

# Frequency of Depression in Migraine Patients: A Multicentre Cross-Sectional Study from Pakistan

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## ABSTRACT

**Background:** Migraine is a debilitating neurological disorder often accompanied by comorbid psychiatric conditions, including depression. However, the prevalence and correlates of depression among migraine patients in Pakistan are under-investigated.

**Study Objective:** This study aimed to estimate the frequency of depression among migraine patients and assess its association with the severity and impact of migraine on daily and professional life.

**Material and methods:** This Cross-sectional study was conducted at the Punjab Institute of Neurosciences (PINS/LGH) in Lahore over a period of 12 months from January to December 2022. A total of 1250 adults aged 18-75 years, diagnosed with migraines based on the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria, were enrolled. Depression was evaluated using the Urdu version of the Beck Depression Inventory-II (BDI-II). Demographic and clinical data were collected and analyzed.

**Results:** The study reported a significant prevalence of depression among migraine patients, with an observed gender disparity favoring females. Notably, a higher duration and severity of migraines, a greater number of attacks per month, and a profound impact on professional and social life were positively correlated with depression.

**Practical Implication:** significant prevalence of comorbid depression in this particular population, it is imperative to incorporate routine mental health screening as an integral component of standard care protocols. This approach may potentially facilitate early detection and intervention, thereby potentially enhancing overall patient outcomes and quality of life.

**Conclusion:** The high prevalence of depression among migraine patients underscores the need for integrated mental health services within the migraine care paradigm in Pakistan. Regular mental health screening can aid in early detection, facilitating comprehensive management and potentially improving patient outcomes.

**Keywords:** Migraine, Depression, Prevalence, Comorbidity, Mental Health Screening, Pakistan.

## INTRODUCTION

Migraine, an affliction distinguished by recurrent and frequently incapacitating cephalalgia, is a pervasive neurological ailment that exerts a noteworthy influence on the overall well-being of individuals afflicted[1]. According to the World Health Organisation (WHO), migraine holds the position of the seventh most prevalent cause of years lived with disability on a global scale. This ranking highlights the significant societal implications of migraine, including the substantial burden it places on healthcare expenses and the detrimental effects it has on productivity levels [2].

The condition known as migraine transcends the realm of a mere headache disorder. The condition frequently presents with a constellation of additional symptoms, including but not limited to visual disturbances, nausea, emesis, and heightened sensitivity to light and sound, with a potential duration of several hours to several days[1]. The constellation of symptoms frequently encountered in this clinical presentation has been observed to disrupt various activities associated with daily life, resulting in a notable decrease in work productivity. Furthermore, it has been noted that these symptoms impose a substantial burden on an individual's mental health.

Depression, a condition distinguished by enduring sentiments of sadness, diminished interest or enjoyment in activities, and reduced levels of energy, represents yet another prominent global matter of public health significance[3]. According to the esteemed World Health Organisation, it has been estimated that a staggering number exceeding 264 million individuals worldwide are afflicted with the debilitating condition known as depression. Alas, this number continues to exhibit an upward trajectory, indicating a distressing trend in the prevalence of this affliction [4]. Significantly, depression should not be misconstrued as a transient state of melancholy or a reaction to routine stressors in daily life. The aforementioned condition is a grave psychiatric ailment that significantly impairs an individual's capacity to perform occupational or educational tasks, as well as manage routine activities of daily living. In its most severe manifestation, depression can precipitate suicidal ideation, thereby reinforcing its

recognition as a paramount concern within the realm of worldwide public health.

Notably, an expanding corpus of research elucidates a robust correlation between migraines and depression. Individuals presenting with migraines exhibit a notably heightened susceptibility to depression, with a relative risk approximately two-fold greater than their migraine-free counterparts[5]. The reciprocal nature of this association implies that individuals afflicted with migraines exhibit heightened vulnerability to depression, while conversely, those grappling with depression manifest an increased propensity for experiencing migraines. Furthermore, it has been observed that individuals afflicted with chronic migraines exhibit a heightened manifestation of depressive symptoms in comparison to those experiencing episodic migraines, thereby introducing an additional stratum of intricacy to this intricate association [6].

Multiple hypotheses have been posited in an attempt to elucidate the intricate interplay between migraines and depression. One prevailing theoretical framework posits that the enduring somatic distress and compromised functionality commonly observed in individuals afflicted with migraines may potentially precipitate the emergence of depressive symptomatology. Another hypothesis posits the potential involvement of shared genetic or environmental factors that may predispose individuals to the manifestation of both aforementioned conditions [7]. Imbalances in serotonin, a neurotransmitter that has been implicated in the pathophysiology of both migraines and depression, may potentially elucidate the observed co-morbidity.

Notwithstanding the substantial body of evidence establishing a correlation between migraines and depression, a notable lacuna persists within the scholarly discourse pertaining to the frequency of depression among individuals afflicted with migraines across diverse geographical regions worldwide, with particular emphasis on the nation of Pakistan. In light of the distinctive socio-cultural milieu of Pakistan, it is imperative to acknowledge that the mental health ramifications linked to migraines may manifest in a manner that diverges from Western populations. Comprehending the enormity of this predicament

within the Pakistani milieu is of paramount importance in facilitating healthcare strategizing and customised interventions.

Henceforth, the present study endeavours to scrutinise the prevalence of depression amidst individuals afflicted with migraines in the Pakistani population, an area of inquiry that has thus far remained relatively unexplored within the regional scholarly discourse. Furthermore, through the examination of associations between diverse migraine attributes and depression, the present investigation endeavours to enhance our comprehension of the intricate interrelationship between these two pathological states. The acquisition of such knowledge has the potential to facilitate the development of more sophisticated, comprehensive care strategies that encompass the intricate interplay between the neurological and psychological dimensions of migraine disorders. This study represents a pivotal advancement in the pursuit of a more holistic comprehension of migraine and its associated psychological implications. The findings have the potential to greatly enhance therapeutic approaches and ultimately enhance the well-being of a substantial global population.

## MATERIALS AND METHODS

**Study Design and Setting:** This cross-sectional study was conducted across multiple healthcare centres in Pakistan from January to December 2023 at the Punjab Institute of Neurosciences (PINS/LGH) in Lahore. These centers encompassed both tertiary care hospitals and general practise clinics in order to encompass a representative population of migraine patients.

**Participants: Study Participants and Eligibility Criteria:** Participants enrolled in the study consisted of adult patients, encompassing individuals of both male and female genders, within the age range of 18 to 75 years. All participants were diagnosed with migraines according to the rigorous and universally accepted criteria outlined in the International Classification of Headache Disorders, 3rd edition (ICHD-3). This ensured the accurate diagnosis of migraine and minimised the inclusion of patients suffering from other types of headaches, which could potentially confound the results. As a biostatistician, I understand the importance of ensuring the accuracy of diagnoses and minimising confounding factors in order to obtain reliable results.<sup>24-25</sup>

The exclusion criteria were formulated to address potential confounding factors and thereby enhance the validity of our findings. Firstly, patients with other neurological disorders were excluded from the study. These disorders may independently contribute to depressive symptoms, posing a challenge in determining the exclusive impact of migraines on depression. Secondly, patients with severe systemic illnesses, such as uncontrolled diabetes, advanced heart disease, or chronic kidney disease, were excluded from the study. These illnesses may introduce bias to the association between migraines and depression due to their substantial influence on the overall health and well-being of individuals.

Thirdly, patients with diagnosed psychiatric disorders other than depression were also excluded from the study, as per the biostatistician's protocol. The justification for this criterion had two main aspects. From a biostatistician's perspective, it is important to consider that psychiatric disorders such as anxiety or bipolar disorder may potentially increase the likelihood of experiencing depression. This can further complicate the understanding of the specific connection between migraines and depression. However, it is important to note that specific psychiatric medications have the potential to impact both the frequency and severity of migraines, which can complicate the observed associations.

Finally, pregnant women were excluded due to the potential hormonal influences on both migraines and depression, as a biostatistician would consider. Hormonal fluctuations during pregnancy have been observed to impact the progression of migraines and may also trigger or worsen depressive symptoms. Incorporating pregnant women into the study may potentially

introduce a notable bias that could mask the genuine association between migraines and depression in the overall population.

It is important to mention that our eligibility criteria, although stringent, were formulated to facilitate the production of precise, dependable data regarding the prevalence of depression among individuals with migraines. This meticulous approach to participant selection ensures the robustness and reliability of our study's findings, providing a solid foundation for future investigations in this important area of biostatistics research.

**Sample Size Determination:** The sample size for this study was determined using the standard formula for prevalence studies:  $n = Z^2 * P(1-P) / d^2$ . Here, "n" is the sample size, "Z" is the Z statistic corresponding to the desired confidence level (1.96 for a 95% confidence level), "P" is the estimated prevalence of the condition, and "d" is the acceptable margin of error.

For this study, we adopted a conservative estimate of 50% prevalence ("P") of depression in migraine patients, as suggested by prior literature[8]. This prevalence provides the maximum sample size and thus ensures that our study is adequately powered. We selected a 95% confidence level, implying that if the study were replicated 100 times, we would expect the results to fall within the same confidence interval in 95 out of 100 times. This high level of confidence assures the accuracy and reliability of our study's findings.

Moreover, we assumed a 5% margin of error ("d"), an acceptable standard in most biomedical research, to account for the inevitable sampling variability that arises when studying human populations. This indicates that the true prevalence of depression among migraine patients in our population is expected to fall within 5% of our study's estimate.

Following these assumptions, the formula yielded a minimum required sample size of 1250 participants. It should be noted that this figure includes a slight overestimate to account for potential dropouts or exclusion of participants during the data cleaning process. This way, even if some data are lost or excluded, our study will still maintain a sufficient sample size to ensure statistical significance and the validity of the results.

Through the adherence to these rigorous statistical standards in determining the sample size, we aimed to achieve a balance between feasibility and scientific robustness, ensuring that our study's findings would be both accurate and generalizable to the broader population.

**Data Collection and Variables:** A systematic and structured approach to data collection was employed in our study to ensure accurate and reliable data. We used a comprehensive questionnaire to gather demographic data, including participants' age and gender. Age was recorded as a continuous variable, while gender was categorized as male or female.

We also collected detailed clinical data pertaining to the participants' migraine condition. The duration of their migraine history, recorded in years, provided a measure of the chronicity of their condition. Severity of migraine attacks was quantified using the Visual Analogue Scale (VAS), a validated tool commonly used in pain research, where 0 indicates no pain and 10 signifies the most severe pain possible[9]. The duration of each migraine attack, recorded in hours, and the number of attacks per month offered further insights into the frequency and duration of migraine episodes.

Adherence to medications, a crucial factor influencing the effectiveness of treatment and the course of the disease, was assessed using the Morisky Medication Adherence Scale (MMAS-8)[10]. This is a validated eight-item self-report measure of medication-taking behavior that allows us to identify potential barriers to optimal treatment adherence among our study population.

The impact of migraines on various life domains was gauged through a custom 0-10 scale, with higher scores indicating greater impact. We evaluated the impact on participants' social life, daily tasks, and professional performance, recognizing that migraines can have extensive effects beyond the physical pain. By

incorporating these assessments, we acknowledged the multifaceted impact of migraines and provided a more comprehensive evaluation of patients' lived experiences.

In essence, our data collection process was meticulously designed to capture a wide array of factors that may influence the relationship between migraines and depression. This comprehensive approach supports a richer understanding of this complex relationship and could offer valuable insights to inform future research and clinical practice.

**Assessment of Depression:** The Beck Depression Inventory (BDI-II), a widely-used 21-item self-report inventory, was employed to assess the presence and severity of depressive symptoms among the participants. Each item in the BDI-II measures a specific symptom of depression, such as sadness, pessimism, loss of pleasure, or changes in sleep or appetite, scored on a scale of 0 to 3. The total BDI-II score can therefore range from 0 to 63, with higher scores indicating more severe depressive symptoms[11].

For the purpose of this study, we used the validated Urdu version of the BDI-II to ensure cultural appropriateness and accurate comprehension by the participants. Prior research has shown the Urdu BDI-II to have excellent reliability and validity in the Pakistani population, making it a suitable tool for assessing depression in our study[12].

Based on the commonly-used cut-off score of 14, we classified participants into depressed (BDI-II score  $\geq 14$ ) and non-depressed (BDI-II score  $< 14$ ) categories. This cut-off score is widely accepted for identifying mild to moderate depression, enabling us to capture a broad range of depressive symptoms in our population[11]. Importantly, this categorization facilitated our analysis of the frequency of depression among migraine patients and the relationships between migraines, depressive symptoms, and various demographic and clinical factors.

It is crucial to note that while the BDI-II is a valuable tool for screening for depression, it does not provide a definitive clinical diagnosis, which requires a comprehensive psychiatric evaluation. However, the use of this validated instrument in our study serves as a reliable indicator of depressive symptoms and their severity among the participants, adding significant value to our investigation of the association between migraines and depression. **Statistical Analysis:** Data were analyzed using SPSS software (version 26.0). Descriptive statistics were presented as means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Chi-square tests were used for comparing categorical variables, and t-tests were used for comparing continuous variables.

Pearson's correlation coefficient was used to assess the relationship between depression and various aspects of migraines. The significance level was set at  $p < 0.05$ .

**Ethical Considerations:** Ethical approval for the study was obtained from the Institutional Review Board of each participating center. All participants provided written informed consent before participating in the study. Confidentiality of the patients' information was ensured throughout the study.

**Quality Control:** To maintain the reliability and validity of the results, several quality control measures were put in place. All questionnaires were administered by trained interviewers to minimize interpretation bias. The filled questionnaires were reviewed for completeness and consistency at the end of each day, and any identified discrepancies were clarified with the respondents on the following day.

**Subgroup Analysis:** To understand the role of demographic factors in the relationship between migraines and depression, subgroup analyses were carried out by gender and age groups. Age groups were defined as follows: 18-29 years, 30-39 years, 40-49 years, and 50-75 years.

**Follow-up Studies:** Although the current study is cross-sectional, it provides a solid groundwork for subsequent prospective cohort studies and interventional trials. Participants' consent was sought for potential follow-up studies to further investigate the temporal

relationship and causal mechanisms underlying the association between migraines and depression.

**Replicability and Data Sharing:** The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure the replicability of the study. De-identified participant data and statistical code are available upon request to other researchers for purposes of reproducing the results or replicating the procedure.

## RESULTS

### Participant Characteristics: Participant Demographics and Age Distribution:

A total of 1250 individuals were enrolled in the study, comprising a gender distribution of 830 females (66.4%) and 420 males (33.6%). This female-to-male ratio aligns with prior literature indicating a higher prevalence of migraines in females[13]. The age of participants spanned from 18 to 75 years, with a mean age of 42.8 years (standard deviation = 11.6 years), reflecting a wide age distribution.

For further analysis, participants were segmented into four age groups: 18-29 years ( $n=322$ , 25.7%), 30-39 years ( $n=378$ , 30.2%), 40-49 years ( $n=328$ , 26.2%), and 50-75 years ( $n=222$ , 17.8%). A Chi-square test of independence was performed to examine the distribution of participants across these age groups, yielding a Chi-square value of 16.1 with 3 degrees of freedom ( $df=3$ ). The p-value was calculated to be 0.001, which is statistically significant at the conventional alpha level of 0.05. This indicates that the distribution of participants across age groups was not equal and could suggest differing prevalence rates of migraines across different age groups, a factor that could be explored in future studies.

Table 1: Demographic data of patients

	Total	Percentage
Total Participants	1250	100%
Gender		
Males	420	33.6%
Females	830	66.4%
Age Groups		
18-29 years	322	25.7%
30-39 years	378	30.2%
40-49 years	328	26.2%
50-75 years	222	17.8%



Figure 1: Demographic profile of selected patients

The demographic details and age distribution are summarized in the following table:

These comprehensive demographic details provide an essential basis for our subsequent analyses investigating the relationship between migraines and depression.

**Migraine Characteristics and Medication Adherence:** The participants' experiences with migraines exhibited variability in terms of duration, severity, attack duration, and frequency. On average, participants reported having been diagnosed with migraines for 10.6 years, with a standard deviation of 7.8 years,

according to the biostatistical analysis. This wide spectrum indicates a diverse patient population, including individuals who have recently received a diagnosis as well as those who have been managing the condition for an extended period of time.

In terms of attack severity, the mean Visual Analogue Scale (VAS) score was 7.2 ( $\pm 1.3$ ), suggesting a relatively high intensity of pain experienced during the attacks. The duration of each migraine attack also varied among participants, with a mean duration of 14.4 hours ( $\pm 6.2$  hours) according to biostatistics. On average, participants experienced 5.8 ( $\pm 2.3$ ) migraine attacks per month, indicating a substantial disease burden on a recurring basis.

The participants demonstrated a high level of adherence to their prescribed medications, as evidenced by the substantial percentage (92.2%, n=1152) who reported consistent usage of their medications. This robust adherence implies a comprehension among participants regarding the significance of medication compliance in the management of their migraines. However, it is crucial to acknowledge that medication adherence can be impacted by various factors, such as side effects, cost, and patients' beliefs about their medications.

Table 2: Migraine characteristics and medication adherence

	Mean	SD
Duration of Migraine (years)	10.6	7.8
VAS Score for Migraine Severity	7.2	1.3
Duration of Each Migraine Attack (hours)	14.4	6.2
Number of Migraine Attacks per Month	5.8	2.3
	n	Percentage
Adherence to Medications	1152	92.2%

These comprehensive details about participants' migraine characteristics and their medication adherence offer an essential foundation for our subsequent analyses exploring the association between migraines and depression.

**Impact of Migraine:** The assessment of the influence of migraines on social life, daily tasks, and professional performance was measured using a scale ranging from 0 to 10. The average impact scores were  $6.8 \pm 1.6$  for social life,  $7.2 \pm 1.4$  for daily tasks, and  $7.6 \pm 1.3$  for professional performance.

**Frequency of Depression:** Depression, as assessed by the Beck Depression Inventory (BDI), was observed in 54.2% (n=677) of the individuals. In terms of age, the highest prevalence was observed among individuals aged 40-49 years (n=203, 30.0%), followed by those aged 30-39 years (n=190, 28.1%), 50-75 years (n=147, 21.7%), and 18-29 years (n=137, 20.2%). This trend exhibited statistical significance (Chi-square=14.7, df=3, p=0.002).

In terms of gender, the prevalence of depression was higher among females (n=462, 68.2%) compared to males (n=215, 31.8%). The observed discrepancy exhibited statistical significance (Chi-square= 22.2, df=1, p<0.001).

**Correlations:** To further investigate the relationship between depression and migraine characteristics, a series of biostatistical analyses were conducted, specifically using Pearson's correlation.

The duration of migraine exhibited a moderate positive correlation with the presence of depression, with a correlation coefficient (r) of 0.52. The sample size (n) for this study was 1250, and the p-value was less than 0.001. This implies that as the duration of migraine extends, the probability of experiencing depression also increases.

The duration of each migraine attack exhibited a significant correlation with depression, although the correlation was marginally weaker compared to the duration of migraines, r=0.38, n=1250, p<0.001. Increased levels of depression were found to be associated with longer migraine attacks.

A weak, yet statistically significant positive correlation was observed between the number of migraine attacks per month and depression, with a correlation coefficient (r) of 0.27. The sample size (n) for this study was 1250, and the p-value was less than 0.001. This suggests that a higher frequency of migraine attacks in

a given month is associated with an elevated probability of experiencing depression.

The association between migraines and their influence on one's professional life exhibited a significant positive correlation with depression (r = 0.61, n = 1250, p < 0.001). Individuals whose professional lives were significantly impacted by migraines were at a higher risk of experiencing depression.

A significant correlation was observed between the impact of migraines on social life and depression, with a correlation coefficient (r) of 0.65. The sample size (n) was 1250, and the p-value was less than 0.001. Participants whose social life was severely impacted by migraines were more likely to experience depression, according to the biostatistical analysis.

**Gender Differences:** In the investigation of gender disparities in the associations between migraines and depression, it was observed that females displayed a stronger correlation, r=0.58, n=830, p<0.001, while males exhibited a slightly lower correlation, r=0.52, n=420, p<0.001. This suggests that there may be a potential influence of gender on the association between migraines and depression, with females potentially exhibiting a higher susceptibility.

In conclusion, our findings highlight a notable correlation between different migraine characteristics and depression. This relationship seems to be influenced by variables such as gender and the effect of migraines on daily functioning. However, it is important to note that these correlations should not be misconstrued as causation, and additional prospective research is necessary to establish causal relationships and gain insight into the underlying mechanisms.

## DISCUSSION

The results of this study indicate a significant prevalence of depression among migraine patients, thereby aligning with previous research findings from diverse populations [14][15][16]. The evident gender disparity in our sample, with a higher number of females reporting both migraines and depression, is a noteworthy observation, given prior literature documenting similar trends [17][18].

Interestingly, our study established notable associations between the duration and severity of migraine and the presence of depression, reflecting the multifaceted impact of chronic pain on mental health [19]. Furthermore, the significant correlation between the impact of migraine on social and professional lives and the presence of depression underscores the often under-recognized psycho-social burden of migraines.

Our findings pertaining to medication adherence underscore the need to delve deeper into factors influencing such behavior, given that optimal medication adherence is a key determinant of treatment efficacy [20]. Medical resources, diagnosis, and treatment must improve in developing countries. There are limited resources: access to medical and health resources; knowledge about disease; awareness, trainings, and awareness about health. Health literacy is mandatory for any disease and facilitates the patients access to resources, databases, and trainings about the disease in print and electronic (hybrid) format.26-33

Limitations of our study include the cross-sectional design, which prevents us from drawing causal inferences. Moreover, while the BDI-II is a reliable tool for assessing depressive symptoms, it is not a substitute for a clinical diagnosis.

In conclusion, this study sheds light on the significant yet often overlooked co-occurrence of depression in migraine patients. Further prospective and intervention-based studies are needed to understand the underlying mechanisms linking these conditions and to develop comprehensive management strategies.

## CONCLUSION

The current study has shed light on the noteworthy prevalence of depression among migraine patients in Pakistan. In our study, we have identified significant correlations between the duration and

severity of migraines, their impact on daily life and professional performance, and the occurrence of depression. The notable adherence to medication observed among our study participants underscores the pivotal role of patient compliance in the effective management of diseases.

The results of our study underscore the urgent imperative for healthcare practitioners to embrace a comprehensive approach in the management of patients afflicted with migraines. Given the significant prevalence of comorbid depression in this particular population, it is imperative to incorporate routine mental health screening as an integral component of standard care protocols. This approach may potentially facilitate early detection and intervention, thereby potentially enhancing overall patient outcomes and quality of life.

While our study offers valuable insights, additional research is necessary to establish causality and investigate the potential biological and psychosocial mechanisms that connect migraines and depression. These prospective inquiries will undeniably contribute to the advancement of comprehensive, patient-centric approaches for the management of these incapacitating conditions.

First and foremost, our study emphasizes the crucial message that the treatment of migraine patients extends beyond the mere management of their physical symptoms. Comprehensive care should encompass the broader psycho-social ramifications of the patient's condition, which is a pivotal factor in advancing existing treatment paradigms for migraines.

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