

Original Article

Evaluation of Magnetic Resonance Imaging Outcomes in Patients with Migraine Compared to People without Migraine Referring to Allameh Bohlol Gonabadi Hospital, Gonabad, Iran: A Case-Control Study



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ABSTRACT



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Key words:

Magnetic resonance imaging (MRI)
Migraine
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Aims Headache and migraine disorders are among the most significant problems of the present era, which can lead to severe disabilities in daily activities. The present study was designed and conducted to investigate magnetic resonance imaging (MRI) findings in patients with migraine compared with those without migraine who were referred to Allameh Bohlol Gonabadi Hospital in Gonabad, Iran.

Materials & Methods This study followed a case-control design, examining 25 patients with migraine (case group) and 25 individuals without migraine, selected via convenience sampling from those referred to the Neurology Clinic of Allameh Bohlol Gonabadi Hospital (Gonabad, Iran) in 2022-2023. The data collection tools used in this study included a demographic information checklist, a checklist of diagnostic criteria for migraine and its types, a checklist for assessing migraine severity using the Migraine Severity Scale, and a checklist of MRI symptoms. The data were analyzed using SPSS software (version 26) at a significance level of 5%.

Findings The mean (standard deviation) age of the studied medical staff was 35.34 (12.22) years, and 76% of them were females. In this study, the number of lesions (plaques) in patients with migraine (12 lesions) was significantly higher than in the control group (1 lesion); using the appropriate statistical test, a significant difference was observed between the two groups ($P=0.001$), indicating a statistically significant relationship between the increase in the number of cerebral plaques and migraine. Regarding lesion site, the highest prevalence of plaques in patients with migraine was reported in the parietal lobe (8 lesions), followed by the frontal lobe (3 lesions). However, the difference in plaque distribution across different cerebral lobes between the two groups was not statistically significant ($P=1.00$). Additionally, examination of the tissue type revealed that all lesions observed in both groups were located in the deep white matter of the brain.

Conclusion The number of brain lesions or plaques can provide a better understanding of changes in brain structure and function in patients with migraine and can be helpful not only in diagnosis, but also in selecting treatment and monitoring its effectiveness.

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مقاله پژوهشی

بررسی یافته‌های تصویربرداری تشدید مغناطیسی در بیماران مبتلا به میگرن در مقایسه با افراد بدون میگرن مراجعه کننده به بیمارستان علامه بهلول گنابادی: یک مطالعه مورد شاهد

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چکیده

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هدف: اختلالات سردرد و میگرن یکی از مهم‌ترین معضلات عصر حاضر بوده که می‌تواند منجر به ناتوانی‌های شدید در کارهای روزمره گردد. مطالعه حاضر با هدف بررسی یافته‌های تصویربرداری تشدید مغناطیسی در بیماران مبتلا به میگرن در مقایسه با افراد بدون میگرن مراجعه کننده به بیمارستان علامه بهلول گنابادی طراحی و انجام شد.

مواد و روش‌ها: مطالعه حاضر از نوع مورد شاهد بود که به بررسی ۲۵ بیمار مبتلا به میگرن (گروه مورد) و ۲۵ فرد بدون میگرن که با استفاده از روش نمونه‌گیری در دسترس از بین مراجعه‌کنندگان به کلینیک مغز و اعصاب بیمارستان علامه بهلول گنابادی در سال ۱۴۰۱-۱۴۰۲ انتخاب شدند، پرداخت. ابزار گردآوری داده‌ها در این مطالعه چک لیست اطلاعات دموگرافیک، چک لیست معیارهای تشخیصی برای تعیین میگرن و انواع آن، چک لیست ارزیابی شدت میگرن بر اساس مقیاس شدت میگرن و چک لیست علائم تصویربرداری تشدید مغناطیسی بود. داده‌ها با استفاده از نرم افزار SPSS نسخه ۲۶ در سطح معنی داری کمتر از ۵ درصد مورد تجزیه و تحلیل قرار گرفت.

یافته‌ها: میانگین (انحراف معیار) سنی کادر درمان مورد مطالعه ۳۵/۳۴ (۱۲/۲۲) سال بوده و ۷۶ درصد ایشان زن بودند. در این مطالعه، تعداد ضایعات (پلاک‌ها) در بیماران مبتلا به میگرن (۱۲ ضایعه) به‌طور معناداری بیشتر از گروه شاهد (۱ ضایعه) بود؛ که با استفاده از آزمون آماری مناسب، تفاوت معناداری بین دو گروه مشاهده شد ($P=0/001$) که نشان‌دهنده ارتباط آماری معنادار بین افزایش تعداد پلاک‌های مغزی و ابتلا به میگرن است. از نظر محل بروز ضایعات، بیشترین شیوع پلاک‌ها در بیماران مبتلا به میگرن به ترتیب در لوب پاریتال (۸ ضایعه) و سپس در لوب فرونتال (۳ ضایعه) گزارش شد. با این حال، تفاوت توزیع پلاک‌ها در لوب‌های مختلف مغزی بین دو گروه از نظر آماری معنادار نبود ($P=1/00$). همچنین، بررسی نوع بافت درگیر نشان داد که تمام ضایعات مشاهده‌شده در هر دو گروه، در ماده سفید عمقی مغز قرار داشتند.

نتیجه‌گیری: تعداد ضایعات یا پلاک مغزی می‌تواند منجر به درک بهتر تغییرات در ساختار و عملکرد مغز در بیماران مبتلا به میگرن شود و نه تنها در تشخیص، بلکه در انتخاب درمان و حتی در پیگیری درمان نیز کمک کننده باشد.

کلیدواژه‌ها:

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Introduction

Headache disorders are among the most common nervous system disorders [1]. Migraine is one of the most common causes of chronic neurological diseases, with an estimated prevalence of 11.2% of the population. This prevalence increases to 21.3% when probable migraine (all migraine criteria except one) is considered [2]. Moreover, according to the Global Burden of Disease Study, migraine is the second most common neurological disorder worldwide and is responsible for more disability than other neurological disorders [3].

Sudden headache attacks characterize migraine and are closely linked to the nervous and cardiovascular systems [4]. It is one of the most common diseases and a leading cause of parenchymal lesions in the brain, accompanied by symptoms such as nausea and vomiting, as well as visual and olfactory impairment [5]. Generally, the diagnostic criteria for this disease are clinical, and in most cases, a detailed and appropriate history is sufficient.

Migraine headaches are divided into two general categories: common migraine (without aura) and classic migraine (with aura) [6]. Aura or precursor refers to a set of processes that occur before the onset of a headache in an individual, which includes various events; the most common of these is the visual type [7].

Approximately 50% of migraine patients are misdiagnosed and mistreated due to the lack of an accurate diagnostic test [8]. Therefore, the definitive diagnosis of migraine is a serious challenge for neurologists and radiologists. According to the criteria for migraine, the diagnosis of headache is based on a normal neurological examination and the patient's clinical history. One method that can be effective in correctly diagnosing migraine and ruling out differential diagnoses, but is not routinely performed in many of these cases, is magnetic resonance imaging (MRI), which may detect subtle and incidental brain abnormalities that would otherwise go undetected [9]. With the use of new cross-sectional imaging methods, especially MRI, which offers superior tissue differentiation compared to CT in detecting mild brain lesions, a revolution has been made in understanding the pathogenesis of the disease [10].

A qualitative MRI study by Aradi et al. of white matter hypersignal lesions in patients with migraine revealed features such as axonal degeneration, decreased glial cell density, and increased extracellular space due to fluid accumulation, which may result from ischemic changes in cerebral small vessels during migraine attacks [11]. A meta-analysis by Swartz et al. indicated that people with migraine are about four times more likely to acquire such changes in their white matter compared to healthy people of the same age and gender [12].

With advances in imaging, migraine is no longer considered a benign disease as it once was. Negm et al.

have identified migraine as an independent risk factor for structural brain changes on MRI, such as deep white matter hyperintensity (WMH), silent posterior circulation infarcts, and high-signal lesions under the tentorial membrane. White matter hyperintensity refers to lesions that appear on MRI and have features of infarction but do not cause any clinical or other symptoms associated with stroke. These lesions have a standard distribution in the subcortical and deep white matter. In patients with migraine with aura, white matter hyperintensities are observed in 47% of cases in the deep white matter and in 19% in the periventricular area [13]. These lesions are clinically crucial because white matter hyperintensity is associated with increased cognitive impairment and a twofold increased risk of dementia and a threefold increased risk of stroke. Moreover, increased white matter signal increases the risk of late-life depression, physical disability, Parkinson's disease, and urinary system problems [13-16]. A better understanding of changes in brain structure and function in patients with migraine could help not only in diagnosis, but also in treatment selection and even in treatment follow-up [14].

Following current clinical guidelines, imaging studies in patients with migraine are currently performed only to rule out secondary causes. Since MRI is the method of choice for demonstrating functional and anatomical brain abnormalities, recent attention has been focused on MRI findings in this disease. During these studies, some structural changes have been observed in patients with migraine; limited studies have shown the presence of some abnormal brain signals. Anatomical changes have been reported in both the white matter and, to a lesser extent, the gray matter of the brains of migraine sufferers. However, the increased prevalence of these abnormal brain findings compared to the healthy population is still questionable, and contradictory results have been published in this regard, which requires controlled studies to compare brain findings in migraine sufferers with healthy individuals [17]. The present study was designed and conducted to investigate MRI findings in patients with migraine compared with those without migraine who were referred to Allameh Bohlol Gonabadi Hospital in Gonabad, Iran, in 2022-2023.

Materials and Methods

This research followed the protocols of a case-control study, approved by the Research Council of the Faculty of Medicine, Gonabad University of Medical Sciences, Iran, and by the Regional Ethics Committee (IR.GMU.REC.1401.113). The sample size was determined based on the formula for comparing proportions in two independent groups in G Power (version 3.1.9.2) software, considering a Type I error of 0.05 and a test power of 0.8, and the proportion values in the two groups based on a similar study [12] and the variable of changes in the white matter signal in the supratentorial area of the brain, 25 people in

each group, which increased to 28 people in each group by considering a 10% possible dropout.

The research units were selected from patients referred to the Neurology Clinic of Allameh Bohlol Gonabadi Hospital with headache complaints in 2022-2023, using a convenience sampling method. If they met the inclusion criteria and, based on a neurologist's opinion, were divided into two groups —case (with migraine) and control (without migraine) —they were considered for examination.

Inclusion criteria for the case group included having informed and written consent to participate in the study, being under 55 years of age (due to the decrease in the prevalence of migraine and the increase in microvascular events with age, and the inability to differentiate the lesion caused by it from a migraine plaque), having migraine according to the third edition of International Classification of Headache Disorders (ICHD-3), requesting an MRI by a physician, and a definitive diagnosis of migraine by a neurologist.

Inclusion criteria for the control group also included having informed and written consent to participate in the study, being under 55 years of age, people whose headaches, according to the diagnosis of a neurologist, did not meet the diagnostic criteria for migraine, or did not complain of headaches but had other clinical symptoms, or their headache intervals were more than three months, and requesting an MRI by a physician.

The exclusion criteria for the study were a lack of cooperation and failure to perform an MRI.

It should be noted that the MRI of all patients in this study was performed on a Siemens Magnetom Avanto 1.5 Tesla machine at Allameh Bohlol Gonabadi Hospital, using a T2-weighted, axial, 5-mm-thick, 3-mm-slice-spacing flare sequence. This standard applied to all patients.

It is also noteworthy that MRI was necessary for all patients in both the case and control groups, based on the neurologist's diagnosis and as part of their treatment.

The tools employed in this study included a demographic information checklist, a checklist for determining migraine and its type according to the ICHD-3, a checklist for assessing migraine severity using the Migraine Severity (MIGSEV) scale, and a checklist for MRI symptoms.

Demographic Information Checklist

This checklist contained questions about gender and age.

Questionnaire for Determining Migraine and Its Type Based on ICHD-3

To accurately assess the clinical symptoms of primary headache and differentiate its types, Farahani et al. developed a questionnaire based on the ICHD-3 diagnostic criteria for headache. They had it approved by several experts [18].

This clinical questionnaire requires that at least five

attacks occur over a period of 4 to 72 hours (with or without successful treatment) and include at least two of the following:

- 1) Severe
- 2) Unilateral
- 3) Pulsating
- 4) Accompanied by nausea and vomiting
- 5) Accompanied by fear of light (photophobia) or fear of sound (phonophobia).

Moreover, during a headache attack, at least one of the following 2 events must occur:

- 1) Fear of light, fear of sound
- 2) Nausea or vomiting

It is noteworthy that these symptoms can vary and, in children, may include loss of appetite, a tendency to consume large amounts of certain foods, such as cocoa, and a headache that usually lasts 1-2 hours [19].

The validity of this questionnaire was confirmed in a study by Farahani et al., which used content validity assessments by 10 experts in psychology, psychiatry, and neurology. The Lavish method was used in content validity. To determine the questionnaire's reliability, it was administered to a group of 11 people using the test-retest method, then re-administered to the same group after a 2-week interval. The results and diagnoses were the same, thereby confirming the questionnaire's reliability [18].

Checklist for Assessing Migraine Severity Based on the MIGSEV Scale

The standard MIGSEV scale was employed to assess migraine severity, which includes four items (pain intensity, functional disability, nausea, and sensitivity to light/sound).

Each item was scored on a scale of 1-3, and the total score was used to classify the migraine attack severity into three levels: mild (4–6), moderate (7–9), and severe (10–12).

MRI Symptoms Checklist

This checklist includes questions, such as the number of lesions, lobes, and lesion sites observed in the flair sequence of the MRI at Allameh Bohlol Gonabadi Hospital, prepared using previous sources and finalized based on the opinions of relevant experts.

In the present research, after necessary coordination with the authorities of Gonabad University of Medical Sciences and Allameh Bohlol Gonabadi Hospital, by referring to the research environment of the research units from among the patients referring to the neurology clinic based on the inclusion criteria after explaining the study objectives and obtaining informed and written consent to participate in the study, first the demographic information of the patients was recorded. Migraine incidence was determined using a migraine determination questionnaire and its type based on the ICHD-3, and diagnosis by a

neurologist. The researcher also determined migraine severity using the MIGSEV scale. For all patients in both the case and control groups, a neurologist prescribed a brain MRI, and an MRI was performed using an MRI machine at Allameh Bohlol Gonabadi Hospital. The MRI results were recorded in the MRI symptom checklist by a neurologist who was unaware of the patient grouping.

After collecting the data, it was first transferred to SPSS software (version 26) and subjected to statistical analysis. Independent t-tests, chi-square tests, and Fisher's exact tests were used to analyze the data. In addition, the significance level was set at 0.05 or lower.

Results

In this study, 60 patients were divided into two

groups: a case group (n=30) and a control group (n=30). In the case group, two patients were excluded because they were over 55 years old, and three patients were excluded because they did not consent to the MRI. In the control group, one patient was excluded because they were over 55 years old, and four patients were excluded due to not consenting to the MRI.

The mean (standard deviation) age of patients in the case group was 36.24 (10.80) years, and in the control group, it was 34.44 (13.66) years. The majority of patients in both groups were female. There was no statistically significant difference in age and gender between the studied patients in the two groups ($P < 0.05$) (Table 1).

Table 1. Comparison of demographic information of participants in the two groups.

Variable	Group		P-Value
	Case	Control	
	Average (SD)	Average (SD)	
Age	34.44 (13.66)	36.24 (10.80)	$P^* = 0.608$
Gender	Number (%)	Number (%)	
Male	7 (28)	5 (20)	$P^{**} = 0.508$
Female	18 (72)	20 (80)	
Total	25 (100)	25 (100)	

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*Independent t-test; **Chi-square test

The results of the statistical analysis performed in this study showed a statistically significant relationship between the number of plaques and migraine, with the number of lesions (12 lesions in the study group and 1 lesion in the control group) observed in the case group being significantly higher than in the control group ($P = 0.001$) (Table 2). Among the patients with migraine, 44% had severe headaches, and 84% reported headache duration between 4 and 72 hours. Moreover, 72% of the patients had bilateral headaches, and 60% experienced pressure headaches. In 40% of cases, unbearable headaches were reported, and in 76% of cases, the headaches were repeated more than

once a week. In 100% of cases, there were accompanying symptoms, and photophobia and phonophobia were observed in 36% and 88% of cases, respectively. In addition, 68% of cases were associated with nausea, and none of the patients experienced tingling or weakness in their limbs. Furthermore, 96% of the migraines were not accompanied by an aura. All the lesions observed in the two groups were in the deep white matter (Table 3). The most affected area was the parietal lobe, and then the frontal lobe. The results of Fisher's exact test showed no significant difference between the two groups in terms of the lobe where the lesions were located ($P = 0.001$) (Table 4).

Table 2. Comparison of the frequency distribution of research units in two groups based on the number of lesions.

Number of Lesions	Group		P-Value
	Case	Control	
	Number (%)	Number (%)	
Without Lesion	13 (52)	24 (96)	$P^* = 0.001$
One Lesion	7 (28)	1 (4)	
Two Lesions	5 (20)	0 (0)	
Total	25 (100)	25 (100)	

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*Fisher's exact test

Table 3. Frequency distribution of characteristics of headache symptoms in the case group.

Characteristics of Headache Symptoms	Number (%)
Pain Intensity	
Low	3 (12)
Moderate	3 (12)
High	8 (32)

	Very High	11 (44)
Duration of Attack	4-72 hours	21 (84)
	More than 72 hours	4 (16)
Site of the Headache	Unilateral	7 (28)
	Bilateral	18 (72)
Type of Headache	Pulsating	10 (40)
	Pressure	15 (60)
Causing Disability	No	2 (8)
	Mild	7 (28)
	Significant	16 (64)
Tolerability	Yes	4 (16)
	Tolerate hardly	11 (44)
	Unbearable	10 (4)
Number of Attacks	1-2 attacks per month	6 (24)
	More than 1 attack per week	19 (76)
Associated Symptoms	Yes	25 (100)
	No	17 (68)
Having Nausea	Mild	1 (4)
	Severe	2 (8)
	Vomiting	5 (20)
Sensitivity to Light	Yes	9 (36)
	No	16 (64)
Sensitivity to Sound	Yes	22 (88)
	None	3 (12)
Feeling a Spark of Light	Yes	1 (4)
	No	24 (96)
Burning Smell	No	25 (100)
Tingling in the Limbs	No	25 (100)
Motor Weakness	No	25 (100)
Speech Disorder	No	25 (100)
Migraine Severity	Low	7 (28)
	Moderate	10 (4)
	High	8 (32)
Type of Migraine	With Aura	1 (4)
	Without Aura	24 (96)
Type of Aura	Visual	1 (100)

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Table 4. Comparison of the frequency distribution of research units in two groups based on the number of lesions.

Lesion Site	Group		P-Value
	Case	Control	
	Number (%)	Number (%)	
Frontal Lobe	3 (25)	0 (0)	P [*] = 1.000
Parietal Lobe	8 (66.7)	1 (100)	
Frontal and Parietal Lobes	5 (20)	0 (0)	
Total	13 (100)	1 (100)	

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*Fisher's exact test

Discussion

Migraine is one of the primary headache types that

involves the neurovascular and cerebral parts. Approximately 50% of patients with migraine are misdiagnosed and mistreated due to the lack of an

accurate diagnostic test. Therefore, the definitive diagnosis of migraine is a serious challenge for neurologists and radiologists. With the use of new cross-sectional imaging methods, especially MRI, which offers excellent tissue differentiation compared to CT, a revolution has occurred in understanding the pathogenesis of the disease. The present study was conducted to determine and compare MRI findings in individuals with and without migraine. In this study, 25 patients who had been previously diagnosed with migraine and 25 people who did not have migraine were examined.

The findings from brain imaging in this work indicated that the prevalence of white matter lesions in migraine patients was significantly higher than in healthy subjects. In the case group, 28% of subjects had 1 lesion, 20% had 2 lesions, and only 52% had none. In contrast, the control group consisted of only one subject (4%) with a lesion, and 96% had no brain lesions. This significant difference was also confirmed by statistical testing, and the two groups differed significantly in the number of lesions ($P=0.001$). These results suggest that the likelihood of structural changes in the brain's white matter is substantially higher in patients with migraine.

In terms of lesion distribution, in the case group, the majority of lesions were observed in the parietal lobe (66.7%), followed by the frontal lobe (25%), and then in both lobes simultaneously (20%). In the control group, the only lesion observed was also in the parietal lobe. However, a strict statistical test revealed no significant difference between the two groups in the site of the lobe involved ($P=1.00$). This result means that although the number of lesions in migraine patients is higher, their distribution in the cerebral lobes is not statistically significantly different from the control group.

Furthermore, the site of all lesions observed in both groups was reported to be in the deep white matter. This similarity in lesion site suggests that, regardless of grouping, the pattern of brain damage occurred predominantly in deep white matter regions, which may be related to specific features of cerebral blood flow or to the sensitivity of these regions to migraine-related physiological phenomena. Overall, these findings emphasize the possible role of migraine in the induction or facilitation of subcortical brain damage.

The results of the studies by Barzin et al. [15] and Kamson et al. [20] on brain lesions in patients with migraine showed that lesions were mainly located in the deep white matter, with most cases occurring in the frontal and parietal lobes. In the study conducted by Alaei et al., the number of brain areas in which plaques or lesions caused by migraine were observed was

significantly higher in patients with migraine headaches than in people without migraine headaches. They also stated that after examining selected brain areas for the presence of plaques, the results showed that the most lesions observed in the group with migraine headaches were observed in the parietal and frontal lobes, respectively. Moreover, in Alaei et al., the number of brain areas involved in patients with migraine headaches was significantly higher than in patients without headaches [21]. In addition, in another study conducted in 2012, Alaei et al. reported the presence of abnormal findings in the brain parenchyma MRI of patients with migraine [12]. These results were consistent with those of our study, although the study population of Alaei et al. consisted of patients with multiple sclerosis (MS).

In studies conducted by Hamdy et al. [22] and Gee et al. [23], the number of plaques observed in MRI was significantly higher in people with migraine headaches than in people without migraine. Tortorella et al., after examining three groups of patients with migraine, MS with migraine, and MS without migraine, stated that the most lesions were observed in the migraine group [24]. In connection with these results, it should be noted that one of the causes of headaches in patients with migraine may be these lesions or plaques observed in the central nervous system. In connection with this, in the study by Sandyk and Awerbuch, the presence of a cerebral plaque was associated with an increased likelihood of headaches with migraine characteristics [25].

In a study on 45 patients with migraine, Gozke et al. found that 28.8% of patients had foci of lesions in the white matter of the brain, of which 61.5% had migraine with aura and the rest had migraine without aura. The signal of foci of lesions in the white matter of the brain was higher in patients with aura than in patients without aura, and it was observed that the number of white matter lesions increased with the increasing number of attacks per month [26]. Other studies have also indicated that MRI outcomes in migraine patients demonstrate a higher risk of white matter abnormalities [27]. The results of a meta-analysis by Swartz et al. showed that people with migraine are about four times more likely to have such changes in their white matter compared to healthy people of the same age and gender [28].

Abnormal findings on MRI of the brain parenchyma of migraine patients help to diagnose the disease. The MRI has been indicated to detect high-signal lesions in the subcortical white matter of migraine patients, and there is a direct relationship between the signs of brain lesions, the onset of migraine, and the severity of the disease. By performing an MRI in patients with

migraine symptoms, it is possible to rule out anatomical brain lesions, such as cortical lesions (e.g., in the occipital lobe, which can cause visual auras) or masses, and cerebrovascular lesions that mimic other migraine symptoms [29]. However, the cause of lesions in the white matter of migraine patients is still not well understood. Possible causes include gliosis, edema, local infarction due to microembolism, and even myelin destruction in the above areas. One of the pathological features of migraine lesions is hemorrhage without vascular wall destruction (vasospasm) and with increased vascular wall permeability. Migraine is likened to a four-way process that involves genetic predisposition to environmental hemodynamic or metabolic factors [30]. A work conducted by Aradi et al. in a qualitative study of MRI hypersignal lesions in the white matter of the brain of patients with migraine indicated features, such as axonal destruction, reduced density of glial cells, and increased extracellular space, due to fluid accumulation, which could be the effect of ischemic changes in small cerebral vessels during migraine attacks [31]. The demonstration of the presence of hypersignal foci in the brain parenchyma of patients with migraine can be considered a diagnostic finding of the disease. It can even be used in the follow-up of patient treatment.

The results of the present study on determining clinical symptoms in people with migraine indicated that most of the research units in the case group experienced considerably high headache intensity (44%), and the duration of the attack in 84% of cases was between 4 and 72 hours. The site of the headache was bilateral in 72% of patients, and in 64% of patients, it caused significant disability. In the studied patients, more than one attack per week occurred in 76% of cases. In all cases, the attacks were accompanied by symptoms, and in 68% of patients, nausea was not observed. Sensitivity to light was observed in 36% of patients, and sensitivity to sound was observed in 88%. The sensation of light flashes was observed in only one patient (4%). A burning sensation, motor weakness, and speech disorder were not reported in any of the patients. Migraine severity was low, moderate, and high in 28%, 40%, and 32% of patients, respectively. Only one of the studied patients had migraine with aura, which was visual.

Consistent with our study's results, Barzin et al. reported that most migraine headaches were of the tension type [15]. In another work, Mottaghi et al. reported moderate pain intensity in migraine patients and eight migraine attacks per month [32]. Meanwhile, in a study by Alaei et al., 93.3% of migraine sufferers had unilateral headaches [12].

Studies on migraine have indicated that migraine attacks have a significant impact on work, family, and social life. Headache-related disability is a primary concern in migraine patients, as it reduces quality of life and work ability [33]. According to the World Health Organization (WHO), migraine is the 19th leading cause of disability in life years [34]. Moreover, Azimi et al. state in this regard: "Headache attacks usually last from 2-3 hours to 2-3 days and are accompanied by dizziness, nausea, and sensitivity to light and sound. Although these pains start unilaterally, they continue to involve the entire head" [35].

The results of a study conducted by Azizi et al. revealed that most headaches in patients with migraine are accompanied by nausea, vomiting, and photophobia. The onset of headaches in their study population was typically in the temporal, frontal, or occipital region, and in most cases, it occurred on one side of the head. In this study, only 30% of patients experienced bilateral headaches. The duration of headaches in their study ranged from 4 to 72 hours and was highly disabling [36].

The results of the present work and the above studies demonstrated that migraine symptoms are almost the same in all populations and cause functional disability in patients in all studies. The differences in our results compared to other studies in the field of migraine could be attributed to variations in MRI devices (imaging technology) or to differences in the stage of disease among the patients studied. However, despite the slight differences observed, our results confirm those of the literature.

An interesting and unexpected finding in the present study was that only 4% of patients with migraine reported experiencing migraine with aura, which is in marked contrast to most global epidemiological reports. According to comprehensive studies published in recent years, the prevalence of migraine with aura in the general population has been reported to be between 25% and 30% [37, 38]. This significant discrepancy underscores the need for a more comprehensive analysis that considers epidemiological, cultural, and methodological contexts.

One possible reason for this difference may be differences in patients' cultural structures and health literacy. In many societies, especially in developing countries, patients' awareness of migraine precursor symptoms (e.g., visual or sensory auras) is low, and these symptoms are sometimes perceived as normal or anxiety-provoking phenomena and are not reported. In the present study, patients may have failed to match their experiences with scientific definitions of aura, leading to an underestimation of its prevalence. In addition, the data collection method and tools used to

identify aura play a key role in this difference, as larger studies, such as those by Ha et al. (2024), employed a combination of clinical interviews and detailed self-assessment tests to cover a broader range of auras [38]. Another point is the demographic characteristics of the patients in the present study. Studies have reported that the prevalence of migraine with aura is influenced by gender, age, race, and geographic variables [39]. For instance, some studies in Asian populations, particularly in the Middle East, have reported a lower prevalence of aura compared to European populations, which may be related to genetic, environmental, or lifestyle differences [40, 41]. Finally, the unexpected finding of this study could be a starting point for more in-depth research into the true prevalence of aura in Middle Eastern or Persian-speaking communities. Comparative studies across countries, the use of more accurate diagnostic tools, and patient education to better recognize aura symptoms could lead to a more precise delineation of this phenomenon in specific populations.

The limitations of this study include the lack of cooperation from some patients due to severe headaches, unwillingness to undergo MRI, or refusal to complete the questionnaire, despite attempts to gain their consent to participate. Additionally, some patients were referred to other medical centers for MRI and continued treatment, making it impossible to examine them, and they were therefore excluded from the study. This limitation increased the sampling time, which we hope will be conducted in future studies with a larger sample size to generalize these data and results. However, the use of standard tools to diagnose and assess the severity of migraine symptoms, in conjunction with a neurologist's opinion, was one of the study's strengths, which increased confidence in the results obtained. Finally, it is suggested that similar studies be conducted with larger sample sizes and broader populations to improve the generalizability of

the results.

Conclusion

The prevalence of brain lesions or plaques in patients with migraine is higher than in healthy individuals. Timely and accurate diagnosis of migraine using history and MRI results can play an essential role in improving symptoms of this disease, reducing headache attacks, and preventing the progression of brain lesions and ultimately stroke.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Regional Research Ethics Committees of Gonabad University of Medical Sciences (IR.GMU.REC.1401.113)

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Authors' contributions

All authors contributed to this research project.

Conflicts of interest

The authors declare that they have no conflict of interest.

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References

- [1]. Khaninezhad L, Valiee S, Moradi Y, Mahmoudi M. The effect of a caring program based on Pender's health promotion model on caregiver burden in family caregivers of patients with chronic heart failure: A quasi-experimental study. *J Educ Health Promot*. 2024;13(1):303. [DOI: 10.4103/jehp.jehp_1024_23] [PMID]
- [2]. Henri J, Redon S, Donnet A. Study of severe migraine in general medicine. *Rev Neurol (Paris)*. 2023;179(9):993-9. [DOI: 10.1016/j.neurol.2023.01.730] [PMID]
- [3]. Mohammadi M, Kankam SB, Salehi S, Mohamadi M, Mohammadi A, Firoozabadi SRD, et al. The association between multiple sclerosis and migraine: A meta-analysis. *Mult Scler Relat Disord*. 2023;79:104954. [DOI: 10.1016/j.msard.2023.104954] [PMID]
- [4]. Ahmed RN, Alkhaffaf WH, Naif MM, Al Mahdawi AM. MRI findings in migraine headache in different age groups and relation to Aura. *Curr Pediatric Res*. 2021. [Link]
- [5]. Al-Hashel JY, Abokalawa F, Toma R, Algubari A, Ahmed SF. Worsening of migraine headache with fasting Ramadan. *Clin Neurol Neurosurg*. 2021;209:106899. [DOI: 10.1016/j.clineuro.2021.106899] [PMID]
- [6]. Gunawardane SP, Kramer ME, Bearden JM, Resar JR, Lawton JS, Allison DB, et al. Chronic migraine with aura as a neurologic manifestation of an atrial myxoma - A case report. *Int J Surg Case Rep*. 2022;92:106894. [DOI: 10.1016/j.ijscr.2022.106894] [PMID]
- [7]. Kaniecki R. Migraine with brainstem aura. In: Swanson JW, Matharu M, editors. *Handbook of Clinical Neurology*. 2024;199:367-79. [DOI: 10.1016/B978-0-12-823357-3.00019-7] [PMID]
- [8]. Ebadi M, Ebrahimimofared M, Sadeghi R, Rezaei Ashtiani A, Eghbalejad Mofrad AM, Faraji F, et al. Migraine symptoms in patients with MRI white matter hyperintensity before and after treatment. *J Positive School Psychol*. 2022;6(7):40-7. [Link]

- [9]. Alturkustani A, Bock Y, Bajunaid K, Lingawi S, Baeesa S. Significant incidental brain magnetic resonance imaging findings in migraine headache patients: Retrospective cross-sectional study. *Clin Neurol Neurosurg.* 2020;196:106019. [\[DOI: 10.1016/j.clineuro.2020.106019\]](#) [\[PMID\]](#)
- [10]. Schwedt TJ, Chiang C-C, Chong CD, Dodick DW. Functional MRI of migraine. *Lancet Neurol.* 2015;14(1):81-91. [\[DOI: 10.1016/S1474-4422\(14\)70193-0\]](#) [\[PMID\]](#)
- [11]. Aradi M, Schwarcz A, Perlaki G, Orsi G, Kovács N, Trauninger A, et al. Quantitative MRI studies of chronic brain white matter hyperintensities in migraine patients. *Headache.* 2013;53(5):752-63. [\[DOI: 10.1111/head.12013\]](#) [\[PMID\]](#)
- [12]. Alaei A, Barzin M, Zarvani A, Abedini SM. Evaluation of cerebral MRI findings in migrainous patients compared with non-migrainous individuals. *J Mazandaran Univ Med Sci.* 2013;22(98):59-65. [\[Link\]](#)
- [13]. Negm M, Housseini AM, Abdelfatah M, Asran A. Relation between migraine pattern and white matter hyperintensities in brain magnetic resonance imaging. *Egypt J Neurol Psychiatr Neurosurg.* 2018;54(1):24. [\[DOI: 10.1186/s41983-018-0027-x\]](#) [\[PMID\]](#)
- [14]. Ashina S, Bentivegna E, Martelletti P, Eikermann-Haerter K. Structural and functional brain changes in migraine. *Pain Ther.* 2021;10(1):211-23. [\[DOI: 10.1007/s40122-021-00240-5\]](#) [\[PMID\]](#)
- [15]. Barzin M, Alaei AR, Gholian Jooibari S. MRI findings in patients with headache referred to Imam Khomeini hospital, Sari, Iran, from October 2007 to February 2009. *J Mazandaran Univ Med Sci.* 2010;20(75):65-9. [\[Link\]](#)
- [16]. Messina R, Rocca MA, Colombo B, Valsasina P, Horsfield MA, Copetti M, et al. Cortical abnormalities in patients with migraine: a surface-based analysis. *Radiology.* 2013;268(1):170-80. [\[DOI: 10.1148/radiol.13122004\]](#) [\[PMID\]](#)
- [17]. Schramm S, Börner C, Reichert M, Baum T, Zimmer C, Heinen F, et al. Functional magnetic resonance imaging in migraine: A systematic review. *Cephalalgia.* 2023;43(2). [\[DOI: 10.1177/03331024221128278\]](#) [\[PMID\]](#)
- [18]. Moshkani-Farahani D, Tavalaei S, Fathi-Ashtiani A, Ahmadi K. The effectiveness of neurofeedback on the treatment of primary headaches in military personnel. *J Military Med.* 2016;17(4):231-9. [\[Link\]](#)
- [19]. Waldman SD. Migraine headache. In: Waldman SD ,editor. *Atlas of common pain syndromes* (15th ed). New York (NY): Elsevier; 2024.:6-9. [\[DOI:10.1016/B978-0-443-11105-1.00002-9\]](#)
- [20]. Kamson DO, Illés Z, Aradi M, Orsi G, Perlaki G, Leél-Össy E, et al. Volumetric comparisons of supratentorial white matter hyperintensities on FLAIR MRI in patients with migraine and multiple sclerosis. *J Clin Neurosci.* 2012;19(5):696-701. [\[DOI: 10.1016/j.jocn.2011.07.044\]](#) [\[PMID\]](#)
- [21]. Alaei A, Cheraghmakani H, Agh Arkakeli AM. Comparing the number, size, and location of multiple sclerosis plaques in patients with and without migraines. *J Mazandaran Univ Med Sci.* 2016;26(139):53-65. [\[Link\]](#)
- [22]. Hamdy SM, Elmazny A, Abdel-Naseer M, Shalaby NM, Shehata HS, Kishk NA, et al. Interferon-beta-induced headache in patients with multiple sclerosis: frequency and characterization. *J Pain Res.* 2020:537-45. [\[DOI: 10.2147/JPR.S230680\]](#) [\[PMID\]](#)
- [23]. Gee JR, Chang J, Dublin AB, Vijayan N. The association of brainstem lesions with migraine-like headache: An imaging study of multiple sclerosis. *Headache.* 2005;45(6):670-7. [\[DOI: 10.1111/j.1526-4610.2005.05136.x\]](#) [\[PMID\]](#)
- [24]. Tortorella P, Rocca MA, Colombo B, Annovazzi P, Comi G, Filippi M. Assessment of MRI abnormalities of the brainstem from patients with migraine and multiple sclerosis. *J Neurol Sci.* 2006;244(1-2):137-41. [\[DOI: 10.1016/j.jns.2006.01.015\]](#) [\[PMID\]](#)
- [25]. Sandyk R, Awerbuch GI. The co-occurrence of multiple sclerosis and migraine headache: the serotonergic link. *Int J Neurosci.* 1994;76(3-4):249-56. [\[DOI: 10.3109/00207459408986007\]](#) [\[PMID\]](#)
- [26]. Gözke E, Öre O, Dortcan N, Unal Z, Cetinkaya M. Cranial magnetic resonance imaging findings in patients with migraine. *Headache.* 2004;44(2):166-9. [\[DOI: 10.1111/j.1526-4610.2004.04034.x\]](#) [\[PMID\]](#)
- [27]. Wang S-J, Chen P-K, Fuh J-L. Comorbidities of migraine. *Front Neurol.* 2010;1:16. [\[DOI: 10.3389/fneur.2010.00016\]](#) [\[PMID\]](#)
- [28]. Swartz RH, Kern RZ. Migraine is associated with magnetic resonance imaging white matter abnormalities: a meta-analysis. *Arch Neurol.* 2004;61(9):1366-8. [\[DOI: 10.1001/archneur.61.9.1366\]](#) [\[PMID\]](#)
- [29]. Shams PN, Plant GT. Migraine-like visual aura due to focal cerebral lesions: case series and review. *Surv Ophthalmol.* 2011;56(2):135-61. [\[DOI: 10.1016/j.survophthal.2010.07.005\]](#) [\[PMID\]](#)
- [30]. Cole A, Aube M. Late-onset migraine with intracerebral hemorrhage: a recognizable syndrome. *Neurology.* 1987;37(suppl 1):238. [\[Link\]](#)
- [31]. Aradi M, Schwarcz A, Perlaki G, Orsi G, Kovács N, Trauninger A, et al. Quantitative MRI studies of chronic brain white matter hyperintensities in migraine patients. *Headache.* 2013;53(5):752-63. [\[DOI: 10.1111/head.12013\]](#) [\[PMID\]](#)
- [32]. Mottaghi T, Askari G, Khorvash F, Maracy M, Ghiasvand R. Effect of vitamin D supplementation on symptoms and C-reactive protein among patients with migraine. *Koomesh.* 2015;16(2):207-12. [\[Link\]](#)
- [33]. Nematgorgani S, Gholi Z, Razeghi Jahromi S, Togha M, Karimzadeh F. The effect of vitamins B on improving the symptoms of migraine: an overview. *Neurosci J Shafaye Khatam.* 2020;8(2):119-29. [\[DOI: 10.29252/shefa.8.2.119\]](#)
- [34]. Munvar MS, Gan GH. Vitamin supplementation as possible prophylactic treatment against migraine with aura and menstrual migraine. *BioMed Res Int.* 2015;2015(1):469529. [\[DOI: 10.1155/2015/469529\]](#) [\[PMID\]](#)
- [35]. Azimi Z, Haghayegh SA, Norouzi M. The moderating role of sleep quality in the relationship between state-trait anxiety with severity of symptoms in patients with a migraine headache diagnosis. *Health Psychol.* 2019;8(30):26-38. [\[DOI: 10.30473/hpi.2019.39807.3965\]](#)
- [36]. Azizi M, Agha-Mohammadiyan Shaarbaf HR, Mashhadi A, Asghari-Ebrahimabadi M. The comparison of psychological status in people suffering from migraine with healthy people. *J Sabzevar Univ Med Sci.* 2016;23(4):706-13. [\[PMID\]](#)
- [37]. Makhlof HA, Hassan AK, Almosilhy NA, Osman ASA, Ramadan S, Abouelmagd ME. Exploring the association between statins use or HMG-CoA reductase inhibition and migraine: a systematic review and meta-analysis. *J Headache Pain.* 2025;26(1):23. [\[DOI: 10.1186/s10194-025-01957-w\]](#) [\[PMID\]](#)
- [38]. Ha WS, Nguyen VK, Chu MK. Epidemiological linkage between migraine and diabetes mellitus: a systematic review and meta-analysis. *J Headache Pain.* 2024;25:158. [\[DOI: 10.1186/s10194-024-01868-2\]](#) [\[PMID\]](#)
- [39]. Vityala Y, Garg R, Ausvi S, Shantaram M, Tippabathini S, Reddy LHB, et al. Effect of combined oral contraceptives on menstrual migraine frequency and severity: a narrative review. *Explor Drug Sci.* 2024;2(6):666-76. [\[DOI: 10.37349/eds.2024.00067\]](#)
- [40]. Amiri P, Kazeminasab S, Nejadghaderi SA, Mohammadinasab R, Pourfathi H, Araj-Khodaei M, et al. Migraine: a review on its history, global epidemiology, risk factors, and comorbidities. *Front Neurol.* 2022; 12: 800605. [\[PMID\]](#) [\[DOI: 10.3389/fneur.2021.800605\]](#)
- [41]. Genc H, Baykan B, Bolay H, Uluduz D, Unal-Cevik I, Kissani N, et

al. Cross-sectional, hospital-based analysis of headache types using ICHD-3 criteria in the Middle East, Asia, and Africa: the

Head-MENAA study. J Headache Pain. 2023;24:24.
[\[DOI: 10.1186/s10194-023-01555-8\]](https://doi.org/10.1186/s10194-023-01555-8) [\[PMID\]](#)