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Predictors of chronic migraine remission

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Abstract

Background Chronic migraine is a debilitating neurological condition that significantly impairs both individual and socioeconomic outcomes. The aim of the present study was to estimate the remission rates of chronic migraine to episodic migraine, and to identify potential predictors of chronic migraine remission. In addition, to assess impact of chronic migraine remission on headache related disability.

Results Out of 300 individuals with chronic migraine (CM) who attended to our institution and continued for follow up in the period from the 1st of January 2021 up to the end of December 2022, approximately 82 cases (27.3%) had remitting CM, while 117 cases (39.0%) had persistent CM, and 101 cases (33.7%) had transitional CM. On multivariate model for detection of potential predictors of CM remission revealed that patients with lowest headache frequency (15–19 frequency/month) were much more likely to remit (OR = 577.826, 95% CI: 15.259 to 21,881.228, $P = 0.001$) than those with high-frequency CM (25–30 frequency/month), patients with non CM with allodynia (0–2) were more likely to remit (OR = 139.374, 95% CI: 4.634 to 419.879, $P = 0.004$) compared to those with moderate to severe CM with allodynia (≥ 6). Additionally, those using Topiramate or beta-blockers were more likely to achieve remission (OR = 23.325, 95% CI: 3.289 to 165.400, $P = 0.002$, and OR = 34.205, 95%CI: 3.591 to 325.842, $P = 0.002$, respectively), and also non-smokers were 11 times more likely to achieve remission compared to smokers (OR = 11.370, 95% CI: 1.702 to 75.934, $P = 0.012$).

Conclusion These findings identified several potential predictors of remission among patients with chronic headache. However, the majority of these prognostic factors are modifiable.

Keywords Chronic migraine, Episodic migraine, Remission

Introduction

Headache is now ranked among the most common medical diseases worldwide that cause disability [1]. Migraine is common type of headache, and one of the complicated neuro-inflammatory illnesses. It is characterized by recurring, throbbing headache pain, usually on one side of the head. Nausea and blurred vision are also common side effects. 1.4% of all neurological and mental diseases are caused by migraine headache [2]. Migraine affects an estimated 12% of the population. Global estimates are higher. Chronic migraine (CM) affects 1–2% of the global population. Approximately 2.5% of persons with episodic migraine progress to CM [3].

The International Classification of Headache Disorders—ICHD-3 defines chronic migraine as having headaches for at least 15 days per month for at least 3 months, with at least 8 days per month associated with migraine, while Episodic migraine (EM) is characterized by having migraine from 0 to 14 headache days per month. Global estimates of CM prevalence generally range from 1.4 to 2.2% [3]. While estimated prevalence of medication overuse headache varies among studies, between 0·5% and 7·2%, with a median of 1–2%, depending on the country, the nature of the study sample [4]. Chronic migraine is associated with a

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substantially greater personal and societal burden, more frequent comorbidities, and possibly with persistent and progressive brain abnormalities [5].

There is complexity in the interaction between EM and CM. While most patients with episodic migraine remain that way, 2.5% of persons with episodic migraine per year develop chronic migraine [6], while CM frequently remits to EM (26% transition rate in 2 years) [7]. Age, sex, depression, anxiety, sleep disturbance, obesity, medication compliance, medication over usage, coffee, poor income, allodynia, and other pain disorders comorbidities are some of the characteristics that have been linked to migraine chronification (predictors) [8].

Finding potential determinants of chronic migraine remission and calculating the remission rates of CM to EM are the primary objectives of the current study. Furthermore, to evaluate the effect of long-term migraine remission on headache-related disability.

The aim of the present study was to estimate the remission rates of chronic migraine to episodic migraine, to identify potential predictors of chronic migraine remission and to assess impact of chronic migraine remission on headache-related disability.

Methods

This cross-sectional study was conducted at the Outpatient Headache Clinic, Neuropsychiatric Department at Assiut University Hospital and continued for follow-up during the study period of two years, from January 2021 up to the end of December 2022. A total of 300 patients with chronic migraine who met the inclusion criteria were enrolled in the study. The inclusion criteria included patients aged ≥ 18 years who were diagnosed with chronic migraine according to the International Classification of Headache Disorders (ICHD) criteria [9]. Chronic migraine was defined as headaches occurring on 15 or more days per month for more than 3 months, with features of migraine headaches on at least 8 days per month, persistent CM was defined as headache meeting criteria of CM in 2 years of follow-up, remitting CM was defined as headache meeting criteria of episodic migraine in 2 years of follow-up, while transitional CM was defined as headache not meeting criteria of CM nor episodic migraine in 2 years of follow-up. Both male and female patients were included in the study. Patients with other neurological diseases, chronic medical conditions, or those who refused to participate or missed follow-up were excluded from the study. The study adhered to the guidelines of Assiut University's Ethical Committee (IRB no. 17101400). Eligible patients who express their willingness to participate will be asked to provide written informed consent before enrollment in the study.

All patients who met the previously mentioned criteria underwent a complete assessment, which included a full history, a complete general examination, and a full neurological examination according to the prepared specialized sheet.

The predictor variables associated with chronic migraine remission were assessed at baseline. This may include age, sex, body mass index (BMI), age of onset, medication use, coffee consumption, smoking status, headache frequency, and use of preventive medication. These variables were analyzed to identify potential predictors of remission.

Participants underwent assessments of depression and anxiety using standardized scales. The Hamilton Depression Rating Scale (HAM-D) was used to assess the severity of depressive symptoms. The scale consists of several items that evaluate the presence and intensity of symptoms such as depressed mood, guilt feelings, sleep disturbances, and changes in appetite. The scores on the HAM-D range from 0 to 52, with higher scores indicating more severe depressive symptoms [10].

The Hamilton Anxiety Rating Scale (HAM-A) was employed to measure the severity of anxiety symptoms. The scale comprises various items that assess symptoms such as tension, nervousness, trembling, and worry. The HAM-A scores range from 0 to 56, with higher scores indicating more severe anxiety symptoms [11].

The Migraine-Specific Quality of Life Questionnaire (MSQ) was utilized to evaluate the impact of chronic migraine on quality of life. This questionnaire consists of multiple domains that assess different aspects of quality of life, including the impact of migraines on daily activities, social functioning, and emotional well-being. The MSQ provides scores for each domain, with lower scores indicating a greater negative impact on quality of life [12].

Disability related to chronic migraine was assessed using the Migraine Disability Assessment Scale (MIDAS). This scale measures the impact of migraine on daily functioning and productivity. It includes questions about the number of headache days, the impact of headaches on various activities, and the need for bed rest or missed work or school. The MIDAS score ranges from 0 to 270, with higher scores indicating greater disability [13].

Additionally, the 12-item Allodynia Symptom Checklist was used to assess symptoms of allodynia, which is the experience of pain or discomfort in response to non-painful stimuli. The checklist includes items related to the presence and severity of allodynia symptoms. The scores on the checklist range from 0 to 36, with higher scores indicating a higher presence and severity of allodynia symptoms [14].

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

Data were gathered, edited, coded, and entered into the IBM SPSS (Statistical Package for Social Science, version 20). The qualitative data were presented as number (percentage) while quantitative data were presented as mean ± standard deviation (SD) or median (range). The comparison between categorical data was done by using Chi-square test or Fisher exact test when the expected frequency in any cell was less than 5. Comparison of quantitative variables was done Mann–Whitney U. Correlation between various variables was done using Pearson correlation test. Odds ratio (OR) with 95% Confidence Interval (CI) and Logistic Regression was calculated for prediction of CM remission. *P*-value set significant at 0.05 level.

Results

Out of 300 individuals with chronic migraine (CM) who attended to our institution and continued for follow-up in the period from the 1st of January 2021 up to the end of December 2022, approximately 82 cases (27.3%) had remitting CM, while 117 cases (39.0%) had persistent CM, and 101 cases (33.7%) had transitional CM (Fig. 1).

More than half of the studied cases (52.2%) aged less than 40 years old, 18.1% aged 40–49 years, 11.6% aged 50–59 years, and 18.1% aged ≥ 60 years. Out of 199 studied participants, 33 cases (16.6%) were males, and 166 cases (83.4%) were females. About half of the studied cases (51.3%) have normal BMI, 71 cases (35.7%) had overweight, and 13.1% were obese. No significant difference was observed between patients with persistent and remitting CM regarding to their age, sex, BMI, and age of onset ($P > 0.05$, for all).

Meanwhile, a higher prevalence of persistent headaches was observed between patients receiving Acetaminophen, NSAIDs, Ergotamine, Triptans, combined OTC, or OTC overuse. Also, a higher prevalence of persistent headache was observed between patients drinking coffee, smokers, those with higher headache frequencies, and those with higher allodynia ($P < 0.05$ for all). In addition, patients receiving current preventive therapy, beta blockers, or topiramate have a lower prevalence of persistent headaches ($P < 0.05$ for all) (Table 1).

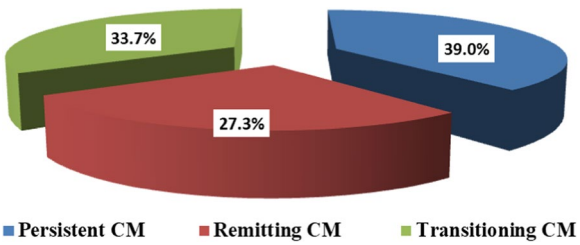

Fig. 1 Two-year transition rates relative to chronic migraine status among the studied participants

Regarding to depression (according to HAMD questionnaire); 39.2% suffered from depression (38.7% had mild depression, and only one case had moderate depression). After 2 years of follow-up, 37.2% still suffered from depression (36.7% had mild depression, and only one had moderate depression). Higher prevalence of depression was observed among patients with persistent headache at baseline and after 2 years of follow-up as compared to patients with remitting headache ($P < 0.001$).

Regarding to anxiety (according to HAMA questionnaire), only one case suffered from mild to moderate anxiety. After 2 years of follow-up, two cases were suffered from mild to moderate anxiety. Patients with persistent headache have higher mean HAMA score, at baseline and after 2 years of follow-up, as compared to patients with remitting headache ($P < 0.001$).

By assessing disabilities among the studied participants using MIDAS questionnaire, we observed that, 38 cases (19.1%) had no or little disability, 61 cases (30.7%) had mild disability, 75 cases (37.7%) had moderate disability, and 25 cases (12.6%) had severe disability. Higher severity of disabilities was observed among patients with persistent headache compared to patients with remitting headache both at baseline and after 2 years of follow-up, as ($P < 0.001$).

To assessing the quality of life (QOL) among migraine patients, we used MSQ questionnaire and we observed that patients with remitting headache have significantly higher mean MSQ score compared to patients with persistent headache (at baseline; median (range) was 44 (30–69) versus 60 (30–72), $P < 0.001$), and after 2 years of follow-up; median (range) was 39 (25–68) versus 70 (48–78), $P < 0.001$) in both studied groups, respectively (Table 2).

Table 3 summarizes potential predictors of CM remission among the studied participants. Those with lowest headache frequency (15–19 frequency/month) were much more likely to remit (OR = 577.826, 95% CI: 15.259 to 21,881.228, $P = 0.001$) than those with high-frequency CM (25–30 frequency/month). Those with non CM with allodynia (0–2) were more likely to remit (OR = 139.374, 95% CI: 4.634 to 419.879, $P = 0.004$) compared to those with moderate to severe CM with allodynia (≥ 6).

Additionally, those using Topiramate or beta-blockers were more likely to achieve remission (OR = 23.325, 95%

Table 1 Baseline demographic characteristics and susceptible risk factors for persistent CM

Demographic data	Total ($n=199$)		Persistent CM ($n=117$)		Remitting CM ($n=82$)		*P* value
Age groups							
18–29 years	52	(26.1)	31	(26.5)	21	(25.6)	0.386
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							
Male	33	(16.6)	15	(12.8)	18	(22.0)	0.088
Female	166	(83.4)	102	(87.2)	64	(78.0)	
BMI							
Normal 18.5–24.9	102	(51.3)	59	(50.4)	43	(52.4)	0.765
Overweight 25–29.9	71	(35.7)	41	(35.0)	30	(36.6)	
Obese ≥ 30	26	(13.1)	17	(14.5)	9	(11.0)	
Risk factors							
Age of onset groups							
18–29 years	84	(42.2)	53	(45.3)	31	(37.8)	0.534
30–39 years	42	(21.1)	26	(22.2)	16	(19.5)	
40–49 years	29	(14.6)	17	(14.5)	12	(14.6)	
50–59 years	24	(12.1)	12	(10.3)	12	(14.6)	
≥ 60 years	20	(10.1)	9	(7.7)	11	(13.4)	
Medication							
Acetaminophen use	142	(71.4)	101	(86.3)	41	(50.0)	**< 0.001**
NSAID use	134	(67.3)	99	(84.6)	35	(42.7)	**< 0.001**
Ergotamine use	90	(45.2)	69	(59.0)	21	(25.6)	**< 0.001**
Triptans use	136	(68.3)	92	(78.6)	44	(53.7)	**< 0.001**
Barbiturates use	35	(17.6)	24	(20.7)	11	(13.3)	0.174
Opiates use	26	(13.1)	18	(15.5)	8	(9.6)	0.255
Combined OTC use	157	(78.9)	110	(94.0)	47	(57.3)	**< 0.001**
OTC overuse	91	(45.7)	81	(69.2)	10	(12.2)	**< 0.001**
Prescription overuse	130	(65.3)	71	(60.7)	59	(72.0)	0.100
Drink coffee							
No	79	(39.7)	35	(29.9)	44	(53.7)	**0.001**
Yes	120	(60.3)	82	(70.1)	38	(46.3)	
Smoking							
No	73	(36.7)	33	(28.2)	40	(48.8)	**0.003**
Yes	126	(63.3)	84	(71.8)	42	(51.2)	
Headache frequency/month							
15–19	51	(25.6)	1	(0.9)	50	(61.0)	**< 0.001**
20–24	52	(26.1)	22	(18.8)	30	(36.6)	
25–30	96	(48.2)	94	(80.3)	2	(2.4)	
Allodynia at baseline							
None (0–2)	64	(32.2)	3	(2.6)	61	(74.4)	**< 0.001**
Mild (3–5)	60	(30.2)	40	(34.2)	20	(24.4)	
Moderate (6–8)	61	(30.7)	60	(51.3)	1	(1.2)	
Severe (≥ 9)	14	(7.0)	14	(12.0)	0	(0.0)	

Table 1 (continued)

Demographic data	Total ($n=199$)		Persistent CM ($n=117$)		Remitting CM ($n=82$)		*P* value
Allodynia after follow up							
None (0–2)	72	(36.2)	4	(3.4)	68	(82.9)	**< 0.001**
Mild (3–5)	53	(26.6)	39	(33.3)	14	(17.1)	
Moderate (6–8)	59	(29.6)	59	(50.4)	0	(0.0)	
Severe (≥ 9)	15	(7.5)	15	(12.8)	0	(0.0)	
Preventive medication							
Current preventive use	125	(62.8)	64	(54.7)	61	(74.4)	**0.005**
Amitryptylline use	85	(42.7)	44	(37.6)	41	(50.0)	0.082
Valproic acid use	27	(13.6)	15	(12.8)	12	(14.6)	0.713
Beta blocker use	43	(36.1)	16	(13.8)	27	(32.5)	**0.002**
Topiramate use	70	(35.2)	22	(18.8)	48	(58.5)	**< 0.001**
Anti-depressants use	37	(18.6)	19	(16.2)	18	(22.0)	0.308

Data are presented as number (percentage). Significance defined by $P<0.05$

BMI body mass index, *CM* chronic migraine

CI: 3.289 to 165.400, $P=0.002$, and OR = 34.205, 95%CI: 3.591 to 325.842, $P=0.002$, respectively).

Also non-smokers were 11 times more likely to achieve remission compared to smokers (OR = 11.370, 95% CI: 1.702–75.934, $P=0.012$).

Discussion

In the general population, the prevalence of CM ranges from 1 to 4%; it affects women more frequently than males and peaks between the ages of 18 and 50. CM not only results in a lower QOL but also has a large socioeconomic cost due to lost productivity and working days [15]. Investigating the risk factors of headache frequency in CM is crucial for identifying associated factors and optimizing treatment paradigms. Only a small number of studies document CM remission [16].

Findings in the current study indicate that more than one-third (39.0%) of sufferers with CM in a baseline year continue persistent over the subsequent 2 years of follow-up. Conversely, true remission occurs in only 27.3% of those with CM, and 33.7% had transitional CM.

Transitioning CM is defined as migraine that met CM criteria at baseline and either CM, low-frequency EM (LFEM), high-frequency EM (HFEM), chronic or episodic tension-type headache, probable migraine, no headache, or other episodic headache in subsequent years and did not meet persistent or remitting CM criteria [17].

Given that CM sometimes persists and sometimes remits, factors predicting remission were evaluated. Headache frequency per month, CM associated with allodynia, using medications as Topiramate or Beta-blockers, and smoking status were significant predictors for persistence or achieving remission among sufferers with CM.

Headache frequency was a significant independent predictor of CM remission, with higher headache frequency associated with lower rates of remission. This finding could be attributed to the fact that more frequent headaches were linked to more days with moderate-to-severe headaches, more frequent use of acute headache medications, more headache-related disability, and ultimately a lower QOL [18]. In contrast, a reduction in headache frequency may also translate into improvements in health-related QOL [19]. Thus, patients with higher headache frequency have a poorer outcome.

However, evidence from previous studies was contradictory. Similar findings were reported by [7, 20, 21] who reported that lower baseline headache frequency was a significant predictive factor for the remission of chronic migraine. Moreover, it was found to be linked to a decrease in migraine days at follow-up but also to an increased risk of allodynia and more drug use days [22]. Also, recently Henning and colleagues reported that there was a lower chance of remission for participants whose baseline headache frequency was higher (0.90, 0.84–0.97) [16].

Conversely, research showed that there was no difference in the incidence of headaches between those who responded and those who did not to preventive treatment [23], and higher baseline headache frequency did not predict treatment-induced remission of chronic migraine [24].

Evidence has accumulated that migraine progression and disability are influenced also by cutaneous allodynia, the perception of non-noxious thermal or mechanical stimuli as painful [25]. It was reported that allodynia

Table 2 Difference in the HAMD, HAMA, MIDAS, and MSQ questionnaires at baseline and after 2 years of follow-up among respondents with persistent CM versus those with remitting CM

Questionnaires	Total ($n=199$)		Persistent CM ($n=117$)		Remitting CM ($n=82$)		*P* value
1. HAMD							
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)	
Median (range)	5 (2–20)		7 (3–17)		3.5 (2–20)		**< 0.001**
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)	
Median (range)	5 (0–20)		7 (1–20)		2 (0–7)		**< 0.001**
2. HAMA							
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)	
Median (range)	5 (2–20)		5 (2–20)		4 (2–12)		**< 0.001**
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)	
Median (range)	5 (0–19)		7 (2–19)		2 (0–6)		**< 0.001**
3. MIDAS							
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)	
Median (range)	11 (2–25)		15 (3–25)		6 (2–20)		**< 0.001**
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)	
Median (range)	11 (0–30)		17 (2–30)		3 (0–11)		**< 0.001**
4. MSQ							
At baseline							
Median (range)	52 (30–72)		44 (30–69)		60 (30–72)		**< 0.001**
After 2 years of follow-up							
Median (range)	50 (25–78)		39 (25–68)		70 (48–78)		**< 0.001**

HAMD Hamilton Depression Rating Scale, *HAMA* Hamilton Anxiety Rating Scale, *MIDAS* Migraine Disability Assessment Test, *MSQ* Migraine specific quality. Data are presented as median (range), or number (percentage). Significance defined by $P < 0.05$

affected 63% of migraineurs in the population and was associated with female sex, frequency, severity, and most of the diagnostic symptoms of migraine [26]. In the current study, the prevalence estimates of allodynia among our studied cases were 67.9%. Also, we observed that allodynia is more common and more severe in

Table 3 Multivariate model for potential predictors of CM remission

Variables	Multivariate analysis		
	OR	95% CI	*P* value
Headache frequency/month			
15–19	577.826	15.259–21,881.228	**0.001**
20–24	35.726	2.471–516.597	**0.009**
25–30	1		
Allodynia			
Non (0–2)	139.374	4.634–419.879	**0.004**
Mild (3–5)	4.642	0.259–83.147	0.297
Moderate to severe (≥ 6)	1		
Drink coffee			
No	4.323	0.945–19.781	0.059
Yes	1		
Topiramate use			
No	1		
Yes	23.325	3.289–165.400	**0.002**
Beta-blockers use			
No	1		
Yes	34.205	3.591–325.842	**0.002**
Smoking			
No	11.370	1.702–75.934	**0.012**
Yes	1		

CI confidence interval, *OR* odds ratio. *P* value is significant ≤ 0.05

individuals with persistent migraine compared with those with remitting migraine. This finding was confirmed in the logistic regression analysis as we observed that patients with non-CM with allodynia (0–2) were more likely to remit (OR = 69.557, 95% CI: 4.013–1205.592, $P = 0.004$) compared to those with moderate to severe CM with allodynia (≥ 6). In line with this finding, Manack and colleagues stated that the absence of allodynia has been shown to be associated with remission [7], and Louter and colleagues reported that allodynia is more common in those with chronic migraine than in people with episodic migraine and suggests a higher risk of migraine chronification [22].

Medication overuse (use of acute medications on more than 10 or 15 days per month, depending on the medication class) is common among people with CM. For some people with migraine, despite taking greater amounts of acute headache medication, they develop an increase in monthly headache days [27]. In the current study, we observed that regular intake of analgesics was associated with persistent migraine. However, regression analysis revealed that medication utilization by class, and OTC/prescription overuse did not significantly predict CM remission. Similar finding was reported by Manack and colleagues [7].

Evidence for the efficacy of oral agents in CM is generally extrapolated from studies in patients with high-frequency EM [28]. Thus, preventive treatment is intended to facilitate the transition from CM to EM, but the real-world benefits of this remission have yet to be quantified. In the present study, the current use of preventive medications facilitated the achievement of remission. In the regression analysis model, we observed that those using Topiramate were more likely to achieve remission (OR = 12.561, 95% CI: 2.736–57.672, $P = 0.001$). Thus, we suggested that preventive medications may also increase remission rates, but effects may be offset by other unmeasured or inadequately measured confounders.

In line with the current study, Manack and colleagues reported that the use of preventive medications was associated with a lower rate of remission [7]. The author explains this finding as follows: persons with CM who receive preventive medication may be more likely to have other factors, such as high attack frequency, associated with a reduced chance of remission [7].

The most popular class of medications for treating migraines in prevention are beta-blockers, which can reduce migraine frequency by more than 50% with an efficacy of roughly 50%. The effectiveness of metoprolol, a selective beta1-blocker, and propranolol, a nonselective beta-blocker, has been repeatedly shown by evidence. Atenolol, nadolol, timolol, and bisoprolol are also shown to be effective [29]. This comes in agreement with the current finding as we observed that receiving Beta-blockers was effective in achieving remission among the studied cases.

Caffeine can cause migraine headaches by increasing urinary magnesium loss, most likely by inhibiting magnesium reabsorption. Caffeine may cause headaches by reducing magnesium levels, which affects neuromuscular conduction and nerve transmission and is beneficial in chronic pain syndromes including migraines. One probable migraine trigger is dehydration. Caffeinated coffee, in higher dosages, has an acute diuretic effect, which can lead to dehydration [30]. This could explain the current finding that drinking coffee was more prevalent among patients with persistent headache, and patients not drinking coffee were four times more likely to achieve remission in regression analysis model, with borderline significance. Similar finding was reported by previous literature [8].

It was discovered that smoking and migraines were related. A retrospective examination of data from the annual health survey revealed a positive correlation between the prevalence of migraines and daily smoking [31]. There is debate over the pathophysiology of smoking and nicotine use in the beginning of migraines,

as both substances directly affect the central nervous system [32]. In the present study, smoking was found to be associated with persisting headache. Participants who did not smoke were more likely to experience remission of migraine. Similar finding was reported by Gong Q and colleagues [33].

Disability, anxiety, and depression are common risk factors of chronic migraine [34]. In the current study, we observed that patients with persistent headache suffered from higher disabilities, lower quality of life (QOL), and associated with other psychiatric comorbidities as depression, anxiety. This finding was supported by previous studies [35].

Manack and colleagues showed that disability is significantly influenced by persistence and remission. Remitted CM patients showed reductions in headache-related disability, but those with persistent CM showed increases in headache-related disability [7].

Patients with CM showed more impairment, a lower quality of life, and higher levels of anxiety and depression than those with EM, according to data gathered by the International Burden of Migraine Study (IBMS) from multiple countries in Western Europe, North America, and the Asia/Pacific areas [36, 37]. Also in line with the current study, the recent meta-analysis of Xu and colleagues reported that depression, anxiety are among modifiable risk factors for the transformation of EM to CM [38].

In fact, CM and depression are recognized risk factors for suicidal thoughts or behaviors in those who suffer from migraine [39, 40]. This finding highlights the need for proper prevention and management to avoid these catastrophic outcomes.

Conclusion

The current study identified several potential predictors for persistence or remission among patients with CM. Headache frequency per month, CM associated with allodynia, using medications as Topiramate or beta-blockers, and smoking status were significant predictors for achieving remission among sufferers with CM. The majority of these prognostic factors are modifiable. The results further emphasize the necessity for conducting further long-term studies on the prognostic variables for chronic headaches.

Abbreviations

ASC	Allodynia symptom checklist
BMI	Body mass index
CDH	Chronic daily headache
CI	Confidence interval
CM	Chronic migraine
CRP	C-reactive protein
CT	Computed tomography
EM	Episodic migraine
Ham-A	Hamelton anxiety rating scale
Ham-D	Hamelton depression rating scale
HFEM	High-frequency episodic migraine
HIT	Headache impact test
IBMS	International burden of migraine study
ICHD	International classification of headache disorders
IRB	Institutional review board
LFEM	Low-frequency episodic migraine
MIDAS	Migraine disability assessment test
MOH	Medication overuse headache
MRI	Magnetic resonance imaging
MSQ	Migraine specific quality of life questionnaire
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
OTC	Over the counter
QOL	Quality of life

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Author contributions

TR recruited participants, analysis, and interpreted data, and contributed in writing the manuscript. AH wrote the manuscript and analysis of data. MA and HF; recruited participants, helped in data entry, analysed, and generated result sheets and revised data interpretation and manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study adhered to the guidelines of Assiut University's Ethical Committee (IRB no: 17101400). All enrolled cases were provided an informed written consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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