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PREVALENCE OF DEPRESSION IN PATIENTS WITH MIGRAINE, A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL

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BACKGROUND
Headache is one of the most common presenting complaints in patients attending primary care centers and the majority of them have primary headache syndromes. Depressive disorders are among the leading causes of disability globally and can further complicate the clinical manifestation if coupled with other comorbidities. Therefore, the primary objective of our study was to determine the prevalence of depression in migraine patients presenting at a tertiary care hospital to better understand the leading causes of the disease.

METHODS
A cross-sectional study was carried out between December 2019 and June 2020 (six months) including 66 migraine patients between 18 and 45 years of age presenting to the neurology outpatient clinics at a tertiary care hospital in Karachi, Pakistan. Non-probability convenience-based sampling technique was used to calculate the sample size, and the data was collected via face-to-face interviews. The first section of the questionnaire consisted of socio-demographic factors such as age, gender, educational, occupational, and marital status in addition to the clinical characteristics such as the duration of the disease and the frequency of migraine attacks. The second section assessed the depressive symptoms of the participants using the Patient Health Questionnaire-9 (PHQ-9) and any patient with a score of five or more was considered as suffering from a depressive disorder. All statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 23.0.

RESULTS
Out of a total of 66 participants, almost two-third (n=43, 65.2%) were males, while nearly one-third (n=23, 34.9%) were females. The average age of the patients was 27.59±5.37 years. The frequency of depression was observed in approximately three-quarters (n=49, 74.2%) of the migraine patients in our study. The prevalence of depression was only significantly associated with disease duration (p=0.027) and the number of migraine attacks (p=0.015).

CONCLUSION
In conclusion, the prevalence of depression was found to be significantly high among migraine patients, therefore migraine might be related to depression. Depression should not be ignored while evaluating migraine subjects for good prognosis and management of the disease.

KEYWORDS migraine, psychiatric disorders, depression

INTRODUCTION
Migraine is a chronic neurological disorder that is characterized by pulsating headache (i.e. feeling of fullness over the forehead) that occurs in recurrent attacks and is often unilateral [1]. It can be accompanied by other clinical manifestations including

nausea, vomiting, vertigo, photophobia, and phonophobia (i.e. sensitivity of light and sound) [1, 2]. It is classified as the third most common disease with an estimated prevalence of 14.7% globally [3]. It is ranked as the seventh most disabling disorder worldwide responsible for 2.9% of all years of life lost to disability [1, 3].

Depression comprises symptoms of feeling melancholic, lack of spirit, loss of enjoyment, changes in appetite, sleep, and low energy resulting in increased lethargy lasting for two weeks [4]. Clinically significant depression is associated with low quality of life and has been recognized as the major contributor to suicide and disability burden globally by the World Health Organization (WHO) [4, 5].

A bi-directional association seems to exist between depression and migraine, with each disorder enhancing the possibility of the other [6]. Published literature suggests rates of psychiatric comorbidity to range between 69% and 87% among migraine patients [7, 8]. The findings of a pooled meta-analyses reported that depression is nearly two times more frequent in subjects with migraine than in people unaffected by headache [9]. Another study conducted in England demonstrated a relationship between migraines and affective disorders, particularly depression [10]. Lastly, a study carried out in Taiwan demonstrated greater than three-quarters (78%) of the population with transformed migraine have psychiatric comorbidity with more than half (57%) suffering from major depression [11].

Psychiatric comorbidity such as depression complicates the management of migraine patients and results in poor prognosis. The mechanisms underlying migraine are reported to be highly complex and a wide heterogeneity exists with a proportion of the population being fully functional while others experiencing serious disabilities such as encountering social, affective, and occupational limitations. Much of this heterogeneity is accounted for by the presence of comorbidities including psychiatric illnesses [9]. Hence, the primary objective of this study was to determine the frequency of depression in migraine patients presenting to the neurology department in our part hospital. A secondary aim was to determine the impact of socio-demographic and clinical factors on the observed depression prevalence in migraine patients.

METHODS
STUDY SETTING AND DESIGN
This was a cross-sectional study conducted between December 2019 and June 2020. Over six months'

duration at the neurology out-patient clinic of a tertiary care hospital in Karachi, Pakistan.

Sample size, inclusion and exclusion criteria
Non-probability convenience-based sampling technique was used to calculate the sample size of 66 patients. The sample population included all patients between 18-45 years of age and either gender (i.e. male or female) having a history of migraine headache of two months' duration. All patients were labeled as having depression as per operational definition. However, we excluded all individuals already taking anti-depressant medications. We also excluded all patients with major medical disorders including diabetes, myocardial infarction, and hypertension (as per medical record). Ethical approval was obtained from the Institutional Review Board.

SAMPLING TECHNIQUE AND DATA COLLECTION
All data were collected via an interviewer-administered-questionnaire. The principal investigator explained the purpose and the methodology of the study to all migraine patients. Those migraine patients who agreed to participate were also asked to give both verbal and written informed consent before their inclusion in the study. A well-standardized two-section questionnaire was designed to collect data for this study. The first section of the questionnaire was based on the participant's socio-demographic characteristics including gender, age, educational, occupational, monthly income, and marital status in addition to the clinical factors such as duration of the disease and the frequency of migraine attacks. The second section consisted of questions about the Patient Health Questionnaire-9 (PHQ-9) [12] utilized to assess the frequency of depression among migraine patients based on recommended duration (two weeks) and scores mentioned as follows: mild depression (a score of 5-9), moderate depression (a score of 10-14), moderately severe (a score of 15-19) and severe depression (a score of 20 or above). Depressive disorder was labeled as positive for a score of ≥5 otherwise it was labeled as negative. The questionnaire was also reviewed by two senior neurologists for validity and reliability (reliability index 0.85).

STATISTICAL ANALYSIS
All statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 23.0. Frequencies and percentages were computed for categorical variables like sex, marital status, education status, occupation status, monthly income, and depression. Mean and standard deviations were

computed for continuous variables like age and duration of illness. Effect modifiers like age, sex, duration of illness, marital status, education status, occupational status, and socioeconomic status were controlled through stratification by applying Chi-square and Fischer's exact test. A p-value of ≤0.05 was considered statistically significant.

RESULTS
SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PARTICIPANTS
A total of 66 migraine patients participated in this study. The mean age of the patients was 27.59±5.37 years. The median duration of the migraine disease in our sample population was two [interquartile range (IQR)=1] months while the median number of migraine attacks was 3 (IQR=1).

Nearly three-fifth (n=39, 59.1%) of our sample population were males while (n=27, 40.9%) were females. Nearly two-third (n=43, 65.2%) of patients were married while (n=23, 34.8%) were unmarried. The highest proportion of migraine patients in our study were graduates (n=26, 39.4%) followed by (n=11, 16.7%) in intermediate level, while equal proportions of our participants were not formally educated and received secondary degrees (n=8, 12.1%). Equal proportions received primary and master degrees (n=6, 9.1%). The highest proportion of participants in our survey were privately employed (n=30, 45.5%) followed by government employees (n=13, 19.7%) and industrial workers (n=14, 21.2%). Half of the patients (n=33, 50.0%) earned a monthly income of less than 30,000 rupees, followed by (n=31, 46.9%) earned between 31,000 and 70,000 rupees, while a very minor proportion (n=2, 3.03%) earned greater than 70,000 rupees (Table 1).

Socio-demographic characteristics	N (%)
Gender	
Male	39 (59.1)
Female	27 (40.9)
Marital status	
Married	43 (65.2)
Unmarried	23 (34.8)
Educational status	
Illiterate	8 (12.1)
Primary	6 (9.1)
Secondary	8 (12.1)
Matric	1 (1.5)
Intermediate	11 (16.7)
Graduate	26 (39.4)
Master	6 (9.1)
Occupational status	
Government employee	13 (19.7)
Private job	30 (45.5)
Industrial worker	14 (21.2)
House worker	9 (13.6)
Monthly income (rupees)	
<30,000	33 (50.0)
31,000-70,000	31 (46.9)
>70,000	2 (3.03)

Table 1: Sociodemographic characteristics of the participants
Prevalence of depression among the participants and its association with socio-demographic and clinical factors

Nearly three-quarters (n=49, 74.2%) of our participants were suffering from depression as determined using the PHQ-9 questionnaire, as illustrated in Figure 1.
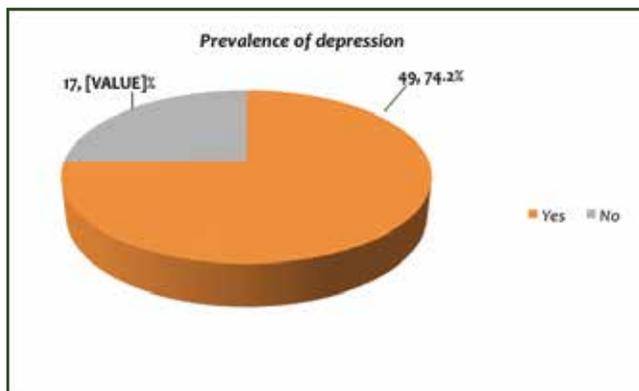

Figure 1: Prevalence of depression in migraine patients
The highest prevalence of depression (n=28, 57.1%) was observed in patients aged 26-30 years, however, this did not reach statistical significance (p=0.708). Depression was more common in male patients (n=27, 55.1%) in comparison to females (n=22,

44.9%), however, the difference was not statistically significant (p=0.263). Furthermore, depression was not significantly associated with the marital status of the patients (p=0.525).

In contrast, depression was significantly associated with the disease duration (p=0.027) as nearly three-quarters (n=37, 75.5%) of the depressed participants had a disease duration of two to three months while only a quarter (n=12, 24.5%) of migraine patients that had depression reported a disease duration of greater than three months. Depression was also significantly associated with the number of migraine attacks (p=0.015) as a greater proportion (n=36, 73.5%) of patients that had depression experienced two to three migraine attacks in comparison to those with four to five migraine attacks (n=13, 26.5%) (Table 2).

Variables		Prevalence of depression		p-value
		Yes (N=49, 74.8%)	No (N=17, 25.2%)	
Age (years)	≤ 25	10 (20.4%)	5 (29.4%)	0.708
	26 to 30	28 (57.1%)	8 (47.1%)	
	31 to 40	11 (22.4%)	4 (23.5%)	
Gender	Male	27 (55.1%)	12 (70.6%)	0.263
	Female	22 (44.9%)	5 (29.4%)	
Marital status	Married	33 (67.3%)	10 (58.8%)	0.525
	Unmarried	16 (32.7%)	7 (41.2%)	
Duration of disease (months)	2 to 3	37 (75.5%)	17 (100%)	0.027
	>3	12 (24.5%)	0 (0%)	
Number of migraine attacks	2 to 3	36 (73.5%)	17 (100%)	0.015
	4 to 5	13 (26.5%)	0 (0%)	
Monthly income (rupees)	<30,000	22 (44.9%)	11 (64.7%)	0.309
	31,000 to 70,000	25 (51.0%)	6 (35.2%)	
	>70,000	2 (4.1%)	0 (0%)	
Educational status	Illiterate	7 (14.3%)	1 (5.9%)	0.110
	Primary	3 (6.1%)	3 (17.6%)	
	Secondary	6 (12.2%)	2 (11.8%)	
	Metric	0 (0%)	1 (5.9%)	
	Intermediate	6 (12.2%)	5 (29.4%)	
	Graduate	21 (42.9%)	5 (29.4%)	
	Master	6 (12.2%)	0 (0%)	
Occupation	Government employee	12 (24.5%)	1 (5.9%)	0.419
	Private employee	21 (42.9%)	9 (52.9%)	
	Industrial worker	10 (20.4%)	4 (23.5%)	
	House worker	6 (12.2%)	3 (17.6%)	

Table 2: Association of socio-demographic and clinical characteristics with a prevalence of depression in migraine patients

DISCUSSION

Our results report a high prevalence of depression amongst patients with Migraines. These migraine attacks are also reported to be associated with nausea and changes in vision. This neurological disorder affects the quality of life (QOL) of an individual and results in significant loss of productivity [13, 14]. The proportion of the migraine burden is contributed by the coexisting set of psychiatric disorders namely depression, anxiety, phobias, and panic attacks. Breslau and his colleagues in their study demonstrated this relationship between migraine and depression by reporting a three-fold increased risk of depression in migraine patients compared to non-migraine ones while those who had depression without a previous history of migraine were also three times more likely to develop migraine compared with non-depressed patients [15]. Studying the relationship between migraine and depression is essential for diagnosis and management. This cross-sectional study comprised 66 patients presenting with migraine headaches with a mean age of 27.59±5.37 years with most of the patients between 26 and 30 years of age. The onset of migraine occurs from childhood being more prevalent between 20-30 years and declining after 40 years of age. Hence, the prevalence increases from the first to fourth decades and declines thereafter [16]. Migraines are reported to be precipitated by multiple environmental and genetic factors with nearly two-thirds of cases having a familial association [17]. Additionally, women are three times more susceptible to migraine attacks compared to men and this difference is reported to be hormonally-driven [18, 19]. Nearly 18% of women and 6% of men suffer a migraine annually, with a lifetime risk of 43% and 18% respectively in the United States [17]. In Europe, 12-28% of people get affected by migraine once in their lifetime with about 14-35% of adult women and 6-15% of adult men getting at least once yearly [18]. However, in our study, 59.1% of males and 40.9% of females reported migraine headaches. Our study reported higher migraine prevalence because it was conducted in a developing country with a significant percentage of the population living below poverty with greater depression rates.

Migraine significantly affects the functional capacity of an individual making most of the daily tasks impossible to perform. Published literature reports that migraine is also negatively associated with years of schooling and grades. Migraine makes it difficult to maintain regular attendance and concentrate on studies. Students with migraine headaches are often forced to miss school and even if they attend school, their productivity is remarkably reduced. It increases the cost of remaining in school to the extent that it hinders learning, it can be considered as reducing the returns to remain in school [14, 20, 21].

Our study provides the hindsight that depression is as common among migraine sufferers as patients

suffering from other chronic diseases. The frequency of depression among migraine subjects was observed to be 74.2%. Wang et al in a study comprising subjects over 65 years reported that the risk of current depression was greater in migraine than in non-migraine patients [22]. Merikangas et al. in their study comprising 457 younger subjects reported an increased risk of developing major depression and anxiety disorders compared with controls [23]. A population-based case-control study conducted by Lipton et al. confirmed a higher risk of current depression among patients suffering from migraines [14]. Swartz et al. studied psychiatric illnesses as possible risk factors for migraine onset with a prospective follow-up of 13 years and demonstrated that only a history of phobic disorder predicted migraine onset [24].

Jelinski et al. reported that certain clinical and demographic factors are independently associated with depression in a population of patients with headaches. These factors included younger age and unemployment, obtaining financial support through disability pension or welfare, and being divorced, separated, or widowed [25]. In contrast, stratification analysis in our study demonstrated that the rate of depression was not significantly associated with monthly income, educational status, occupation. Monthly income was used as a parameter to measure the socio-economic status of the participants.

However, some limitations of our study must be considered. Our study comprised of small sample size, and recruited migraine subjects from only a single tertiary care center, which limits the generalizability of our results. Bipolar disorder was not identified in our sample population but can be a cause of depression in a general population. These limitations should be taken into consideration when extrapolating our results to other migraine subjects. Nonetheless, we feel that the results observed in this small sample provide a platform for further investigations into the interaction between migraine and depression by including a large sample population from primary care settings that serve a variety of ethnic populations.

CONCLUSION

In conclusion, migraine is consistently related to depression. This association can have several important clinical implications as the prevalence of depression was found to be significantly high among migraine patients. For good prognosis and management of the disease, physicians should evaluate for the presence of depression among migraine subjects, both the disorders should be taken into account when formulating an effective treatment plan. Treatment of one disorder can prevent further progression to one or both of them and result in a good prognosis. A suitable therapeutic approach among migraine subjects can reduce the disability burden among these subjects, hence reducing health-care resources and economic burden.

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