Original Article

Primary Headache with Relapsing Remitting Multiple Sclerosis

Prevalence of Primary Headache in Iraqi Patients with Relapsing Remitting Multiple Sclerosis

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ABSTRACT

Objective: To find out how many multiple sclerosis patients experienced headaches.
Study Design: A cross-sectional study
Place and Duration of Study: This study was conducted at the Neurology Clinic located in Al-Sadiq Teaching Hospital in Babylon Governorate, Iraq from 15th September 2025 to 28th February 2026.
Methods: 151 multiple sclerosis patients were included. The demographic data and multiple sclerosis information such as age, sex, Expanded Disability Status Scale score, time of diagnosis, number of lesions, and type(s) of headache(s).
Results: Majority of the patients 105 (69.5%) were females and rest were males 46 (30.5%). Most patients had an Expanded Disability Status Scale score of zero (69, 45.7%) i.e. 1 (63, 41.7%) at scores of 1, 2 (13, 8.6%), or three; of the patients; 89 (58.9%) had a history of chronic headache but 62 (41.1%) did not. Most patients were 69 reported migraine as the type of headache they had the most often (highly significant), although tensions and/or unspecified headaches were reported to occur less frequently than migraines. It is important to note that (i.e, sensory deficits) were the most frequent presenting signs at the time of diagnosis. The largest number of multiple sclerosis patients was in the 15-25 years age range (86, 57%) followed closely by 25-35 years (39, 26%) and 35-45 years (26, 17%).
Conclusion: The prevalence of headaches in multiple sclerosis patients. The two most commonly reported headaches by patients were migraine and tension-type headaches. This indicates that focused education on the recognition and management of headache in multiple sclerosis patients may improve their quality of life.
Key Words: Multiple sclerosis patients, Headache characteristics, Pain management

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INTRODUCTION

Multiple sclerosis (MS) is a persistent inflammatory, demyelinating, neurodegenerative, and autoimmune disease of the central nervous system (CNS), resulting in gliosis and plaque formation in many parts of the brain and spinal cord.[1] Globally, 2,860,000 people were affected with MS in 2020.[2] Female MS patients are three times more common than male MS patients; the majority of new MS diagnoses are between the ages of 20 and 40.[3]

Its cause is unknown, but numerous factors contribute to its development including immune dysregulation, family genetics, geographic location, viral infections and stress.[4] The manner in which MS presents to patients varies widely from benign forms to rapidly progressing, debilitating MS diseases.[5,6]

Headache is one of the most frequently seen conditions seen in clinical medicine.[7] Overall, approximately 89% of people will experience at least one headache or headache disorder sometime during their lives.[8] While migraine has been classified as a neurological condition that causes repeated episodes of severe unilateral headache with vomiting, nausea, photophobia and phonophobia, it is further defined as beginning as the culmination of a series of processes occurring within the CNS that increase a person's susceptibility to environmental stimuli. Migraine has also been linked to increased activity of the trigeminal nerve and unexplained amounts of calcitonin gene-related peptide (CGRP) released from the trigeminovascular system.[9]

In order to understand the high rates of migraine seen in patients with MS, many different mechanisms have been suggested. To begin with, histological evidence from postmortem samples suggests that inflammation of the meninges may play a role in the development of migraine headaches through the presence of lymphoid follicle-like structures located within the meninges and gyri.[10] Cortical demyelination secondary to

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inflammatory processes may act as an explanation for migraines, as it is known to result in faster cortical spreading depression in rodent models of migraine.[11] Furthermore, the location of the lesions may also be a factor; one retrospective study demonstrated that patients displaying MS lesions in the midbrain periaqueductal gray area are more likely to develop migraine.[12] Similar demographic and epidemiological patterns exist between MS and migraine, as both are more prevalent among women, young adults and Caucasians.[1] Patients with MS and migraine comorbidity are more likely to experience significant neurological impairment, fatigue, depression and stress than those without migraine.[13] The headaches, especially migraines and tension-type headaches, are a frequent occurrence among MS patients and have been reported to have a prevalence higher than 50%.[14] A retrospective review indicated that 55.6% of MS patients reported experiencing headaches. Among those, 61.7% experienced migraine headaches, 25.3% tension-type headaches, and 13% mixed-type headaches.[15] Due to the conflicting rates reported concerning migraine among individuals with MS, along with the increasing incidence of MS patients being identified in the Babylon governorate of Iraq, the current study will investigate the prevalence of headaches amongst MS patients in the Babylon region.

METHODS

This was a cross-sectional study took place at Neurology Clinic at Al-Sadiq Teaching Hospital, Iraq from 15th September 2025 to 28th February 2026 vide letter No. 3439/QM/Approval/JSDJNEHU Dated 07.07.2025 and 151 patients were enrolled. Initially, a list was made of patients with multiple sclerosis (MS). All patients who participated had a definitive MS diagnosis and met the revised McDonald Criteria 2017. Each participant had provided informed consent to participate in the study. Any patients who were unable to provide adequate cooperation for study purposes or suffered from other causes of headache were excluded from the study. Each patient underwent a comprehensive clinical history examination where data were collected on the patient's age, sex, and whether they were taking MS-related medications or antidepressant medications. Statistical analyses were performed via the SPSS-27. An independent sample T test was used to evaluate the differences between two independent means. The associations between categorical variables were evaluated using both the Pearson chi-square test and Fisher's exact probability test. A statistical significance level for each analysis was established at $p \leq 0.05$.

RESULTS

The average age of patients was 30.00±9.07. Less than half of the patients were within 20-30 years old age group (N=68; 45%). The average age of diagnosis was 25.74±7.21. More than half of the patients (N=79; 52.3%) were diagnosed between 20-30 years. The majority of the patients were females (N=105; 69.5%). According to figure 1 (sensory, motor, cerebellar, optic, and trigeminal), sensory symptoms were the most frequent initial presentation for less than half of the patients (N=69, 45.7%). For motor symptoms, there were 19 patients (12.6%); for cerebellar symptoms (13 patients, 8.6%); for optic nerves (44 patients, 29.1%) and trigeminal involvement was present in six patients (4%) [Table 1].

Less than half of patients (N=69, 45.7%) presented with a normal neurological exam and no disability (score 0). The remaining 63 patients (41.7%) had no disability but minimal signs in one functional system (FS), (i.e. score 1), 13 patients (8.6%) presented with minimal disability in one FS (i.e. score 2), and there were only six patients (4%) who had moderate disability in one FS but mild disability in three or four FS with no impairment to their ability to walk (i.e. score 3) [Table 2].

Finally, regarding primary headaches (i.e. presence or absence) and type of primary headache (i.e. migraine vs. tension type), 89 patients (58.9%) with multiple sclerosis (MS) reported the presence of a primary headache, with less than three-quarters of these patients (N=64, 71.9%) suffering from migraines (Table 3). The mean current ages of MS patients with and without headaches had no statistically significant difference. Whereas a statistically significant difference was found in the mean age of MS patients reporting primary headaches (24.55±5.83 years) versus those that did not report primary headaches (27.35±8.39 years) at the time of diagnosis (Table 4).

In females, 65.1% developed primary headaches compared to less than half (49.34%) of males. Of patients presenting to the doctor with optic symptoms (i.e. visual disturbance due to optic neuritis), 95% developed primary headache, as well as all patients who had presented initially with trigeminal symptoms. In contrast to this, only 2 out of the 7 (28%) of patients who initially presented to the doctor with motor symptoms developed primary headaches. With respect to EDSS scores, the majority of patients with a score of 0 (i.e. no disability) and those who with a score of 1 both developed primary headaches (63.8% and 68.3%, respectively), whereas all patients with EDSS scores of 3 were headache-free (Table 5).

Patients with migraine (i.e. primary recurrent headache disorder) exhibited both a statistically significant reduction in the mean current age and a statistically significant reduction in the mean age at diagnosis versus those who developed tension-type (i.e. secondary headache disorder) headache. The majority of females (77.9%) developed migraines, whereas less than 50% of males (n=47.5%) developed tension-type headache. Of the patients presenting with optic and

trigeminal symptoms as their first presentation of MS, 95.56% developed migraines, while 0% developed tension-type headache.

Table No. 1: Distribution of patients with multiple sclerosis according to sociodemographic characteristics (N=151)

Sociodemographic characteristics	No.	%
Age (years)		
10 – 20	17	11.3
21 – 30	68	45.0
31-40	39	25.8
40 – 50	22	14.6
> 50	5	3.3
Age at diagnosis (year)		
10 – 20	25	16.5
21 – 30	79	52.3
31-40	46	30.5
> 40	1	0.7
Gender		
Male	46	30.5
Female	105	69.5

Table No. 2: Distribution of patients with multiple sclerosis according to expanded disability status scale (N=151).

Expanded Disability Status Scale	No.	%
Normal neurological exam, no disability in any FS (score 0)	69	45.7
No disability, minimal signs in one FS (score 1)	63	41.7
Minimal disability in one FS (score 2)	13	8.6
Moderate disability in one FS, or mild disability in three or four FS. No impairment to walking (score 3)	6	4.0

Table No. 3: Distribution of patients with multiple sclerosis according to primary headache

Variable	No.	%
Primary headache		
Present	89	58.9
Absent	62	41.1
Type of headache		
Migraine	64	71.9
Tension headache	25	28.1

Table No. 4: The mean differences of age of patients (years) and age of diagnosis (years) according to primary headache (N=151)

Variable	Primary headache	No.	Mean±SD	P-value
Age (years)	Present	89	30.00±9.34	1.000
	Absent	62	30.00±8.75	
Age at diagnosis (years)	Present	89	24.55±5.83	0.023
	Absent	62	27.45±8.59	

Patients with a score of 0 and score of 3 on the expanded disability status scale were the most likely to develop migraine headaches (84.1%) while one patient (i.e. 50%) with a score of 2 developed tension-type headaches (Table 5).

Table No. 5: The association between primary headache among patients with multiple sclerosis and study variables (N=151)

Variable	Primary headache		P value
	Present (n-89)	Absent (n=62)	
Gender			
Male	21 (45.7%)	25 (54.3%)	0.028
Female	68 (64.8%)	37 (35.2%	
First presentation			
Sensory	33 (47.8%)	36 (52.2%)	<0.001
Motor	2 (10.5%)	17 (89.5%)	
Cerebellar	6 (46.2%)	7 (53.8%)	
Optic	42 (95.55)	2 (4.5%)	
Trigeminal	6 (100%)	-	
EDSS			
Score 0	44 (63.8%)	25 (36.2%)	<0.001
Score 1	43 (68.3%)	20 (31.7%)	
Score 2	2 (15.4%)	11 (84.6%)	
Score 3	-	6 (100%)	

Table No. 6: The comparison between types of primary headache among patients with multiple sclerosis that developed headache according to study variables (N=89)

Variable	Types of primary headache		P value
	Migraine (N=64)	Tension headache (N=25)	
Age of patient (years)	28.69±9.19)	33.36±9.03)	0.033
Age of diagnosis (years)	22.75±2.44	29.16±8.84	0.001
Gender			
Male	11 (52.4%)	10 (47.6%)	0.023
Female	53 (77.9%)	15 (22.1%)	
First presentation			
Sensory	21 (63.6%)	12 (36.4%)	<0.001
Motor	-	2 (100%)	
Cerebellar	1 (16.7%)	5 (83.3%)	
Optic	36 (85.7%)	6 (14.3%)	
Trigeminal	6 (100%)	-	
EDSS			
Score 0	37 (84.1%)	7 (15.9%)	0.019
Score 1	26 (60.5%)	17 (39.5%)	
Score 2	1 (50%)	1 (50%)	

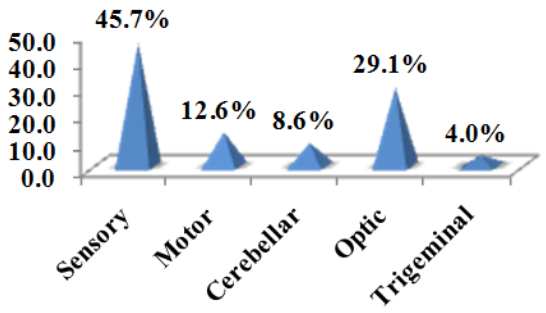

Figure No. 1: Distribution of patients with multiple sclerosis according to first presentation

DISCUSSION

This study showed a statistically significant association between having multiple sclerosis (MS) and experiencing migraine headaches, which indicates that people with MS are more likely to experience migraine headaches versus individuals who do not have MS. In the past 15 years, there has been a dramatic increase in MS, largely due to advances in understanding the basic pathophysiology of MS and the introduction of the first disease modifying therapies (DMTs) to treat this complicated disorder.[16,17] Because of the concerted effort over the last 20 years to create comprehensive longitudinal databases of MS patients, researchers now have the ability to study the effects of inherited (genetic) and non-inherited (environmental) factors on MS susceptibility and disease progression; thus improving individualization of risk assessment for persons at risk for developing MS, as well as evaluating the potential for implementing prevention strategies. Additionally, factors have been identified that provide guidance for treatment decisions; such as predicting individual responses to specific medications.[18]

Mirmosayyeb et al[19] performed a meta-analysis, which included 11,372 MS patients, and reported a total incidence of migraine headache of 31%. In addition, there was an enormous range of studies (2–67%) on how many people suffer from migraine throughout different countries with considerable differences between continents. In another meta-analysis by Wang et al[20] that analysed 3560 people with MS, the overall estimated prevalence of migraine was 27% with each individual study varying from 16.7% to 47%. Lastly, in a recent study of 18955 MS patients reviewed from a national inpatient sample database, the prevalence of migraine was 7%.[21] One reason for the variations in the frequency of the prevalence of migraine is due to case mix differences relating to age, sex, ethnicity, body mass, co-morbidities and other demographic and clinical factors.

Numerous hypotheses have been developed to explain the increased incidence of headache in MS patients, including decreased serotonin levels in the cerebrospinal fluid (CSF), decreased sympathetic nervous system activity, alterations in cytokine production and the development of B-cell (follicular) structures in the meninges and/or along the cerebral gyri.[22,23] Other studies have demonstrated a relationship between demyelinating lesions within the central nervous system (CNS). Multiple studies have correlated MS lesions by the brainstem, dorsal C2 horn, and peri-aqueductal gray matter to severe migraine headache.[24,25] The headache associated with the development of migraines in MS are due to some combination of shared genetic or environmental factors affected by hormonal fluctuations. This has been supported by studies showing that both disease activity of MS and the frequency of migraine attacks decrease in pregnancy.[26] It has been demonstrated a decrease in T8+ lymphocytes, which are believed to be among the primary cells associated with the immune response in both MS patients and headache patients, which could suggest an alteration of immunity is an additional factor.[11,15,19]

CONCLUSION

Multiple sclerosis patients have a more than 2-fold increased chance of experiencing headaches compared to the general population and may benefit from early intervention and the avoidance of known headache triggers during the initial stages of their multiple sclerosis diagnosis.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Saif Mohammed Tawfeeq Algburi, Raed M. Kathim
Drafting or Revising Critically:	Wahab Ebdan, ustafa Makki Ajam
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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