transient changes in cerebral blood flow. Other proposed mechanisms include endothelial dysfunction, repeated episodes of cerebral hypoperfusion, neurovascular inflammation, and small-vessel abnormalities (6-8). Even with these proposed mechanisms, clinicians are still uncertain about the clinical significance of these lesions. Some studies suggest that they are incidental radiological findings without major clinical consequences, whereas others have associated them with cognitive impairment, altered brain function, and an increased risk of future cerebrovascular events (9-11). Furthermore, published studies have reported inconsistent findings regarding the influence of migraine subtype, aura, disease duration, and headache frequency on the development of these lesions.

Most of the available evidence has come from Europe and North America. There is limited research from South Asian countries, where genetic background, environmental factors, vascular risk factors, and healthcare access may differ from Western populations (12,13).

Migraine is also a major public health problem in Pakistan. A nationwide population-based survey reported that approximately 22.9% of adults suffer from migraine, making it one of the most prevalent primary headache disorders in the country (14). However, very few local studies have evaluated MRI findings and white matter hyperintensities among Pakistani patients with migraine.

Therefore, this study was conducted to determine the frequency and radiological characteristics of white matter hyperintensities on MRI in patients with migraine at a tertiary care hospital in Pakistan. The findings of this study may help improve the understanding of migraine-related brain changes and support better interpretation of MRI findings in clinical practice.

Methods

This descriptive cross-sectional study was conducted at the Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, over a period of six months after obtaining ethical approval from the Institutional Ethical

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Committee (Approval No. A/28/EC/17/2025, dated 25/06/2025). A total of 400 patients aged 18 to 60 years with migraine were included using a non-probability consecutive sampling method. The sample size was calculated based on an expected frequency of 63.9%, with a 95% confidence level and 5% margin of error. Migraine was diagnosed according to the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria (2). Patients with other neurological disorders, head trauma, infections, tumors, contraindications for MRI or who were pregnant were excluded. After obtaining written consent, patients' data including age, gender, type, duration and frequency of migraine were recorded. Other conditions such as hypertension and diabetes were also checked to decrease their effect on the results. All patients underwent MRI of the brain using a 1.5 Tesla scanner with T2 and FLAIR sequences. The white matter hyperintensities were identified as bright areas on MRI and were assessed by a trained radiologist who was unaware of the patients' details (4). These lesions were evaluated on the basis of their presence, location, size and severity using the Fazekas scale.

Representative MRI images demonstrating different grades and anatomical distribution of white matter hyperintensities (WMHs) were selected from the study participants after anonymization to illustrate the typical radiological findings observed in this cohort (Figure 1). In addition, the results of the multivariable binary logistic regression analysis were graphically presented as a forest plot showing adjusted odds ratios (AORs) with corresponding 95% confidence intervals for factors associated with WMHs (Figure 2).

The data were analyzed using SPSS version 28. Continuous variables were summarized as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test. Multivariable binary logistic regression analysis was subsequently performed to identify independent predictors of white matter hyperintensities (WMHs). Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated. A p-value <0.05 was considered statistically significant.

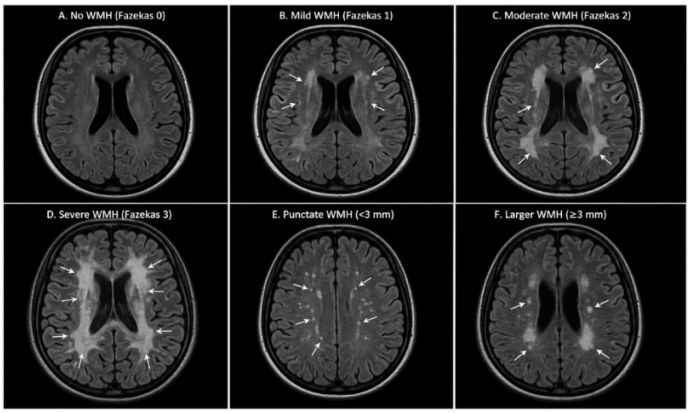

Figure 1: Representative axial fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) images demonstrating white matter hyperintensities (WMHs) in patients with migraine. (A). No WMHs (Fazekas Grade 0). (B). Mild punctate deep white matter hyperintensities (Fazekas Grade 1). (C). Moderate white matter hyperintensities with early confluence of lesions (Fazekas Grade 2). (D). Severe confluent periventricular and deep white matter hyperintensities (Fazekas Grade 3). (E). Representative punctate WMHs measuring <3 mm. (F). Representative larger WMHs measuring ≥3 mm. White arrows indicate the representative WMHs.

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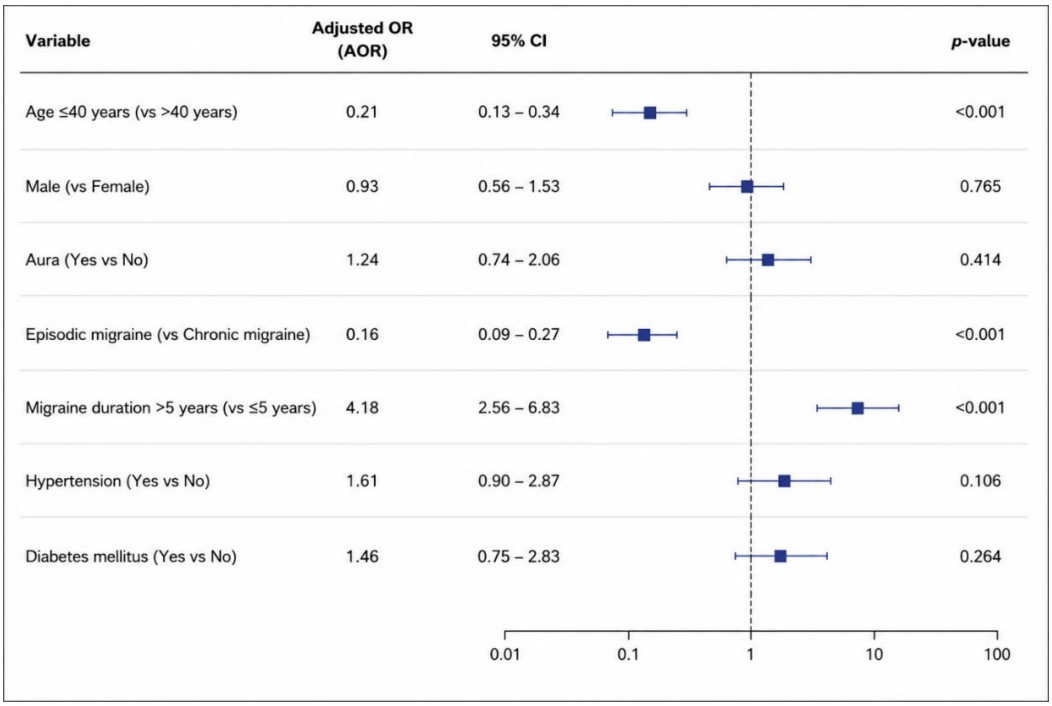

Figure 2: Forest plot showing adjusted odds ratios (AORs) with 95% confidence intervals (CIs) for factors associated with white matter hyperintensities (WMHs) based on multivariable binary logistic regression analysis. Age greater than 40 years, chronic migraine, and migraine duration exceeding five years were identified as significant independent predictors of WMHs.

Results

A total of 400 patients diagnosed with migraine were included in the study. The mean age of the participants was 34.6 ± 9.8 years. Females constituted the majority of the study population (65.5%), while males accounted for 34.5% (Table 1).

Table 1: Demographic Characteristics of Patients (n = 400)

Variable	Frequency (n)	Percentage (%)
Age ≤ 40 years	248	62.0
Age > 40 years	152	38.0
Male	138	34.5
Female	262	65.5

White matter hyperintensities (WMHs) were identified in **248 (62.0%)** patients, whereas **152 (38.0%)** patients had no WMHs on MRI (Figure 3).

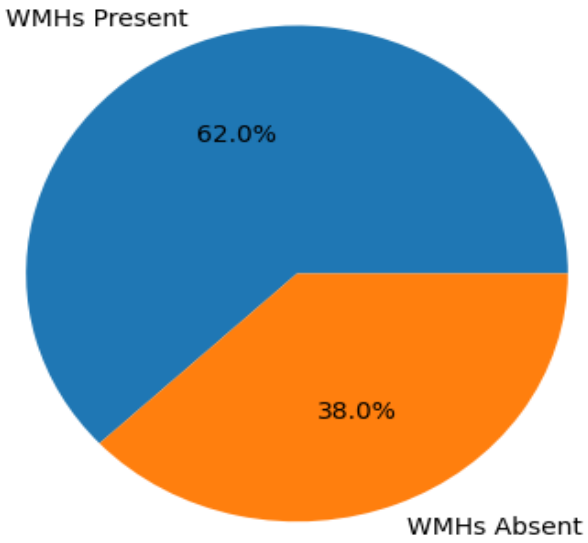

Figure 3: Frequency of White Matter Hyperintensities in Migraine Patients

Among patients with WMHs, most lesions measured less than 3 mm (73.4%). The frontal lobe was the most frequently involved region (91.9%), followed by the deep white matter (70.2%), parietal lobe (41.1%), periventricular region (38.7%), temporal lobe (23.4%), and

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occipital lobe (7.3%). The predominance of frontal and deep white matter involvement indicates that these regions are particularly susceptible to migraine-related structural changes (Table 2, Figure 4).

Table 2: Characteristics of WMHs (n = 248)

Feature	Frequency (n)	Percentage (%)
<3 mm	182	73.4
≥3 mm	66	26.6
Frontal lobe	228	91.9
Parietal lobe	102	41.1
Temporal lobe	58	23.4
Occipital lobe	18	7.3
Periventricular	96	38.7
Deep white matter	174	70.2

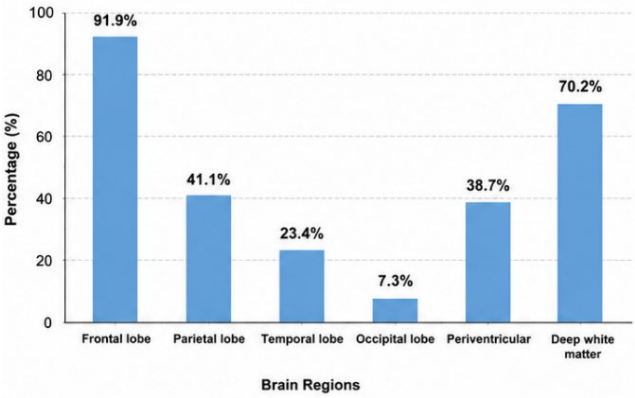

Figure 4: Distribution of WMHs Across Different Brain Regions

Assessment of lesion severity using the **Fazekas scale** showed that most patients had **Grade 1** lesions (**44.0%**), followed by **Grade 2 (14.5%)** and **Grade 3 (3.5%)**, while **38.0%** of patients had no white matter lesions (Grade 0) (**Table 3, Figure 5**).

Table 3: Fazekas Scale Distribution (n = 400)

Fazekas Grade	Frequency (n)	Percentage (%)
Grade 0	152	38.0
Grade 1	176	44.0
Grade 2	58	14.5
Grade 3	14	3.5

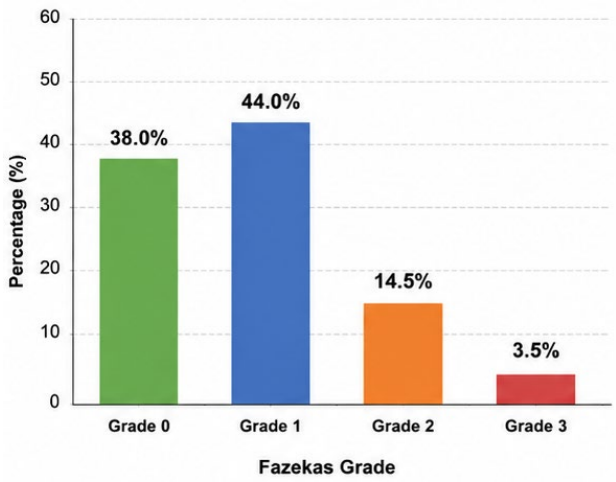

Figure 5: Severity of WMHs Based on Fazekas Scale

The association between WMHs and clinical variables is presented in Table 4. WMHs were significantly more frequent among patients aged >40 years (78.4% vs. 54.2%; p<0.001), those with chronic migraine (72.5% vs. 58.1%; p=0.01), and those with a migraine duration >5 years (69.3% vs. 52.6%; p=0.003). No statistically significant association was observed between WMHs and gender (p=0.18) or migraine aura status (p=0.27). Representative MRI images demonstrating different grades and distribution of WMHs are shown in Figure 5.

Table 4: Association of White Matter Hyperintensities (WMHs) with Clinical Variables

Variable	WMHs Present n (%)	WMHs Absent n (%)	*p*-value
Age			**<0.001**
≤40 years	134 (54.2)	114 (45.8)	
>40 years	119 (78.4)	33 (21.6)	
Gender			**0.18**
Male	80 (58.0)	58 (42.0)	
Female	168 (64.1)	94 (35.9)	
Migraine aura			**0.27**
With aura	93 (66.1)	47 (33.9)	
Without aura	155 (60.1)	105 (39.9)	
Migraine type			**0.01**
Episodic	147 (58.1)	106 (41.9)	
Chronic	101 (72.5)	38 (27.5)	
Migraine duration			**0.003**
≤5 years	110 (52.6)	99 (47.4)	
>5 years	138 (69.3)	61 (30.7)	

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Footnote: Data are presented as number (percentage). Associations between categorical variables were assessed using the Chi-square test. A *p*-value <0.05 was considered statistically significant.

Binary logistic regression analysis was performed to identify independent predictors of white matter hyperintensities (WMHs). After adjustment for gender, aura, hypertension, and diabetes, patients aged >40 years had significantly higher odds of WMHs than younger patients (AOR for ≤40 vs >40 = 0.21, 95% CI: 0.13–0.34; p<0.001). Chronic migraine was independently associated with WMHs, whereas patients with episodic migraine had significantly lower odds of WMHs (AOR = 0.16, 95% CI: 0.09–0.27; p<0.001). Migraine duration >5 years was also an independent predictor of WMHs (AOR = 4.18, 95% CI: 2.56–6.83; p<0.001). Gender (p=0.765), migraine aura (p=0.414), hypertension (p=0.106), and diabetes mellitus (p=0.264) were not independently associated with WMHs (Table 5).

Table 5: Multivariable Binary Logistic Regression Analysis of Factors Associated with White Matter Hyperintensities (WMHs)

Variable	Adjusted OR	95% CI	p-value
Age ≤40 years (vs >40 years)	0.21	0.13–0.34	<0.001
Male (vs Female)	0.93	0.56–1.53	0.765
Aura (Yes vs No)	1.24	0.74–2.06	0.414
Episodic migraine (vs Chronic migraine)	0.16	0.09–0.27	<0.001
Migraine duration >5 years (vs ≤5 years)	4.18	2.56–6.83	<0.001
Hypertension (Yes vs No)	1.61	0.90–2.87	0.106
Diabetes mellitus (Yes vs No)	1.46	0.75–2.83	0.264

OR: Odds ratio; **CI:** Confidence interval. Outcome variable: Presence of white matter hyperintensities (WMHs). Variables with **p < 0.05** were considered statistically significant.

The adjusted odds ratios and corresponding 95% confidence intervals derived from the multivariable binary logistic regression analysis are illustrated in Figure 2.

Discussion

This study evaluated the frequency and radiological characteristics of white matter hyperintensities (WMHs) in patients with migraine using MRI. The results showed the presence of WMHs in 62% of patients. This frequency is similar to the prevalence reported by (5) who found WMHs in approximately 63.9% of migraine patients. Similar frequencies have been also reported in several international studies suggesting that WMHs are a common neuroimaging finding in migraine patients (3,5). Recent studies have also confirmed that WMHs are frequently detected in migraine patients using modern MRI techniques supporting the reliability of the present findings (15). The consistency of these findings supports the reliability of the present results and indicates that migraine is associated with structural changes in the cerebral white matter.

An important finding in this study was the significant association between increasing age and the presence of WMHs. Patients older than 40 years showed a higher frequency of lesions compared with younger patients. Similar observations have been reported by several investigators who found that advancing age is an independent predictor of white matter abnormalities in migraine patients (7,8). Age-related vascular changes, endothelial dysfunction, and cumulative exposure to migraine-related ischemic events may contribute to the development of these lesions over time (6,7). Recent evidence also suggests that age-related impairment of cerebral small vessels and reduced vascular repair mechanisms may increase

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susceptibility to white matter injury in patients with migraine (16). Repeated episodes of altered cerebral blood flow may result in subtle injury to white matter, leading to the appearance of hyperintense lesions on MRI.

Although WMHs were slightly more common among female patients, the difference was not statistically significant. Migraine itself is more prevalent in women because of hormonal influences and genetic susceptibility (1,2). However, previous studies have also reported that gender alone may not be a strong determinant of WMH development once migraine has occurred (5). Similar findings in the present study suggest that factors such as age, disease duration, and attack frequency may have a greater influence on lesion formation than gender.

The relationship between migraine subtype and WMHs remains controversial. In the present study, no significant difference was found between migraine with aura and migraine without aura. Some studies and meta-analyses have shown a stronger association of migraine with aura and white matter lesions, suggesting that cortical spreading depression and transient cerebral hypoperfusion may be more pronounced in patients with aura (11). Other investigators, however, have demonstrated no significant difference between the migraine subtypes, which is consistent with the present study (12,13). More recent studies have also suggested that factors such as disease burden and vascular risk profile may play a greater role than aura status in the development of WMHs (17). These conflicting findings indicate that aura alone may not be a reliable predictor of white matter abnormalities and that other contributing factors may be involved.

Migraine severity seemed to play an important role in the development of WMHs. Patients with chronic migraine showed a higher lesion frequency compared to patients with episodic migraine. Similar findings have been reported in previous studies where a higher headache burden was associated with increased white matter changes (7,9). Frequent migraine attacks may expose the brain to repeated episodes of neurovascular stress, oxidative injury and transient changes of cerebral perfusion. Over time, these mechanisms may contribute to the accumulation of small ischemic changes within the white matter. Persistent activation of the trigeminovascular system and repeated neuroinflammatory responses have also been proposed as possible mechanisms contributing to white matter injury in chronic migraine (18).

Disease duration was also significantly associated with WMHs in the present study. Patients suffering from migraine for more than five years showed a higher frequency of lesions. Previous studies have similarly demonstrated that prolonged migraine history increases the likelihood of detecting WMHs on MRI (6,7). This finding supports the hypothesis that cumulative exposure to migraine-related patho physiological mechanisms, including cortical spreading depression, endothelial dysfunction, inflammatory processes, and recurrent hypoperfusion, may contribute to gradual white matter injury. Recent longitudinal studies have further suggested that prolonged disease duration may increase the cumulative burden of structural brain changes in migraine patients (19).

In the present study, binary logistic regression analysis was performed to identify independent predictors of white matter hyperintensities (WMHs). After adjusting for

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potential confounding variables, age greater than 40 years, chronic migraine, and migraine duration of more than five years remained significant independent predictors of WMHs. Patients with chronic migraine and longer disease duration had significantly higher chances to develop WMHs, whereas gender, migraine aura, hypertension and diabetes mellitus were not independently associated with WMHs. Our findings suggest that the appearance of WMHs is more closely related to age and cumulative migraine burden than to demographic features or common vascular comorbidities. The multivariable analysis further strengthens the observed associations and supports the hypothesis that prolonged exposure to recurrent migraine attacks may contribute to structural white matter alterations detectable on MRI.

Most lesions identified in the present study were located in the frontal lobe and deep white matter regions. Similar distributions have been reported by (5,9), which found that frontal and subcortical white matter are the most commonly affected areas in migraine patients. The frontal region may be particularly vulnerable because of its vascular supply and susceptibility to repeated fluctuations in cerebral blood flow (20,21,22). Most lesions were also <3 mm in size indicating the majority represented mild structural changes rather than extensive brain injury.

The Fazekas scale assessment showed that most lesions were in Grade 1, with only a small number of patients with moderate or severe lesions. Similar results have been reported in previous studies, in which WMHs were mainly mild and clinically asymptomatic (9,13). Recently, MRI-based studies demonstrated that most WMHs related to migraine are punctate, non-confluent lesions that correspond to lower Fazekas grades, supporting the results of this study (21). These results suggest that, although WMHs are common in migraine patients, they are generally limited in extent and may not always indicate significant neurological deficit.

The clinical relevance of WMHs is still not clear. Some authors have proposed that these lesions may be related to cognitive decline, impaired information processing, and increased risk of future cerebrovascular events (9,10). Other studies, however, have found little evidence of clinically significant neurological impairment and have proposed that WMHs may represent incidental radiological findings in many migraine patients (13). More recent evidence indicates that the prognostic significance of these lesions remains uncertain and requires long-term prospective follow-up before definite conclusions can be drawn (23). The present study was not designed to assess long-term neurological outcomes; therefore, the functional significance of these lesions could not be determined.

Conclusion

This study demonstrated that white matter hyperintensities (WMHs) are common MRI findings in patients with migraine and were present in 62% of the study population. Multivariable binary logistic regression analysis again identified older age, chronic migraine and migraine duration of more than 5 years as independent predictors of WMHs. The majority of lesions were small, mild in severity and mainly located in frontal and deep white matter regions. While the clinical significance of these lesions remains unclear, awareness of their characteristic pattern may assist in the interpretation of MRI findings in migraine patients and support clinicians in making informed decisions in the diagnostic

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process. Further longitudinal studies are recommended to determine the long-term clinical implications of WMHs in patients with migraine.

Strength of the Study

A major strength of this study is that it provides local data from Pakistan, where limited information is available regarding MRI findings in migraine patients. The relatively large sample size also improves the reliability of the findings.

Limitations

There are several limitations to this study. First, because of the cross-sectional study design, causal relationships and progression of white matter hyperintensities over time could not be determined. Second, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings. Third, advanced neuroimaging techniques and detailed assessment of cognitive function were not performed. Finally, although major neurological disorders were excluded, residual vascular risk factors may still have influenced the MRI findings. In addition, residual confounding from unmeasured variables cannot be excluded despite multivariable adjustment.

Recommendations

Further studies are recommended to better understand the clinical importance of WMHs in migraine patients. Future longitudinal studies are needed to determine whether these lesions evolve over time or are associated with cognitive decline or increased risk of stroke. Multi-center studies with larger and more diverse populations would help to improve the generalizability of findings. Additionally, future research should investigate the role of advanced imaging techniques and biomarkers to better understand the underlying mechanisms of WMHs in migraine.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding this study.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	