Head & Face Medicine

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Migraine and MRI: uncovering potential associations

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Abstract

Objective This study aims to investigate the association between patients with migraine headaches and brain magnetic resonance imaging (MRI) findings.

Background Migraine is a frequently encountered primary headache disorder with a disproportionate female predominance. Diagnosis is usually based on the patient's clinical history with neuroimaging reserved for severe or atypical presentations to exclude other pathologies. Migraine patients often experience a profound impact on their quality of life.

Methods A retrospective study was conducted at King Abdullah University Hospital, Jordan, involving patients with a clinical diagnosis of migraine who had undergone MRI brain imaging between January 2021 to March 2023. Descriptive data were documented, with two independent neuro-radiologists interpreting MRI findings.

Results Our study included 670 migraine patients (510 females; mean age, 40.3 years). White matter hyperintensity lesions were found in 309 patients (46.1%), significantly affecting older age groups with a mean age of 46.8 years ($p > 0.001$). Additionally, gender played a role, with a higher prevalence of these lesions in female migraine patients, accounting for 79.6% ($p = 0.05$). Multiple logistic regression analysis proved age to be an independent risk factor for the presence of white matter hyperintensity lesions (OR: 1.0688, 95% CI: 1.0546–1.0831, $p > 0.001$).

Conclusion White matter hyperintensity lesions were seen in the MRI imaging of a subset of migraine patients. Patients with these lesions tend to be older and of female gender. However, the clinical significance of these findings remains unclear.

Keywords Headache, Migraine, Neuroimaging, MRI

Introduction

Migraine, a prevalent debilitating primary headache disorder, typically affects women at twice the rate of men [1]. It is characterized by recurrent, asymmetric, pulsating headaches that can last anywhere from 4 to 72 h and are often accompanied by symptoms such as nausea, photophobia, phonophobia, and autonomic nervous system dysfunction [2]. Migraine is categorized into two main types: migraine with aura, also known as classic migraine, which is characterized by one or more reversible neurological symptoms that precede the episode and usually affect vision, sensation, speech and movement

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[3]; and migraine without aura commonly referred to as common migraine, which occurs without these preceding neurological disturbances [4]. Other classification for Migraine is based on its frequency and severity, specifically the number of monthly migraine days (MMDs) [5]. Patients who experience headaches on at least 15 days per month with at least 8 of those days meeting the diagnostic criteria of migraine are known to have Chronic Migraine. In contrast, Episodic Migraine is defined as experiencing fewer than 15 headaches per month [6].

Approximately one in three migraine patients may experience transient focal neurological symptoms, with a smaller subset suffering from a more severe form, in which migraine attacks transform into persistent daily headaches; Emerging evidence suggests that repeated headache episodes may lead to long-term changes in the central nervous system (CNS) [7]. The diagnosis of migraine is typically made using the International Headache Society's diagnostic criteria with little emphasis on neuro-imaging [8]. Appropriateness Criteria of the American College of Radiology (ACR) does not advise the routine use of neuroimaging in the evaluation of adults with migraine headaches [9]. However, in cases of atypical clinical presentations, the presence of red flags, or abnormal neurological examinations, neuroimaging techniques such as MRI and CT scans, along with other diagnostic procedures, may be warranted to rule out secondary headaches [8]. Data regarding their respective sensitivity in non-acute headache cases are currently insufficient.

MRI stands out over CT scan in the evaluation of brain Parenchymal lesion [10], due to its superior resolution, discrimination, and advanced sequences such as T1-weighted images, T2/fluid-attenuated inversion recovery (FLAIR), susceptibility-weighted imaging (SWI) or other T2*-weighted sequences [11], making it a promising imaging technique for chronic headaches while also avoiding the radiation associated with CT scans [12]. It is common to detect nonspecific white matter lesions in the brain of migraine patients through MRI; however, it has not been demonstrated that the severity of symptoms, management, or prognosis of the condition is influenced by these findings [13].

The primary objective of this study is to comprehensively evaluate and understand MRI findings in migraine patients and to correlate them with age and gender. This research aims to contribute to the development of improved diagnostic and therapeutic strategies for individuals impacted by this condition.

Patients and methods

A retrospective study was conducted at King Abdullah University Hospital, Ramtha, Jordan between January 2021 to March 2023. The study protocol was approved by the Institutional Review Board at King Abdullah University Hospital (KAUH), Jordan.

Participants

Patients with a clinical diagnosis of migraine headaches and normal neurological evaluation who had undergone MRI brain imaging were enrolled in our study. Primary headaches other than migraine, headaches caused by other underlying conditions (secondary headaches), those with a history of neurological surgery, and patients with intracranial masses were excluded from our study.

Imaging acquisition and evaluation

Axial lumbar MRI scans were acquired using 3T MRI scanner (Philips) with both T1-weighted and T2-weighted sequences to assess brain morphology and any associated pathology. Specific imaging parameters included slice thickness [4 mm], FOV [68.6 × 28.3 cm], TR [2525.68 ms], and TE [120 ms]. Assessment of the MRI images was done independently by two board-certified neuro-radiologists (K.A and K.Z.A), any discrepancies were resolved after a thorough discussion amongst them. MRI findings were classified into two categories: normal and abnormal white matter hyperintensity lesions. The presence of any other incidental parenchymal abnormalities observed on MRI and whether patients were admitted due to migraine were also recorded. Patient's demographics including age and gender were reviewed.

Statistical analysis

Jamovi 2.3.28 was used to analyze our data. For descriptive statistics, frequencies, mean (measures of central tendency), and standard deviation (measures of dispersion) were utilized for metric variables, while percentages were used for categorical variables. Our numerical data was found to be non-parametric using Shapiro-Wilk test thus Mann-Whitney U test was used. Chi-square test was used to analyze our qualitative data, and multiple logistic regression was employed to control for potential confounding factors. Statistical significance was considered with p-value < 0.05.

Results

Table 1 presents an overview of patients' characteristics. A total of 670 migraine patients were enrolled in this study with a mean age of 40.3 years (SD, 14.5), there was a notable female predominance with a total of 510 patients (76.1%).

White matter hyperintensity lesions on T2/Flair MRI were noticed in 309 migraine patients (46.1%) with the remaining patients not showing any significant findings ($n = 361$ (53.9%)). Migraine patients who exhibited white matter hyperintensity lesions were observed to significantly affect older age groups with a mean age of 46.8

Table 1 Baseline characteristics of participants ($n=670$)

Variable	Value
Age in years	
Mean	40.3
Median	41.0
SD	14.5
Gender, *n* (%)	
Male	160 (23.9)
Female	510 (76.1)
White matter findings on T2/Flair, *n* (%)	
Hyperintensity lesions	309 (46.1)
None	361 (53.9)

n = number, SD = standard deviation.

Table 2 Relation between white matter hyperintensity lesions in MRI and gender, age

Variable	White matter lesions on T2/FLAIR images		*P* value
	abnormal high T2/FLAIR foci	None	
Age in years			**> .001***
Mean	46.8	34.7	
Median	47.0	33.0	
SD	13.6	13.0	
IQR	39.0–55.0	24.0–45.0	
Gender, *n* (%)			**.05***
Male	63 (20.4)	97 (26.9)	
Female	246 (79.6)	264 (73.1)	
Total	309	361	

p values for Mann Whitney test *(Age)*

p values for chi-square test *(Gender)*

*Statistically significant at $p \leq 0.05$

Table 3 Frequencies of any other parenchymal abnormalities in MRI

Any other parenchymal abnormalities	*N* (%)
None	573 (85.5)
Arachnoid cyst	21 (3.1)
Brain atrophy inappropriate for patient's age.	5 (0.7)
Chronic ischemic changes	13 (1.9)
Cyst	5 (0.7)
DVA	8 (1.2)
Empty sella turcica	5 (0.7)
Infarction	5 (0.7)
Meningioma	11 (1.6)
Cavernoma	3 (0.4)
Others	21 (3.1)

years. In contrast, patients with no imaging findings were typically younger with a mean age of 34.7 years Fig. 1. Patients gender also played a significant role in the presence of white matter foci in which females displayed a higher number of cases ($n=246$) accounting for 79.6% of the total number of patients with abnormal imaging foci Table 2.

Multivariate logistic regression was conducted with the aim of eliminating confounding factors Table 4. Age was found to be an independent risk factor for white matter hyperintensity lesions (OR: 1.0688, 95% CI: 1.0546–1.0831, $p=>0.001$) while gender was found to be insignificant (OR: 1.1283, 95% CI: 0.7537–1.6893, $p=0.558$). Table 3 summarizes the frequencies of various other parenchymal abnormalities seen in the patient's MRI such as cysts, brain infarcts, and masses (e.g., cavernoma, meningioma). Migraine-related admissions to the hospital were minimal with most patients being discharged Fig. 1.

Discussion

Headache is one of the most prevalent conditions for which adult patients seek medical attention [14]. Approximately 12% of the population is diagnosed with migraine [15] with a higher prevalence in females across all age groups [16]. Migraine and tension-type headache predominate as common causes of headache in children [17, 18].

There are major concerns over the long-term effects of migraine on brain health due to its great prevalence and the substantial burden it creates on both individuals

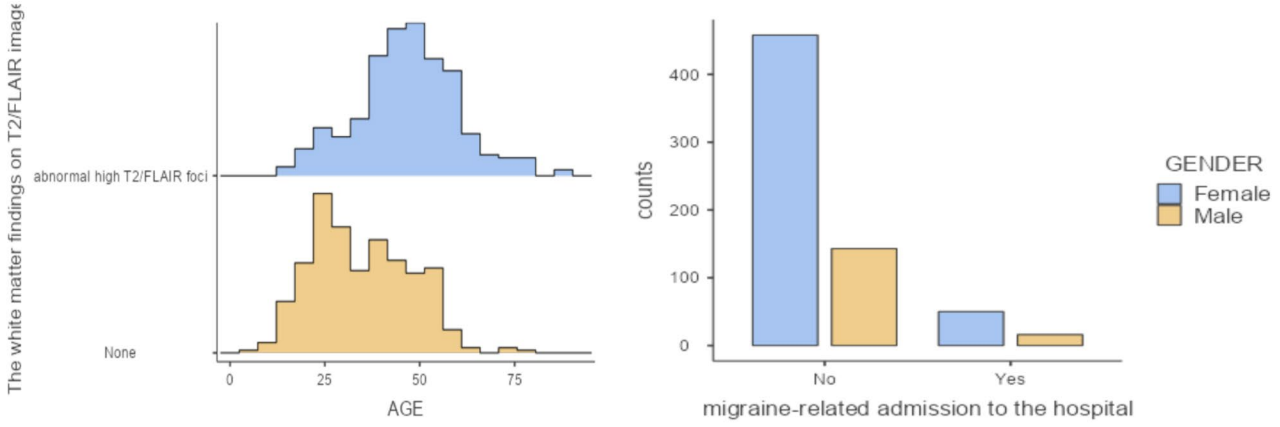

Fig. 1 Distribution of MRI findings with age and migraine-related admissions

Table 4 Predictors of white matter hyperintensity lesions in MRI by multiple logistic regression

Predictor	Odds ratio (OR)	95% Confidence Interval		*P* value
		Lower	*Upper*	
Age	1.0688	1.0546	1.0831	**> .001***
Gender:				
Female-Male	1.1283	0.7537	1.6893	.558

*Statistically significant at $p \leq 0.05$

and healthcare systems [19]. The neurological effects of migraine have drawn more attention as our knowledge of the condition grows. The correlation between migraine and white matter hyperintensity (WMHI) lesions, which has been noted in numerous studies [20–22], is one of the main issues. These lesions are thought to be markers of chronic migraine, with potential implications for cognitive function and other neurological outcomes [23, 24].

Migraine is a well-established cause of WMHI lesions, with a meta-analysis by Swartz and Kern et al. showing a four-fold increased risk of white matter injury in migraineurs [25]. WMHI lesions in migraine patients are a sign of chronification [26] thus longer duration and higher frequency of the headaches are associated with increased numbers of WMHI lesions [27].

Some studies explored the potential origin of these white matter lesions in migraine patients. One theory suggests an ischemic origin, with the blood vasculature initially undergoing vasoconstriction with signs of cerebral ischemia during migraine attacks, followed by vasodilation leading to the characteristic throbbing headache [28]. We found 13 patients with chronic ischemic changes, accounting for 1.9% of the total patients. However, the clinical significance of these lesions remains unclear [29]. Another study suggests that high blood pressure is significantly associated with increased risk of WMHI lesions [30]. Other factors have been thought to play a role in the pathogenesis of these lesions which include dysfunction of the mitochondria [31], endothelial instability [32], immune-mediated white matter demyelination [33], dyslipidemia, smoking [34], "glutamatergic excitotoxicity" [35],and drugs with vasoactive characteristics [36].

In contrast to Alturkustania [37] et al.'s 57.1% report, our analysis identified 309 (46.1%) migraine patients with aberrant MRI findings. This disparity could result from variations in sample size, ethnicity, and environmental circumstances. Alturkustania et al.'s study may have had more statistical power with a bigger sample size, and differences in WMHI prevalence may have been explained by ethnic and environmental factors, including lifestyle differences and genetic predispositions. Larger, multicenter, or longitudinal studies should be used in future research to examine these parameters in greater detail and elucidate their involvement in WMHI lesions in migraineurs. Notably, in our study, migraine patients were mostly females accounting for 76.1% which is consistent across the literature [20, 38]. Kruit et al. observed that female migraineurs face a higher risk of developing high numbers of WMHI lesions, particularly in the deep white matter [38].

Additionally, we observed that migraine patients with white matter hyperintensity lesions were found to significantly affect older age groups (mean age, 46.8), which aligns with the findings reported by Alturkustania et al., who observed abnormal MRI imaging in patients > 40 years of age [37]. In our study, incidental findings such as arachnoid cysts, meningiomas, and cavernomas were reported in 3.1%, 1.6%, and 0.4% of patients, respectively. These findings, although less common, may have clinical relevance in understanding the broader spectrum of structural brain abnormalities in migraine patients. Similar rates were reported by Alturkustania et al., with 2.9%, 1.4%, and 0.7%, respectively. While these incidental findings are not directly linked to the presence of WMHI lesions, their occurrence in migraine patients may warrant further investigation to determine if there is any association with disease severity or other clinical factors [37].

More research is necessary to fully understand the clinical consequences of the correlation between white matter hyperintensity (WMHI) lesions and migraine. WMHI lesions may indicate more than just a chronic migraine marker, albeit the precise connection between these lesions and migraine is yet unclear. When these lesions are found in migraine patients, clinical practitioners may decide to examine them more closely for any long-term neurological effects, such as cognitive deterioration or the emergence of other neurological or vascular conditions. WMHI lesions could be used as a predictor of migraine progression or treatment response if more study confirms a causal relationship. Long-term patient outcomes may be enhanced by more focused therapy approaches that are based on an understanding of the pathophysiology of these injuries, possibly emphasizing neuroprotection or vascular health.

This study, while contributing valuable insights into the relationship between migraine and MRI-detected white matter hyperintensity (WMHI) lesions, presents certain limitations that warrant consideration. The retrospective design limits the ability to establish causation, with potential biases from reliance on pre-existing medical records and selection bias for patients who underwent MRI. Being a single-center study, our findings may not be generalizable to broader populations due to demographic and regional variations. The predominance of female patients (76.1%) reflects epidemiological trends but restricts gender-specific analysis, and the sample size and

age distribution may not fully represent all migraineurs. Additionally, the study lacked robust clinical correlation, focusing solely on identifying WMHI lesions without assessing their impact on migraine characteristics or treatment outcomes. The cross-sectional nature precludes understanding the progression of WMHI lesions or their role in chronic migraine. Confounding factors such as hypertension, diabetes, smoking, obesity, physical inactivity, and the use of vasoactive medications were not fully accounted for, limiting etiological conclusions. While two neuroradiologists independently interpreted the MRIs, interobserver variability and lack of standardized assessment criteria may affect reliability. Incidental findings like arachnoid cysts and meningiomas were noted but not explored for clinical relevance. Ethnic and environmental factors, as well as variations in MRI protocols, further limit generalizability. To address these issues, future multicenter, longitudinal studies with diverse populations and comprehensive clinical evaluations are needed to better understand WMHI lesions and their implications for migraine patients.

Conclusion

Our study adds valuable insights to migraine and its association with neuroimaging findings, primarily focusing on MRI-detected white matter hyperintensity lesions. These lesions were identified in a substantial proportion of our migraine patient cohort, indicating their relevance to the condition. Our study's findings are anticipated to make significant contributions to the ongoing exploration of migraine prognosis, treatment strategies, and broader clinical implications. A notable correlation emerged between these lesions and patient age, underlining the potential age-related aspects of migraine and its structural brain changes. Although gender did not appear to be a significant influencing factor in lesion presence, other contributing elements may warrant further exploration.

Author contributions

Conceptualization, K.A. and K.Al. ,; methodology, K.A and K.Al; investigation, M.B and A.A; data curation, M.B and A.A; writing—original draft preparation, M.B and A.A writing—review and editing, K.A, M.B, A.A; supervision, K.A and K.Al; funding acquisition, N/A. All authors have read and agreed to the published version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors declare no conflict of interest.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board of Jordan University of Science and Technology. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

Informed consent

Statement: Informed consent was obtained from all individual participants included in the study. Participants were fully informed about the purpose of the research, the procedures involved, potential risks and benefits, and their rights to withdraw from the study at any time without any consequences. The confidentiality and anonymity of all participants were maintained throughout the study.

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