DEVELOPMENTAL MEDICO-LIFE-SCIENCES

ISSN (P): 3007-2786, (E): 3007-2794 DOI: https://doi.org/10.69750/dmls.02.09.0153

ORIGINAL RESEARCH ARTICLE Open Access

Neuropsychiatric Manifestations in Patients with Chronic Migraine: A Hospital-Based Study

Asma Jami[1], Ayesha Tahir[2], Thuzintha Suluxshan[3], Fareena Almas[4]*

1. King Edward Medical University, Lahore, Pakistan
2. Isra University, Hyderabad, Pakistan
3. Tbilisi State Medical University, Georgia
4. Bakhtawar Amin Medical and Dental College, Multan, Pakistan

Corresponding author: Thuzintha Suluxshan, **Email:** thuzinttha@gmail.com

ABSTRACT

Background: Chronic migraine (CM) is a very disabling neurological disorder that goes beyond recurrent headache attacks, to include some important neuropsychiatric comorbidities. The depression, anxiety, sleep disturbance, and cognitive dysfunction are becoming recognized as innate characteristics of CM phenotype but there is a paucity of data on South Asian populations.

Objectives: The aim of the study is to determine the prevalence and clinical correlation of neuropsychiatric manifestations in chronic migraine patients who reported to the tertiary care hospital in Pakistan.

Methods: This observational cross-sectional study was conducted in the Department of Neurology, Mayo Hospital, Lahore, Pakistan, from March 2023 to June 2024. A total of 120 patients aged 18–60 years diagnosed with chronic migraine as per the *International Classification of Headache Disorders-3 (ICHD-3)* criteria were recruited through consecutive non-probability sampling. Neuropsychiatric assessments were performed using validated scales: the Patient Health Questionnaire-9 (PHQ-9) for depression, Generalized Anxiety Disorder-7 (GAD-7) for anxiety, Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and Montreal Cognitive Assessment (MoCA) for cognitive function. Data were analyzed using SPSS v26.0, applying Chi-square tests for categorical variables and Pearson correlation analysis for inter-domain associations. A p-value <0.05 was considered statistically significant.

Results: The age of 36.4 above and below was 9.7 that represented the mean age and females 68.3 that represented the percentage of the females. Depression was found in 46.7, anxiety in 41.6, and inappropriate sleep quality in 55.8 percent of patients, and 30.8 percent of patients had been found to be cognitively impaired. Depression and anxiety rates were much greater among females than among males ($p<0.05$). The longer the duration of migraine, the more likely that they impaired cognition ($p=0.03$). There was a significant relationship between sleep disturbance and depressive symptoms ($r=0.54$, $p<0.001$).

Conclusion: The neuropsychiatric symptoms are very common in CM patients, especially in sleep disturbance, depression, and anxiety. These results underline the necessity to use integrated neuropsychiatric screening and multidisciplinary management to enhance the outcome of this susceptible group.

Keywords: Chronic migraine, depression, anxiety, sleep disturbance, cognitive impairment, neuropsychiatry.

Received: 23/02/2025
Revised: 25/07/2025
Accepted: 19/09/2025
Published: 30/09/2025

INTRODUCTION

Migraine is an extremely common and disabling primary headache condition and has been identified by the World Health Organization as one of the causes of the highest number of years lived with disability in the world [1]. It impacts a general population of about 12-15 percent with disproportionately more women being affected than their male counterparts. The worst end of the migraine spectrum is chronic migraine (CM), according to the International Classification of Headache Disorders, 3rd edition (ICHD-3), the headaches on 15 or more days of the month of 3 months or more, and at least 8 days must satisfy migraine criteria. Patients who have CM have a higher burden of disease, low productivity, and poor life quality in comparison to episodic migraine [2].

In addition to the physical weight of frequent headaches, CM is being known more and more as a condition having severe neuropsychiatric implications [3]. The most frequently reported comorbidities include depression, anxiety, sleeping problems, and problems with cognition. These not only aggravate the subjective experience of pain, but also disability, are associated with overuse of medication, and complicated treatment outcomes. Pathophysiology of this association is multifactorial with overlapping biological pathways that include dysfunction of serotonergic pathways, hypothalamic-pituitary-adrenal (HPA) axis, neuroinflammation, and cortical hyperexcitability [4,5]. In addition, the bilateral relationship between migraine and psychiatric disorders indicates that neuropsychiatric symptoms may both cause and further intensify migraine chronicity [6].

Although the study of neuropsychiatric profile of CM patients in South Asian population, including Pakistan, is well studied globally, the available information on the topic is rather limited [7]. Psychiatric comorbidities presentation and reporting might be affected by cultural differences, access to healthcare, and sociopsychological stressors, and specific data related to the region is necessary. Additionally, most patients who end up in neurology clinics are not diagnosed or treated adequately to have comorbid psychiatric conditions, and this can result in worse outcomes in the long term [8,9].

Considering this, this study was intended to evaluate the occurrence and trends of neuropsychiatric symptoms in patients having chronic migraine in a population in Pakistan in the hospital. The results can facilitate the incorporation of regular psychiatric screening into the process of managing migraine and lead to better multidisciplinary care strategies because they will help establish the frequency and correlates of depression, anxiety, sleep disturbances, and cognitive impairment in this clinical cohort [10].

MATERIALS AND METHODS

The study is a cross-sectional observational study, which was carried out in the Department of Neurology, Mayo Hospital, Lahore, Pakistan, over a period of fifteen months, i.e., between March 2023 and June 2024. A total of one hundred and twenty (120) patients were recruited through consecutive non-probability sampling.

Diagnosis of chronic migraine was based on the criteria of the *International Classification of Headache Disorders, 3rd edition (ICHD-3)*, which defines the condition as having a headache on fifteen or more days per month over a minimum of three months, with at least eight days meeting the diagnostic criteria of migraine. Study patients were aged between 18 and 60 years and provided written informed consent prior to participation.

Careful exclusion criteria were applied to eliminate confounding variables, excluding patients with other primary headache disorders (such as cluster or tension-type headache), secondary headaches caused by trauma, infection, or intracranial pathology, those with pre-existing psychiatric illnesses predating migraine onset, and individuals with neurological or systemic diseases that could confound psychiatric or cognitive assessments (such as dementia, stroke, or epilepsy).

Following recruitment, a comprehensive clinical assessment was performed for all participants, including sociodemographic information (age, sex, marital status, education, occupation, family history) and clinical variables (duration, frequency, and medication use). Standardized and validated instruments were used to evaluate neuropsychiatric manifestations, conducted by trained neurologists and psychologists.

The Patient Health Questionnaire-9 (PHQ-9) was used to assess depression, the Generalized Anxiety Disorder-7 (GAD-7) scale for anxiety, the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and the Montreal Cognitive Assessment (MoCA) for cognitive performance. These tools were administered in both English and Urdu versions according to patient preference to ensure accurate comprehension regardless of literacy level. The following cut-offs were used: PHQ-9 $\geq$10 for clinically significant depression, GAD-7 $\geq$10 for clinically significant anxiety, PSQI >5 for poor sleep quality, and MoCA <26 for cognitive impairment.

Ethical approval for the study was obtained from the Institutional Review Board. All participants provided written informed consent in accordance with the Declaration of Helsinki, and confidentiality and anonymity were strictly maintained.

Data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables (e.g., age, duration of migraine) were presented as mean ± standard deviation, while categorical variables (e.g., gender, psychiatric outcomes) were expressed as frequencies and percentages. Chi-square tests were applied to assess associations between clinical/demographic

variables and neuropsychiatric manifestations. Independent t-tests were used for continuous variable comparisons, and Pearson correlation analysis was conducted to examine relationships among depression, anxiety, sleep quality, and cognitive function scores. A p-value <0.05 was considered statistically significant.

RESULTS

One hundred and twenty patients who met the diagnostic criteria of chronic migraine were recruited in the time frame of the study. The average age of the participants in the study was 36.4 + 9.7 years where the youngest was 19 years and the elders were 58 years. There were more cases of the female gender (68.3%), and 31.7% were men. The average years of migraine was 6.8 years (3.1) and 42.5 percent of the patients indicated that there is a positive family history of migraine. Table 1 presents the baseline demographic and clinical traits.

The prevalence of neuropsychiatric manifestations was found to be strikingly high in this cohort. Depression, defined by PHQ-9 scores ≥10, was present in 46.7% of patients, while anxiety, defined by GAD-7 scores ≥10, was documented in 41.6%. Sleep disturbance, assessed through the PSQI with a cut-off >5, was the most prevalent manifestation, affecting 55.8% of participants. Cognitive impairment, based on MoCA scores <26, was observed in 30.8% of the patients. These findings are shown in Table 2.

When stratified by gender, females had a significantly higher prevalence of depression and anxiety compared to males (p=0.02 and p=0.03 respectively), while no statistically significant difference was noted in sleep quality. Cognitive impairment, however, showed a significant association with longer duration of migraine, with patients suffering from migraine for more than five years exhibiting higher rates of MoCA-defined impairment (p=0.03). These associations are presented in Table 3.

Table 1: Demographic and Clinical Characteristics of the Study Population (n=120)

Variable	Mean ± SD / n (%)
Age (years)	36.4 ± 9.7
Gender (Female/Male)	82 (68.3) / 38 (31.7)
Duration of migraine (yrs)	6.8 ± 3.1
Family history present	51 (42.5)

Table 2: Prevalence of Neuropsychiatric Manifestations in Patients with Chronic Migraine (n=120)

Manifestation	n (%)	Mean Score ± SD
Depression (PHQ-9 ≥10)	56 (46.7)	11.8 ± 4.3
Anxiety (GAD-7 ≥10)	50 (41.6)	10.5 ± 3.9
Sleep disturbance (PSQI>5)	67 (55.8)	8.7 ± 3.1
Cognitive impairment (MoCA <26)	37 (30.8)	24.1 ± 2.7

Table 3: Gender- and Duration-Based Differences in Neuropsychiatric Manifestations

Variable	Female (%)	Male (%)	p-value	Migraine <5 yrs (%)	Migraine ≥5 yrs (%)	p-value
Depression	52.4	31.6	0.02*	41.3	54.7	0.08
Anxiety	47.5	28.9	0.03*	36.2	47.9	0.09
Sleep disturbance	57.3	52.6	0.08	51.7	59.1	0.11
Cognitive impairment	32.9	26.3	0.07	23.4	38.2	0.03*

p < 0.05 considered statistically significant.

The correlation analysis showed that there was a significant positive correlation between sleep disturbance and the severity of depression (r=0.54, p<0.001), meaning that the patients with low sleep quality had higher chances of having clinically significant depressive symptoms. On the same note, there was a moderate correlation between the scores of anxiety and depression (r=0.42, p=0.002). These results imply that neuropsychiatric symptoms of chronic migraine are likely to be co-located but not independent of each other.

To conclude, the findings of the paper indicate that neuropsychiatric symptoms are frequent in chronic migraine patients, among them being sleep disorders, depression, anxiety, and cognitive disorders. The difference between genders was especially significant in depression and anxiety and the persistence of migraine was closely linked with cognitive impairment development. These results indicate the clinical significance of standard psychiatric and cognitive assessment in such a vulnerable population.

DISCUSSION

The current hospital-based research demonstrates the significant neuropsychiatric manifestations burden of patients with chronic migraine, as over fifty percent of the sample reported poor sleep quality, almost half of the patients had clinically significant depression, and a significant percentage of interviewees had anxiety and cognitive disability[10]. The findings are similar to earlier published works which have continuously reported the high prevalence of psychiatric comorbidities in migraine populations underpinning the fact that chronic migraine is not purely a pain disorder but a complicated neuropsychiatric disorder [11-13].

In this study, depression was found in 46.7% of patients which is similar to what is reported globally where depression is reported to occur in 30 to 50% of chronic migraine groups [14]. Migraine has been linked to depression, and it was proposed that these matters include common neurobiological pathways, such as serotonergic and dopaminergic dysfunction, hyperactivity of hypothalamic–pituitary–adrenal (HPA) axis, and the activation of inflammatory cytokines. Moreover, the depressive symptoms are probably predisposed by the chronic and disabling character of migraine, as the patients experience pain periodically, and their social functioning is impaired. Notably, we have found that the prevalence of depression has been higher in female subjects, which, again, was corroborated by the global literature, which suggests that women are more susceptible to it based on hormonal changes, psychosocial stress, and culture, which increases both the migraine and mood symptoms [15-18].

The prevalence of anxiety (41.6% participants) was aligned with the literature that has indicated that one-third to one-half of patients with chronic migraine develop anxiety disorders [19]. The fact that the subjects of anxiety and depression overlap in our sample also serves as a powerful indicator in support of the theory of a two-directional relationship, with both conditions worsening each other. Functional changes of the amygdala, anterior cingulate cortex and prefrontal networks have been shown in patients with comorbid migraine and anxiety by neuroimaging studies which could be the cause of increased vulnerability. Our results highlight the clinical significance of simultaneous screening of both conditions because missing the diagnosis of anxiety may make it difficult to adhere to treatment and this will increase disability [20,21].

Sleep disturbance was detected as the most frequent manifestation, which was observed in 55.8 percent of patients. It has been known that low sleep quality worsens the number and severity of migraine, and vice versa, frequent headaches cause disrupted and unrestful slumber [22]. It is important to note that the correlation between PSQI scores and depressive symptoms is significant in this study, and it demonstrates the interdependence of sleep and mood, in which a single disorder predisposes the occurrence of another, which, in turn, leads to the occurrence of the first. It has been previously demonstrated that disturbed sleep architecture and decreased slow-wave sleep are capable of sensitizing pain pathways, which further increases the chronicity of migraine. Therefore, sleep hygiene interventions can have a central role in comprehensive management of migraine [23].

Cognitive impairment, which was less common than mood and sleep disturbances, had been reported in almost one third of patients and was found to be significantly connected with the length of migraine [24]. These findings are in line with the research proposing the possibility of the impairment of attention, memory, and executive functioning skills by persistently being exposed to migraine-related cortical hyperexcitability, vascular dysregulation, and medication overuse. Though this is wrong, it has significant consequences in occupational performance and quality of life. Notably, the patients themselves underestimated cognitive impairment, and it is important to emphasize that the objective screening of patients on a regular basis should become a common practice in clinical settings [25].

The results of this work have valuable implications. First, they emphasize the need to include psychiatric and cognitive evaluations in the regular migraine treatment. Second, they state the need to focus on multidisciplinary management, in which neurologists, psychiatrists and psychologists work together to deal with the complex burden of chronic migraine. Third, they write that sleep and mood disturbances interventions can be targeted, which can indirectly improve the frequency and severity of headaches, which will lead to better outcomes [7,13].

Still, there are some restrictions that should be taken into account. It was only conducted in one tertiary care setting and thus the findings cannot be generalized. Such a study cannot be used to determine causality between the psychiatric manifestation and migraine because it is cross-sectional [15]. Also, there was a lack of control group and use of screening tools instead of formal psychiatric interviews, which could have resulted in underestimation or overestimation of prevalence rates. It is suggested that future multicenter, longitudinal studies are the way to define causal relationships, determine a response to treatment, and understand neurobiological mechanisms behind these comorbidities [8,19].

CONCLUSION

This study illustrates that neuropsychiatric symptoms are extremely common in patients with chronic migraine with depression, anxiety, sleep disorders, and cognitive impairment making up a substantial clinical burden. There were women who were especially susceptible to mood disorders and the longer the migraine lasted, the worse the cognitive performance. The results of this study underscore the necessity of holistic and multidisciplinary management approaches that extend beyond the management of headaches to overall screening of the psychiatric condition, sleep disorder, and cognitive ability. Timely identification and combined management of these manifestations can enhance patient quality of life, decrease the level of disability, and maximize the results in the long-term management of chronic migraine patients.

Conflict of Interest: The authors report no conflicts of interest.

Funding: No external funding was received for this study.

Acknowledgments: We gratefully acknowledge our colleagues and all study participants for their valuable contribution.

Authors' contributions: **A.J.**–Study conception, supervision, and manu-script review.

A.T. – Data collection and statistical analysis.

T.S.–Literature review and manuscript drafting.

F.A.–Discussion writing and final proofreading.

All authors approved the final manuscript.

Data Availability Statement: The data used in this study are available upon reasonable request from the corresponding author, subject to ethical and institutional guidelines.

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This Article May be cited As: Jami A, Tahir A, Suluxshan T, Almas F. Neuropsychiatric manifestations in patients with chronic migraine: A hospital-based study. Dev Med Life Sci. 2024;2(9):5-11. doi:10.69750/dmls.02.09.0153