

**WHITE MATTER HYPER INTENSITIES IN MIGRAINE PATIENTS
OF ALHADA ARMED FORCES HOSPITAL,
TAIF CITY.****Faisal A Althobaiti¹, Abdulrahman A Althobaiti², Maad S Altalhi³, Naif E Alomairi⁴,
Yahea A Alzahrani⁵**Neurology Resident, Department of Neurology, King Fahad General Hospital, Jeddah,
Saudi Arabia.¹Neurology Resident, Department of Neurology, King Abdulaziz Medical City, Jeddah,
Saudi Arabia..²Medical Resident, Department of Medicine, King Abdullah Medical Complex, Jeddah,
Saudi Arabia. .³Assistant Professor and Neurology Consultant, Department of Neurology, Al-Hada Armed Forces
Hospital, Taif, Saudi Arabia..⁴Assistant Professor of Radiology, Consultant of Radiology, college of Medicine,
Taif University, Saudi Arabia.⁵**Article Received:** November 2019 **Accepted:** December 2019 **Published:** January 2020**Abstract:****Introduction:** Migraines are regarded as a common neurologic disease typically characterized by recurrent attacks of severe headaches. Some data have shown a link between migraine diagnosis and presence of white matter hyperintensities in MRI results. However, it remains unclear among the Arab population.**Objective:** The goal of this study is to find the correlation between diagnosis and frequency of migraine attacks besides durations, severity and gender to the presence of white matter hyperintensities in MRI results.**Methods:** The study included two steps. The first step was a survey for an outpatient neurology clinic in Al Hada hospital from the beginning of November 2018 till the end of January 2019. The second step included recording the MRI results of the participants and classifying the presence of white matter hyperintensities using Wahlund classifications for white matter lesions.**Results:** A total of 34 patients were included, and 52.9% had white matter hyperintensity in their MRI. White matter hyperintensity is positively and significantly correlated with age ($p=0.007$) and negatively correlated with head trauma ($p=0.024$). Also, it is clinically correlated with smoking, frequency of headache and tension character of headache.**Conclusion:** white matter hyperintensities in migraine patients are correlated with different clinical features and comorbidities. Further studies focusing on the clinical significance of the presence of white matter hyperintensities in migraine patients are required.**Keywords:** Migraine, White matter, hyperintensity, Saudi Arabia**Corresponding author:****Yahea A Alzahrani,**Assistant Professor of Radiology,
Consultant of Radiology, college of Medicine,
Taif University, Saudi Arabia.

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INTRODUCTION:

Migraines are considered a common neurological disease. In developed countries, the incidence of migraines is up to 20% of the population ¹. Migraines with aura are regarded as a risk factor for ischemic stroke, especially in women. Furthermore, the risk of a migraine is greater in females aged less than 45 years ², and this could be partially due to hormonal factors ³.

Additionally, brain white matter hyperintensities (WMHs) detected by magnetic resonance imaging (MRI) have been found to be present with different neurological diseases such as multiple sclerosis, ischemia and migraine ⁴.

Moreover, some trials showed that females diagnosed with migraines had a significantly higher risk of WMH in their brain compared to males, regardless of migraine subtype or cardiovascular risk factors ⁵. The link between migraines and vascular disorders may be due to the higher incidence of multiple risk factors in patients diagnosed with migraines ⁶. Furthermore, subclinical infarctions were found to be more prevalent in the posterior circulation territory in migraine patients compared with normal persons ^{7,8}. Despite the available data on the link between migraines and WMHs, information is still unclear and scant in some areas ⁹. For instance, the correlation between WMHs and migraines and different races has not been identified, especially in Asians and Arab races ¹⁰. Also, the link between WMHs and the frequency of migraine has not been discussed in the literature ¹¹.

Therefore, this study aims to investigate the correlation between WMHs detected by MRI and frequency of migraine in a Saudi population in the city of Taif.

Materials and Methods:

The design of the study is a retrospective cohort study that was carried out in the neurology clinic at Al-Hada Armed Forces hospital, Taif, Saudi Arabia from the beginning of November 2018 to the end of January 2019. The study included patients from both

genders aged between 18 and 60 years old who were diagnosed with migraines based on guidelines of the American Academy of Neurology and who underwent an MRI after diagnosis.

Patients with other types of headaches, existing neurological disease and those who did not have a brain MRI were excluded.

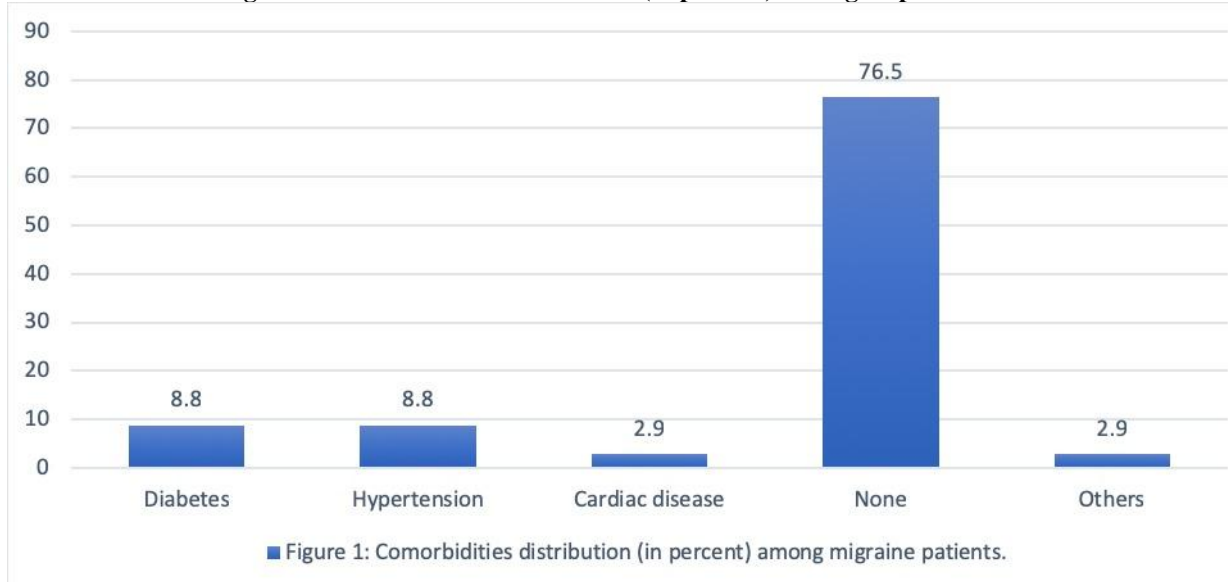
Data collection was done in two steps, The first was a self-administered questionnaire was distributed to patients in the neurology clinic. The used questionnaire was from Cleveland Clinic Canada and Migraine Relief Center and was translated into Arabic. The questionnaire included questions on comorbidities, the presence of aura, different symptoms and any medications.

Secondly, The MRI results of the surveyed patients were recorded, and the findings were classified according to the Wahlund classification for white matter lesions.

Statistical analysis Consisted of recording data in a pre-designed and validated Excel spreadsheet. Data were represented in terms of frequencies and valid percentages for categorical variables. Correlations were calculated using a chi-square test for categorical variables, and significance was denoted when $p\text{-value} < 0.05$. Data was further analyzed using IBM SPSS version 21 (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) to perform all statistical calculations.

RESULTS:

Between November 2018 to January 2019, a total of 34 patients were included in this study as they were diagnosed with migraine headache. The mean age of the patients was 40 ± 13 and 88,2 % of the cohort was comprised of females. All of the responders' demographic data are detailed in (Table 1). It was also observed that 76.5% of the participants did not have any comorbidities, while diabetes and hypertension were the most prevalent comorbidity in those who had comorbidities (8.8%). (Figure 1) shows the distribution of comorbidities among the whole cohort.

Figure 1: Comorbidities distribution (in percent) among responders.**Table 1: Demographic data of participants**

	Frequency	Percent
Gender		
Male	4	11.8
Female	30	88.2
Age Groups		
18-20	5	14.7
21-30	4	11.8
31-40	8	23.5
41-50	9	26.5
51-60	8	23.5
Marital Status		
Single	9	26.5
Married	25	73.5
Educational Level		
Below the high school	16	47.1
High school	7	20.6
Bachelor degree	11	32.4

Almost half of the responders (44.1%) had previous surgery. Additionally, 11.8% had previous head trauma. Family history was also investigated. 32.4% of participants had family history of migraine, while 17.6 % had family history of neurological disorder. Epilepsy was the most common neurological disorder recorded within family history (8.8%). Turning to smoking habits, 79.4% of responders reported that they were non-smokers, while one participant (2.9%) was a smoker (Table 2).

Table 2: Medical history of participants

	Frequency	Percent
Previous surgery		
Yes	15	44.1
No	19	55.9
Type of previous surgery		
No previous surgery	19	55.9
Cholecystectomy	5	14.7
CS	8	23.5
Tonsillectomy	2	5.8
Previous head trauma		
Yes	4	11.8
No	30	88.2
Family history of migraine		
Yes	11	32.4
No	23	67.6
Family history of neurological disease		
Epilepsy	3	8.8
Brain tumor	2	5.9
None	28	82.4
Multiple Sclerosis	1	2.9
Smoking		
Smoking	1	2.9
No smoking	27	79.4
Passive smoking	6	17.6

Frequency of migraines was categorized into daily, weekly and monthly categories. 52.9% of the participants had monthly migraine attacks. As for the duration of headache, 41.2% of responders described their headaches to remain for days without medications, while on medications, only 14.7% had headaches for days. Regarding the severity of headaches, it was described to be severe in spite of medications in 17.6% of responders, while 91.2% of responders had severe headaches without medications to control them. Moreover, the most common headache site was on both sides in 41.2% of the participants. Finally, 47.1% of the participants described their headache as throbbing pain. (Table 3) shows the description of headache among all of the responders.

Table 3: Description of headache.

	Frequency	Percent
Onset of headache		
sudden	19	55.9
gradual	15	44.1
Duration with medication		
Seconds	1	2.9
Minutes	15	44.1
Hours	13	38.2
Days	5	14.7
Duration without medications		
Minutes	3	8.8
Hours	17	50.0
Days	14	41.2
Severity with medications		
Mild	9	26.5
Moderate	19	55.9
Severe	6	17.6
Severity without medications		
Moderate	3	8.8
Severe	31	91.2
Site of headache		
Right side	10	29.4
Left side	8	23.5
Both sides	14	41.2
Forehead	1	2.9
Back of head	1	2.9
Character of headache		
Tension	10	29.4
Stabbing	4	11.8
Throbbing	16	47.1
Pressure (Tight band)	3	8.8
Dull ache	1	2.9

Regarding the presence of aura migraines, most of the patients did not have symptoms of migraines. On the other hand, mood change was the most commonly reported symptom (38.2%) by symptomatic participants, while runny nose was described as the least common symptom (2.9%).

After examining the MRI findings of the 34 participants, patients were classified according to the Wahlund classification as either having partial leukoaraiosis or not having white matter lesions.

The Wahlund classification has four classification levels: level 0 designates no obvious white matter hyperintensity, level 1 designates partial leukoaraiosis, level 2 designates partial leukoaraiosis that begins to fuse and level 3 designates partial leukoaraiosis that is widely fuse and convergent. In our study, 16 patients were classified as level 0, while 18 patients were classified as level 1.

Following this step, the MRI findings were correlated with different demographic data of the whole cohort as well as the features of their headaches in terms of frequency of headache and medical history using a chi-square test with significance designated as $p < 0.05$.

There was a statistically significant difference between MRI findings and the age group of the patients, where the frequency of WMHs increases with increasing age ($p=0.007$). Surprisingly, patients who had previous head trauma showed a significantly lower frequency of WMHs.

One clinically relevant correlation that did not reach statistical significance is smoking. Smokers had a higher incidence of WMHs in their MRI results. Also, the frequency of headache was increased in patients with WMHs. Finally, patients with tension character of headache showed the highest incidence of WMHs. All correlations are shown in (Table 4).

Table 4: Correlations between the presence of white matter hyperintensities and characteristics of migraine headaches

		No white matter lesions (Level 0)	partial leukoaraiosis (Level 1)	P values
Age groups (years)	<20	5	0	0.007*
	21-30	4	0	
	31-40	2	6	
	41-50	2	7	
Gender	Male	2	2	0.9
	Female	14	16	
Chronic disease	Diabetes	1	2	0.25
	Hypertension	0	3	
	Cardiac disease	1	0	
	None	14	12	
Previous head trauma	Yes	4	0	0.024*
	No	12	18	
Family history of migraine	Yes	6	5	0.545
	No	10	13	
Smoking	Smoking	0	1	0.630
	No Smoking	13	14	
	Passive Smoking	3	3	
Frequency of headache	Daily	5	4	0.835
	Weekly	8	10	
	Monthly	3	4	
Onset	Sudden	10	9	0.464
	Gradual	6	9	
Site of headache	Right side	5	5	0.664
	Left side	3	5	
	Both sides	7	7	
	Forehead	1	0	
Character	Tension	3	7	0.395
	Stabbing	3	1	
	Throbbing	9	7	
	Pressure	1	2	
Headache changes	Menstrual cycle	5	1	0.106
	Contraceptive pills	0	1	
	None	11	16	

*Level of significance at $p < 0.05$

DISCUSSION:

Migraine headaches are considered one of the most common neurological diseases and affect millions of people globally⁵. Migraine symptoms can have debilitating effects that can significantly affect the quality of life of migraine patients^{8,10}.

Recently, some studies have discussed the presence of WMHs detected by MRI in patients with migraines^{3, 6, 8}. Yet, correlations between WMHs and different migraine features remain unclear⁷.

The present work explored the link between the presence of WMHs and some migraine features including the demographics of migraine patients in

addition to migraine frequency, onset, site and character in a Saudi population from the city of Taif.

In this study, white matter hyperintensity is positively and significantly correlated with age ($p=0.007$) and negatively correlated with head trauma ($p=0.024$). Additionally, there were clinically relevant correlations with smoking, frequency of headache and tension headaches, though statistical significance was not achieved due to a small sample size.

Previous studies in the medical literature have evaluated the presence of white matter hyperintensities in migraine patients. Seneviratne *et al.*⁶ examined the clinical and radiological correlates

with migraine diagnoses. The study included 44 migraine patients, 19 having WMHs in the frontal lobe. Seneviratne *et al.*⁶ revealed that there is a positive correlation between the presence of WMHs in migraine patients and age, headache frequency and family history.

The findings of Seneviratne *et al.*⁶ agree with the outcomes of the present work. This study has shown a relevant clinical correlation between WMHs in Saudi patients and migraine frequency; however, statistical significance was not achieved due to the small sample size compared with Seneviratne *et al.*⁶. Also, there was a significant correlation between age and WMHs ($p=0.007$).

Rossato *et al.*¹² performed another larger study that included 185 migraine patients and sought to compare white matter distribution of WMHs to different symptoms of aura. Similar to the outcomes of the current work, Rossato *et al.*¹² discovered that aura symptoms in addition to all clinical migraine features do not correlate with migraine distribution.

In the present study, though, distribution of white matter hyperintensity was not examined; instead, the presence or absence of WMHs was evaluated and found to be uncorrelated with any of the migraine symptoms including aura.

These findings were also supported by Trauninger *et al.*⁴, with the largest sample size compared to all previous studies, including 186 patients to detect risk factors for WMHs in migraine patients. Similar to Seneviratne *et al.*⁶ and the present work, Trauninger *et al.*⁴ found a significant correlation between

WMHs and duration of attacks as well as migraine frequency. Trauninger *et al.*⁴ also found a link between WMHs and thyroid dysfunctions and hyperhomocytinemia, which were not evaluated by the present study.

The present study has some limitations. The small survey sample size is the most important limitation that should be considered when evaluating the outcomes of this study. Also, the study was retrospective and included only a single center; these aspects could also affect the reliability of the results and should be considered.

Finally, to our knowledge, this is the first study to evaluate the correlation between the presence of WMHs and various migraine features in Taif, Saudi Arabia.

CONCLUSION:

White matter hyperintensities are found to be correlated with different clinical features as well as

the medical history of migraine patients. Further studies with larger sample sizes are required to detect more risk factors for this radiological finding. Also, future studies should focus on the clinical relevance of the presence of white matter hyperintensities in migraine patients, since they could serve as a prognostic factor for other neurological disorders and ultimately affect the cognitive functions and quality of life of migraine patients.

Authors' contributions:

Faisal Abdulrahman Althobaiti:
Manuscript Preparation and Literature Search
Maad Saad Altalhi:
Manuscript Preparation and Literature Search
Naif Edah Alomairi:
Study design
Yahea Abdullah Alzahrani:
Data Interpretation and Statistical analysis
Abdulrahman Awadh Althobaiti:
Data Collection and Statistical Analysis

Declaration of interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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