Impact of Chronic Migraine Remission on Headache-related Disability

Tarek A. Rageh, Mostafa O. Abdelazez*, Hassan M. Farweez
Neurology Department, Faculty of Medicine, Assiut University, Assiut, Egypt.
Corresponding Author: Mostafa O. Abdelazez
E-mail: mostafa1891994@gmail.com

Abstract:

Background*:* Chronic migraine (CM) is a severe neurological condition that significantly impairs personal and socioeconomic outcomes. The existing research aimed to evaluate the effect of chronic migraine remission on headache-related disability and assess the rate of chronic migraine remission.

Patients and Methods*:* This is a prospective study, which included all diagnosed CM patients according to the diagnostic criteria of chronic migraine of ICHD3, who attended the outpatient Headache Clinic, Neuropsychiatry Department at Assiut University Hospital in the period from the beginning of 2021 up to the end of 2022. Headache Sheets and clinical rating scales related to headache severity and frequency were used to assess headache patterns and the impact of headache severity among CM patients. All were followed up at 24 months.

Results*:* Out of 300 CM patients eligible for the study and complete follow-up, 27.3 % remitted CM, while 39.0% and 33.7 % had persistent CM and transitional CM, respectively. By using Migraine Disability Assessment Test (MIDAS), we found that 50.2% had moderate to severe disability. Based on Migraine Specific Quality of Life Questionnaire (MSQ) score, cases with remitting headaches at baseline had a significantly higher mean score, 59.4 ± 9.9 than those with persistent headaches 43.7 ± 10, $P < 0.001$; the same was observed after 2 years of follow-up; 67.9 ± 7 versus 40 ± 10.4, $P < 0.001$ respectively.

Conclusion: These results confirm that cases with persistent chronic migraine have persistently increased disability compared with cases with remitting chronic migraine.

Keywords: Chronic migraine (CM), remission, headache-related disability.

Introduction:

Headache is now ranked among the most common medical disorders worldwide, causing disability (1). Migraine is a common type of headache and a complex neuro-inflammatory disease. A headache, which is the primary sign of migraine, has long been connected with the condition. Two of the most common signs related to migraines are photophobia and vomiting. (2) Migraine is the most common neurological condition seen in primary care settings. The results of the most recent assessment on the Global Burden

The burden of Illness indicates that migraines are the second biggest reason for disability throughout the globe, and they are the top reason among young women. (3) 12 percent of the population is believed to suffer from migraines. There is a significant increase in global estimations. One to two percent of the world's population suffers from chronic migraine. The shift from

episodic migraine to chronic migraine occurs in around 2.5% of individuals (4).

Episodic migraine is characterized by having 0 to 14 days of migraine per month, whereas Chronic Migraine (CM) is defined as headache for at least three months, with at least 15 days of headache per month and at least 8 days of migraine per month. CM is recognized by the International Classification of Headache Disorders, ICHD-3 (5).

Headache and migraine disorders affect a person's quality of life (QoL) and contribute to an increasing economic burden on the healthcare system. Migraineurs tend to have lower socioeconomic status than those without migraines, and migraineurs lose between 15 and 20 workdays per year. This research was conducted to determine the impact of chronic migraine remission on headache-related disability & its effect on QoL, as well as to evaluate the rate of CM remission.

Patients and Methods

This prospective cohort research was performed at the Headache Outpatient Clinic, Assiut University Hospital. Three hundred CM patients attended the headache outpatient clinic of the Neuropsychiatry Department at Assiut University Hospital and continued to be followed up throughout the study period over two years. Adult Migraineurs of both sexes who fulfilled the diagnostic criteria for chronic migraine of ICHD (5), reporting an average of 15 headache days per month in the past 3 months, and meeting the International Classification of Headache Disorders were enrolled in this observational study. The research was carried out at the Assiut University Hospital Department of Neuropsychiatry in Assiut, Egypt, for two years, starting 1st January 2021 and ending 31st December 2022. Patients who had neurological diseases other than chronic migraine or other chronic medical conditions refused participation in the study, or lost follow-up, and were excluded from the study. The study adhered to the guidelines of the Assiut University Ethics Committee (**IRB** number:17101400). All enrolled patients gave informed consent before participation.

According to the dedicated sheet provided, all cases that met the diagnostic criteria underwent a complete evaluation, including a full history taking, a complete general examination, and a complete neurological examination.

Participants were assessed for depression and anxiety using standardized scales. The severity of depressive signs was assessed with the Hamilton Depression Rating Scale, often known as the HAM-D. The scale consists of several items that evaluate the existence of symptoms as well as their severity, such as depressed mood, guilt feelings, sleep disturbances, and changes in appetite. Values on HAM-D may vary anywhere from 0 to 52, with higher values suggesting signs of depression (6).

To determine the degree of signs of anxiety that were present, the Hamilton Anxiety Rating Scale was used. Signs such as tension, nervousness, shaking, & concern are evaluated using the scale comprising various questions. The scores on the HAM-A range from 0 to 56, with higher scores indicating more severe signs of anxiety (7).

The Migraine-Specific Quality of Life Questionnaire was used to evaluate the impact of chronic migraine on one's quality of life. This questionnaire consists of multiple domains that assess different aspects of quality of life, including migraines' influence on day-to-day activities, social functioning, and emotional well-being. The MSQ indicates scores for each domain, with lower scores indicating a higher degree of detrimental impact on the QoL (8).

Utilizing the Migraine Disability Assessment Scale, we evaluated the degree of disability associated with chronic migraine. This scale measures the influence that migraines have on day-to-day

functioning and productivity. It includes questions about the number of days that headaches were present, the impact of headaches on various activities, and the need to miss work or school (9).

These assessments were performed both at baseline and after a 2-year follow-up period to evaluate changes over time in depression, anxiety, disability, and quality of life.

Statistical Analysis:

All statistical calculations were done using SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 22. Data were statistically described in terms of mean ± standard deviation (±SD), or median and range when not normally distributed, frequencies (number of cases), and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using the Mann-Whitney U test as the data were not normally distributed. For comparing categorical data, a Chi-square ($\chi 2$) test was performed. The exact test was used when the expected frequency was less than 5. P-value set at 0.05 level.

Results

Out of the 300 patients with chronic migraine (CM) who attended the headache clinic between January 1, 2021, and the end of December 2022 and remained followed up, 82 cases (27.3%) had remitting CM, while 117 cases (39.0%) had persistent CM, and 101 cases (33.7%) had transition CM (Figure 1).

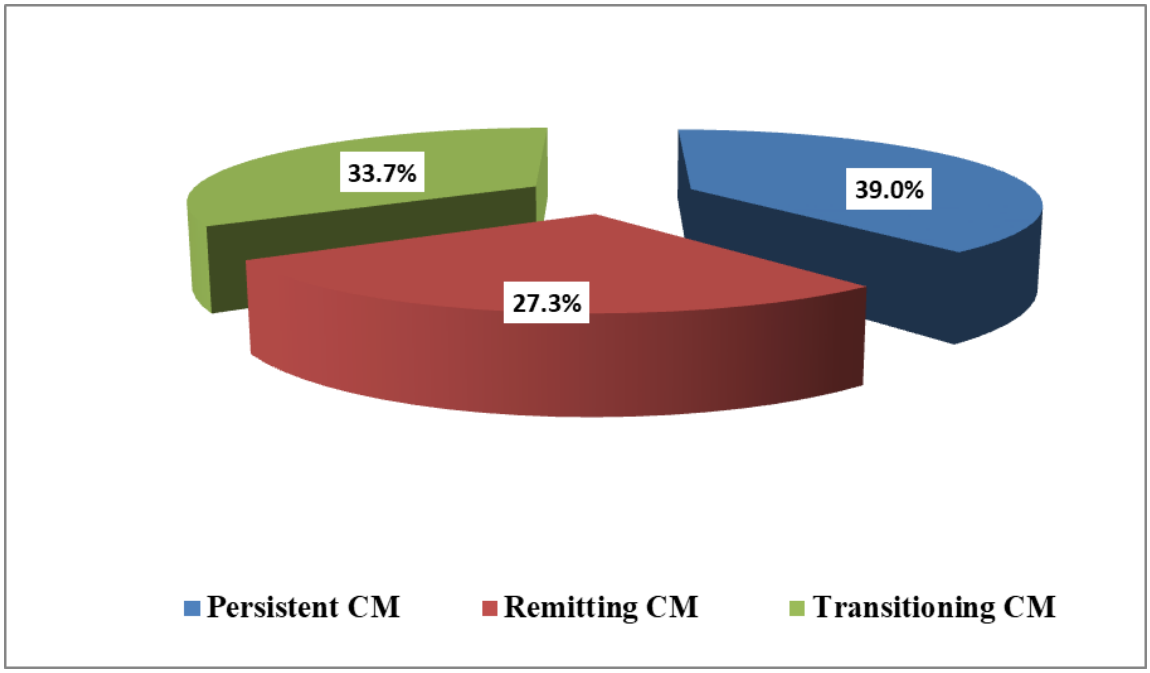

Figure 1: Two-year transition rates relative to chronic migraine status among the studied participants

Demographic Data

More than half of the cases (52.2%) were aged 18- 39 years, and the remaining cases (47.8%) were among older age groups ≥ 40 years. Most cases (83.4%) were female. Concerning BMI, the assessment revealed that overweight is 35.7%, fatty is 13.1%, and overweight is 35.7%. We observed no substantial variances among patients with persistent and remitting CM with respect to age, gender, and BMI (P=0.386, 0.088, 0.765) (**Table 1**).

Table 1: Baseline Demographics & Headache Characteristics of Cases with Recurrent & Persistent CM

Demographic data	Total (n=199)		Persistent CM (n=117)		Remitting CM (n=82)		P value
Age groups							0.386
• 18 - 29 years	52	(26.1)	31	(26.5)	21	(25.6)	
• 30 - 39 years	52	(26.1)	32	(27.4)	20	(24.4)	
• 40 - 49 years	36	(18.1)	25	(21.4)	11	(13.4)	
• 50 - 59 years	23	(11.6)	11	(9.4)	12	(14.6)	
• ≥ 60 years	36	(18.1)	18	(15.4)	18	(22.0)	
Sex							0.088
• Male	33	(16.6)	15	(12.8)	18	(22.0)	
• Female	166	(83.4)	102	(87.2)	64	(78.0)	
BMI							0.765
• Normal 18.5 - 24.9	102	(51.3)	59	(50.4)	43	(52.4)	
• Overweight 25 - 29.9	71	(35.7)	41	(35.0)	30	(36.6)	
• Obese ≥ 30	26	(13.1)	17	(14.5)	9	(11.0)	

Quantitative data are presented as mean ± SD or median (range), and qualitative data are presented as number (percentage). Significance is defined by $p < 0.05$.

HAMD

Out of 300 CM cases, 39.2% suffered from depression (38.7% had mild depression and only one had moderate depression); 37.2% were still depressed after 2 years of follow-up (36.7% had mild depression and only one had moderate depression). At baseline & after 2-year follow-up, a higher prevalence of depression was noted in instances with persistent headaches compared to those with remitting headaches ($p < 0.001$). When comparing the same groups over time, the mean HAMD score increased significantly in cases with persistent headaches and the reverse in cases with remitting headaches, $p < 0.001$, as shown in **Table 2**.

Table 2

HAMD	Total (n=199)		Persistent CM (n=117)		Remitting CM (n=82)		P value[1]
At baseline							
• Absent (< 7)	121	(60.8)	49	(41.9)	72	(87.8)	
• Mild depression (7 - 17)	77	(38.7)	68	(58.1)	9	(11.0)	**< 0.001**
• Moderate depression (18 - 24)	1	(0.5)	0	(0.0)	1	(1.2)	
• Severe depression (>25)	0	(0.0)	0	(0.0)	0	(0.0)	
• Mean ± SD	6.04 ± 3.23		7.20 ± 3.14		4.39 ± 2.59		**< 0.001**
• Median (range)	5 (2 – 20)		7 (3 – 17)		3.5 (2 – 20)		

HAMD	Total (n=199)		Persistent CM (n=117)		Remitting CM (n=82)		P value[1]
After 2 years of follow-up							
• Absent (< 7)	125	(62.8)	44	(37.6)	81	(98.8)	
• Mild depression (7 - 17)	73	(36.7)	72	(61.5)	1	(1.2)	**< 0.001**
• Moderate depression (18 - 24)	1	(0.5)	1	(0.9)	0	(0.0)	
• Severe depression (>25)	0	(0.0)	0	(0.0)	0	(0.0)	
• Mean ± SD	5.48 ± 3.91		7.79 ± 3.38		2.17 ± 1.45		**< 0.001**
• Median (range)	5 (0 – 20)		7 (1 – 20)		2 (0 – 7)		
• **P value[2]**	**< 0.001**		**< 0.001**		**< 0.001**		

HAMD: Hamilton Depression Rating Scale. Quantitative data are presented as mean ± SD or median (range), and qualitative data are presented as number (percentage). Significance is defined by $p < 0.05$.

P value[1]: for comparing the remitting versus persistent CM groups.

P value[2]: for comparing the same group over time.

HAMA: Using the **HAMA** scale, two recorded cases had mild to moderate anxiety. Patients with persistent headaches had higher mean HAMA scores at baseline and after 2 years of follow-up compared to patients with remitting headaches ($P < 0.001$). When the same groups were compared over time, as shown in **Table 3**, patients with persistent headache had significantly higher mean HAMA scores. Only one patient had mild-to-moderate anxiety.

Table 3

HAMA	Total (n=199)		Persistent CM (n=117)		Remitting CM (n=82)		P value[1]
At baseline							
• Mild severity (<17)	198	(99.5)	116	(99.1)	82	(100.0)	
• Mild to moderate severity (18 - 24)	1	(0.5)	1	(0.9)	0	(0.0)	1
• Moderate to severe (25 - 30)	0	(0.0)	0	(0.0)	0	(0.0)	
• Mean ± SD	5.06 ± 2.57		5.65 ± 2.84		4.22 ± 1.85		**< 0.001**
• Median (range)	5 (2 – 20)		5 (2 – 20)		4 (2 – 12)		
After 2 years of follow-up							
• Mild severity (<17)	197	(99.0)	115	(98.3)	82	(100.0)	
• Mild to moderate severity (18 - 24)	2	(1.0)	2	(1.7)	0	(0.0)	0.513
• Moderate to severe (25 - 30)	0	(0.0)	0	(0.0)	0	(0.0)	
• Mean ± SD	5.19 ± 3.49		7.26 ± 3.04		2.22 ± 1.22		**< 0.001**
• Median (range)	5 (0 – 19)		7 (2 – 19)		2 (0 – 6)		
• **P value[2]**	**0.012**		**< 0.001**		**< 0.001**		

HAMA: Hamilton Anxiety Rating Scale.

P value[1]: for comparing the remitting versus persistent CM groups.

P value[2]: for comparing the same group over time.

MIDAS

When the MIDAS questionnaire was used to evaluate the disability of the study subjects, it was observed that 38 (19.1%) had no or little disability, 61 (30.7%) had mild disability, 75 (37.7%) had moderate disability and the remaining 25 (12.6%) had severe disability. Both at baseline & after 2 years of follow-up, a higher severity of disability was noted in cases with persistent headaches compared to instances with remitting headaches (P < 0.001), as demonstrated in **Table 4.**

Table 4

MIDAS	Total (n=199)	Persistent CM (n=117)	Remitting CM (n=82)	P value[1]
At baseline				
• Little or no disability (0 - 5)	38 (19.1)	1 (0.9)	37 (45.1)	
• Mild disability (6 - 10)	61 (30.7)	29 (24.8)	32 (39.0)	**< 0.001**
• Moderate disability (11 - 20)	75 (37.7)	62 (53.0)	13 (15.9)	
• Severe disability (>= 21)	25 (12.6)	25 (21.4)	0 (0.0)	
• Mean ± SD	11.71 ± 6.26	14.84 ± 5.63	7.24 ± 3.99	**< 0.001**
• Median (range)	11 (2 – 25)	15 (3 – 25)	6 (2 – 20)	
After 2 years of follow-up				
• None (0 - 5)	78 (39.2)	3 (2.6)	75 (91.5)	
• Mild (6 - 10)	19 (9.5)	13 (11.1)	6 (7.3)	**< 0.001**
• Moderate (11 - 20)	55 (27.6)	54 (46.2)	1 (1.2)	
• Severe (>= 21)	47 (23.6)	47 (40.2)	0 (0.0)	
• Mean ± SD	11.81 ± 8.80	17.65 ± 6.75	3.49 ± 2.18	**< 0.001**
• Median (range)	11 (0 – 30)	17 (2 – 30)	3 (0 – 11)	
• **P value[2]**	**0.003**	**< 0.001**	**< 0.001**	

CM: Chronic Migraine.
MIDAS: The Migraine Disability Assessment Test.
P value1: For comparing the remitting versus persistent CM groups.
P value[2]: For comparing the same group over time.

MSQ

Using the MSQ questionnaire to evaluate the QoL of migraine cases, it was noted that patients with remitting headache had significantly higher mean MSQ scores than patients with persistent headaches. When comparing the same groups over time, as shown in Table 5, a substantial reduction in MSQ scores was noted in patients with persistent headaches, while a substantial increase in MSQ scores was noted from baseline to 2-year follow-up in patients with remitting headache (P < 0.001 for both groups).

Table 5

MSQ	Total (n=199)	Persistent CM (n=117)	Remitting CM (n=82)	P value[1]
At baseline				**< 0.001**
• Mean ± SD	50.16 ± 12.62	43.66 ± 9.99	59.43 ± 9.90	
• Median (range)	52 (30 – 72)	44 (30 – 69)	60 (30 – 72)	
After 2 years of FU				**< 0.001**
• Mean ± SD	51.49 ± 16.57	39.97 ± 10.44	67.93 ± 7.04	
• Median (range)	50 (25 – 78)	39 (25 – 68)	70 (48 – 78)	
• **P value[2]**	**< 0.001**	**< 0.001**	**< 0.001**	

MSQ: Migraine-specific quality. We present qualitative data as numbers (percentages). Significance is defined by $p < 0.05$.
P value1: For comparing the remitting versus persistent CM groups.
P value[2]: For comparing the same group over time.

Discussion

This research is prospective hospital-based research. Furthermore, in the estimation of the remission rate from CM to EM among CM cases attending the headache Outpatient Clinic at Assiut University Hospital from the beginning of January 2021 to the end of December 2022, we aimed to estimate the effect of remission of CM on headache-related disorders.

Not only is the quality of life diminished, but the loss of paid and unpaid workdays and productivity is also a significant socioeconomic burden. Medical costs alone are three times higher for chronic migraine cases than for episodic migraine patients, and psychiatric comorbidity is more common in CM than in EM. Epidemiological data on South Asia are scarce, but some data suggest that women and those living in rural areas have the highest disease burden (10).

Results showed that over one-third (39.0%) of patients who developed CM in the baseline year persisted at the subsequent 2-year follow-up. Conversely, true remission was seen in only 27.3% of patients with CM, and 33.7% had transitional CM. Similar to the current study, Manack and colleagues found in a 2-year study that approximately 34% of patients with CM persisted at the subsequent 2-year follow-up, true remission was seen in approximately 26% of cases with CM, and 40% had transitional CM (11).

Disability, anxiety, and depression are common risk factors for chronic migraine (12). In the current research, it was observed that cases with persistent headaches had higher disability, and poor QoL was associated with other psychiatric disorders (e.g., depression, anxiety). This finding was supported by previous studies (13).

Manack and colleagues found that persistence and remission of CM favorably affected disability: headache-related disability increased in cases with persistent CM and decreased in cases with remitting CM (11).

In comparison to those with EM, those with chronic migraine had more significant disability, a lower QOL, and higher levels of anxiety and melancholy, according to the International Burden of Migraine Research, which compiled data from some Asia-Pacific, Western European, and North

American countries (14, 15). It is well-established that CM and depression are risk factors for suicidal ideation and behavior in migraine cases (16, 17). This finding underscores the need for appropriate prevention and management to avoid such devastating consequences.

Xu and colleagues conducted a meta-analysis that additionally identified depression and anxiety as modifiable risk factors related to the transition from episodic migraine to chronic migraine (18).

In addition, cases with migraines had greater rates of anxiety, disability, and depression compared to those with tension or cluster headaches. Multiple investigations in the past have demonstrated that depression can be more severe (19), anxiety (19, 20), and disability (21) in migraine cases. Because of the higher frequency and chronicity of pain in migraine patients, anxiety, signs of depression, and disability also appear to be more intense. Zwart and colleagues and Rist and colleagues have also shown a relationship between headache frequency and depression and anxiety in migraine patients (19, 22). Some studies have also found a relationship between chronic pain and depression, anxiety, and disability in migraine patients (15, 23).

Furthermore, it was noted that after 2 years of follow-up, cases with persistent headaches had significantly higher mean scores on the HAMD, HAMA, and MIDAS and significantly lower MSQ scores. This phenomenon can be attributed to the heightened occurrence of negative emotions & effects among cases experiencing headaches; consequently, as the frequency of headache attacks increases, so does the severity of depression and anxiety among headache individuals (24). On the contrary, those who are afflicted with chronic disabling pain may experience a universal alleviation of pain-related symptoms if positive emotions, memories, and thoughts are evoked (25).

Recommendation

It is recommended that chronic migraines be treated properly to avoid their consequences on quality of life.

Conclusion

The current study identified cases with persistent CM that demonstrate a persistent increase in disability and QoL compared to patients with remitting CM.

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