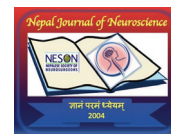


Clinico-epidemiological profile of migraine and its correlation with depression, anxiety and stress in a tertiary care hospital in South India



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Abstract

Introduction: We studied the clinico-epidemiological profile of patients with migraine and to study the correlation of migraine severity with depression, anxiety and stress

Materials and Methods: 98 subjects who were meeting inclusion and exclusion criteria were studied after obtaining informed written consent. Data was collected using prestructured performa and then analysed using SPSS software.

Result: 64.3% patients had unilateral headache and 76.5% had frontal area pain. Migraine with aura was present in 40.8% with commonest aura being visual (85%). Most common visual aura was scotoma (47.5%) and the most common associated symptom was photophobia (83.7%) followed by nausea (78.6%). The most common trigger was sun exposure (70.4%) followed by sleep deprivation (69.4%). Severe disability was present in 26.5% of subjects. Severity of migraine showed significant positive association with those who were taking alternative medicine. Migraine severity showed positive correlation with depression, anxiety and stress with correlation coefficient of 0.506, 0.509, and 0.604 respectively. Maximum correlation was with stress which may be considered as an independent risk factor for severe migraine.

Conclusion: Anxiety, depression and stress were strongly associated with severe migraine. They can act as factors that trigger and perpetuate migraine, of which stress may be considered as an independent risk factor for severe migraine. Early screening and management of depression, anxiety and stress might provide better control of migraine, thus improving the quality of life of migraineurs.

Key words: Migraine, MIDAS score, PHQ9, GAD7, PSS, anxiety, depression, stress

Introduction

Migraine is considered the third most common disease in the world with an estimated global prevalence of 14.7%.¹ In a study done by Biman K Ray et al,² the prevalence of migraine in India was found to be 14.12 %.

Migraine is usually associated with depression, anxiety and stress, which is unrecognised or untreated most of the time. Depression is three times more common in those with migraine than in healthy individuals.³ The coexisting psychiatric issue can worsen migraine and can affect the quality of life of migraineurs. Migraine predominantly affects people who are in their productive life period of 25-55 years. Moreover, it is regarded as the highest cause of years lived with disability (YLDs) amongst those aged 15-49.⁴ Migraine is said to be responsible for 86 million workdays lost per year in UK according to studies.⁴ So this might be particularly important for a developing country like India where the population index is high and the workdays lost can significantly affect the economy. So early identification and management of depression, anxiety and stress can definitely improve quality of life in patients with migraine.

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Materials and Methods

Aim of the study was to study the clinico-epidemiological profile of migraine patients and to study the correlation of migraine severity with depression, anxiety and stress. This cross-sectional observational

study was undertaken for a period of 1 year (2018-2019) in a tertiary care hospital of Kerala. Participants were selected randomly from the patients with migraine visiting the department of Neurology, in the tertiary care hospital during the study period. Those who were meeting the ICHD 3 BETA criteria of migraine⁵ with age between 18 to 60 years were included in the study. Those with associated secondary causes of headache /other primary headache syndromes or those with psychiatric disorders were excluded. The study was done on 98 subjects from whom an informed written consent was taken, they were interviewed and data were collected using a prestructured proforma and detailed clinical examination was done. MIDAS questionnaires were used to assess the severity of migraine. PHQ 9 questionnaires were used to assess depression. GAD -7 questionnaires were used to assess the anxiety disorder. Perceived stress scale (PSS) was used to assess the impact of stress. Neuro imaging (CT scan /MRI brain), blood biochemistry, blood counts and ESR were done in all patients to rule out secondary causes.

Grading of MIDAS score

0-5	Grade I, little or no disability
6-10	Grade II, mild disability
11-20	Grade III, moderate disability
21+	Grade IV, severe disability

Groups based on GAD7 score

no anxiety	<5
mild anxiety	5-9
moderate anxiety	10-14
severe anxiety	>14

Groups based on PHQ9 score

<5	No depression
5-9	Mild depression
10-14	Moderate depression
>14	Severe depression

Groups based on PSS score

0-13	Low stress score
14-26	Moderate stress score
27-40	Severe stress score

Statistical Analysis

Data were collected using a predesigned proforma and subsequently entered into Microsoft Excel spread sheet. Analysis of data was done using SPSS version 16.0. Qualitative measures were measured as proportion and association between qualitative variables was analysed using chi square test. A P value of <0.05 was considered as statistically significant. For analysis using chi square test, MIDAS score was dichotomized into two groups, grade 1-2 into mild and grade 3-4 into severe score. The

correlation coefficient was used for correlation; multiple linear regression analysis was done to assess the predictive value of the variables on severity of migraine.

Results

The total number of subjects included in the study was 98, out of which 25 were males (25.5%) and 73 were females (74.5%). The maximum number of patients belonged to < 30 years of age (40.8%) (Fig-1). 33 subjects (33.7%) had a family history of migraine. 37 subjects (37.8%) had a duration of illness 1-5 years, 26 subjects (26.5%) had a duration of illness of 6-10 years, and 21 subjects (21.4%) had a duration of illness. 64.3% of subjects had unilateral headaches. 76.5% had frontal head ache, 50% had unilateral frontal area pain, temporal area and occipital pain were present for 8.2% and 9.2%, respectively, and bitemporal pain was present in 6.1%. Pain over the neck was present either along with or before head aches in 24.5% of subjects.

Migraine with aura was present in 40.8% of the subjects, of which 85% (n = 34) had visual aura, 7.5% (n = 3) had vertiginous aura, and 7.5% (n = 3) had other types of aura. 47.5% (n = 19) of those with visual aura had scotomas, 25% (n = 10) had fortification spectra, and 12.5% (n = 5) had flashes of light as aura. 55.1% (n = 54) of the subjects had associated vomiting, nausea occurred in 78.6% (n = 77); 83.7% (n = 82) had photophobia; 51% (n = 50) had phonophobia; and 4.1% (n = 4) had other symptoms (1 patient had hemiplegic migraine, the remaining 3 had paresthesias) (Fig 2).

20.5% (n = 15) of females had worsening head aches during menstruation. The most common trigger for migraine exacerbation was sun exposure at 70.4% (n = 69) followed by sleep deprivation in 69.4% (n = 68), mental stress at 42.9%, skipping meals meal in 40.8% (n = 40), loud sounds in 23.5% (n = 23), and physical stress in 17.3% (n=17) (Fig3). Around 48% (n = 47) had received prophylactic treatment at some point during their illness. Compliance to treatment was present in 55.3% (n = 26) of subjects. 31.6% (n = 31) were using alternate medicine either along with prophylaxis or as a sole treatment

Based on the MIDAS score, 26.5% (n = 26) had severe disability while there was no disability for around 27.6% (n = 27) of subjects. Mild and moderate disability occurred in 23.5% (n = 23) and 22.4% (n = 22), respectively. (Fig -4).

Based on the GAD7 scale, 14.3% (n = 14) of subjects had severe anxiety, and 37.8% (n = 37) had no anxiety. It was also noted that 27.6% (n = 27) had mild anxiety and 20.4% (n = 20) had moderate anxiety (Fig- 5). Based on PHQ9, there was no depression in 52% (n = 52)) of subjects, while 5.1% (n = 5) had severe depression, 8.2% (n = 8) had moderately severe depression, 25.5%

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(n = 25) had moderate depression, and 8.2% (n = 8) had mild depression (Fig 6). While using the PSS score, it was found out that 46.9% (n = 46) had a low stress score, 38.8% (n = 38) had moderate stress, and 14.3% (n = 14) had severe stress (Fig- 7).

For analysis of association using the Chi-square test, the MIDAS score was dichotomized into 2 groups, with scores of 3–4 as severe and scores of 1-2 as mild disability. It was noted that those with an age group of <30 years tend to be significantly associated with severe disability ($p = 0.041$). Those for whom the migraine was triggered by mental stress had a more significant migraine disability score ($P = 0.002$). Those who were on alternative medicine were significantly associated with severe disability ($p = 0.003$). Those with a higher anxiety score (GAD7) were

significantly associated with a higher MIDAS score ($P = 0.004$). Higher depression (PHQ score) was significantly associated with a high MIDAS score ($P = 0.012$). High stress, as shown by high PSS score, was significantly associated with a high MIDAS score ($p = 0.001$).

In correlation analysis MIDAS score (fig 8, 9, 10) shows a positive correlation with depression, anxiety, and stress with a Pearson correlation coefficient of 0.506, 0.509, and 0.604 ($p = 0.001$), respectively. And stress shows the highest correlation with migraine severity. A multiple linear regression model was performed to assess the predictive model of the MIDAS score, GAD7, PSS, and PHQ9 had an R value of 0.431, implying that 43.1% of the variation in MIDAS was explained by the predictors.

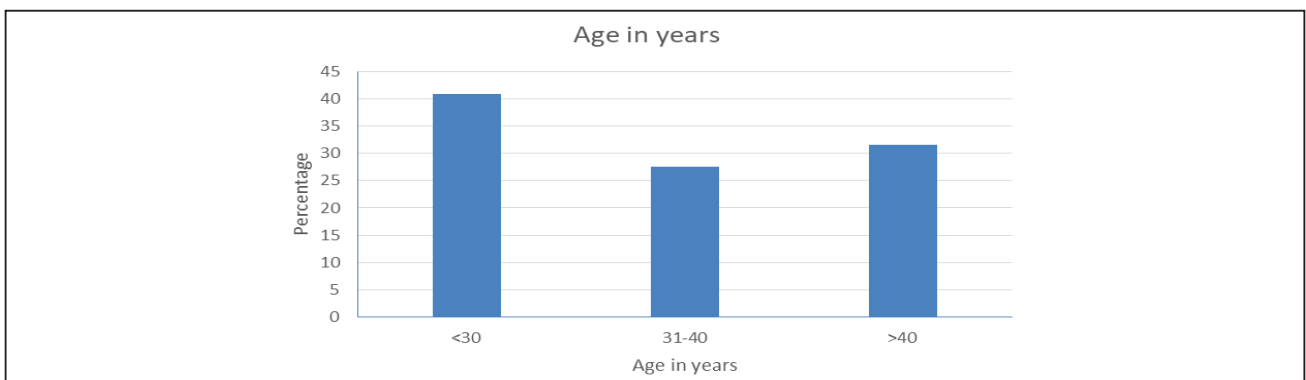


Figure 1: Age distribution

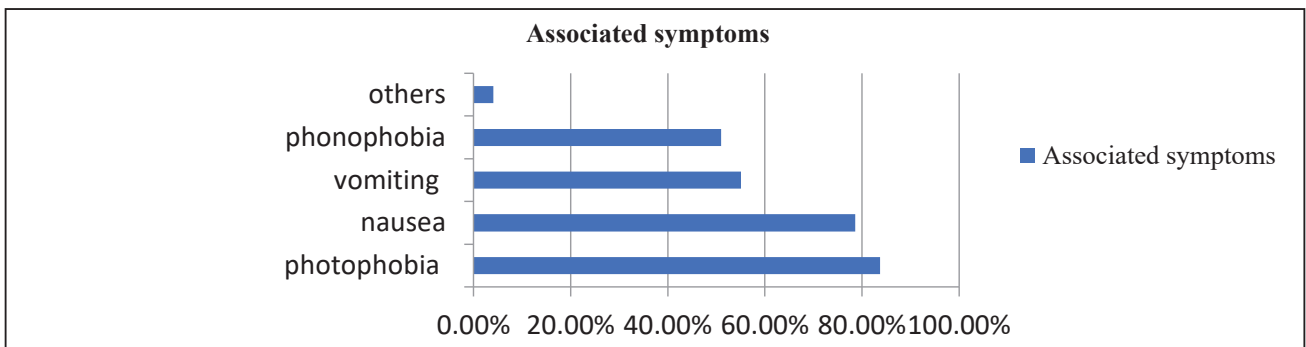


Figure 2: Associated symptoms

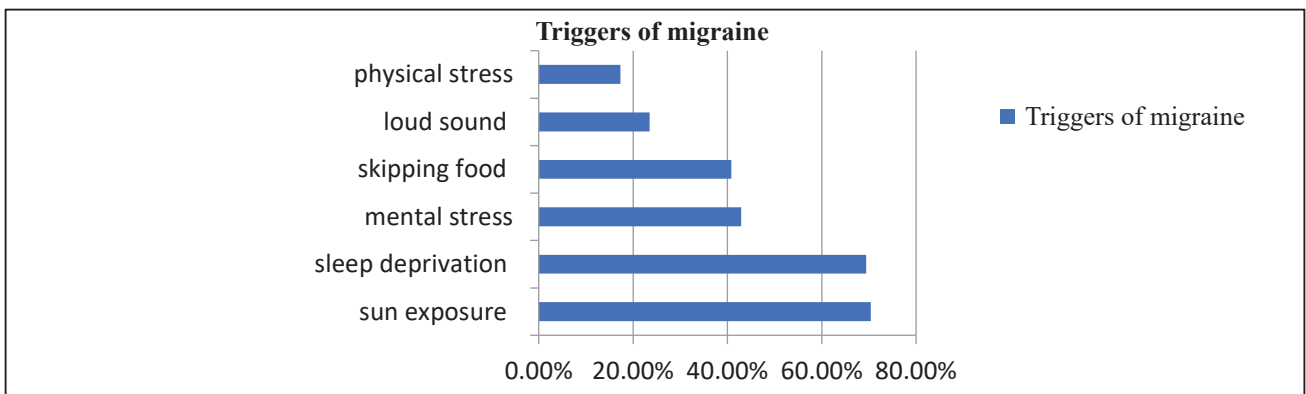


Figure 3: Triggers of migraine

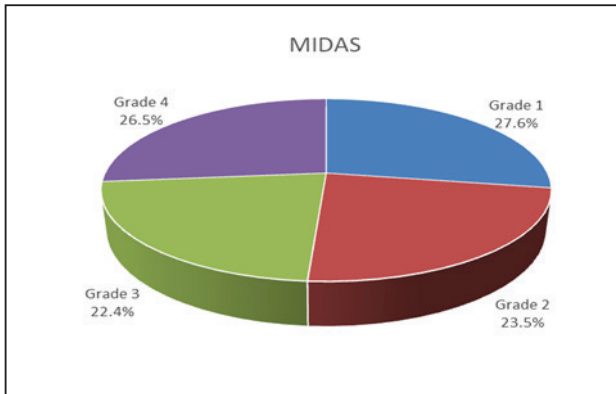


Figure 4: Severity of migraine

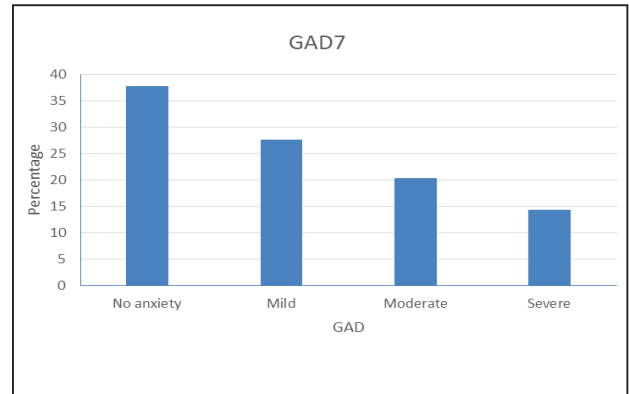


Figure 5: GAD 7

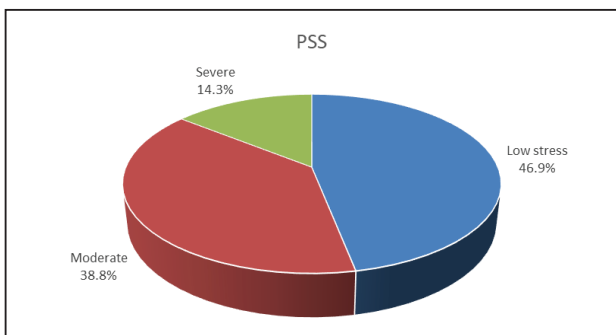


Figure 6: PHQ9

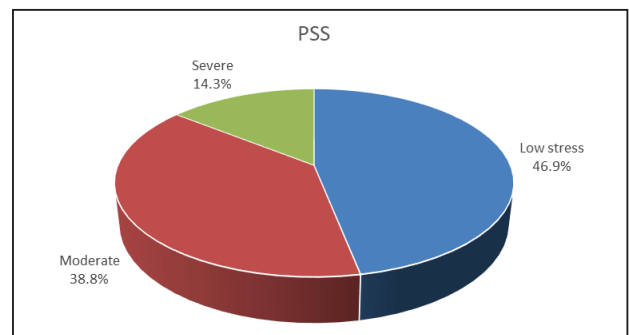


Figure 7: PSS Score

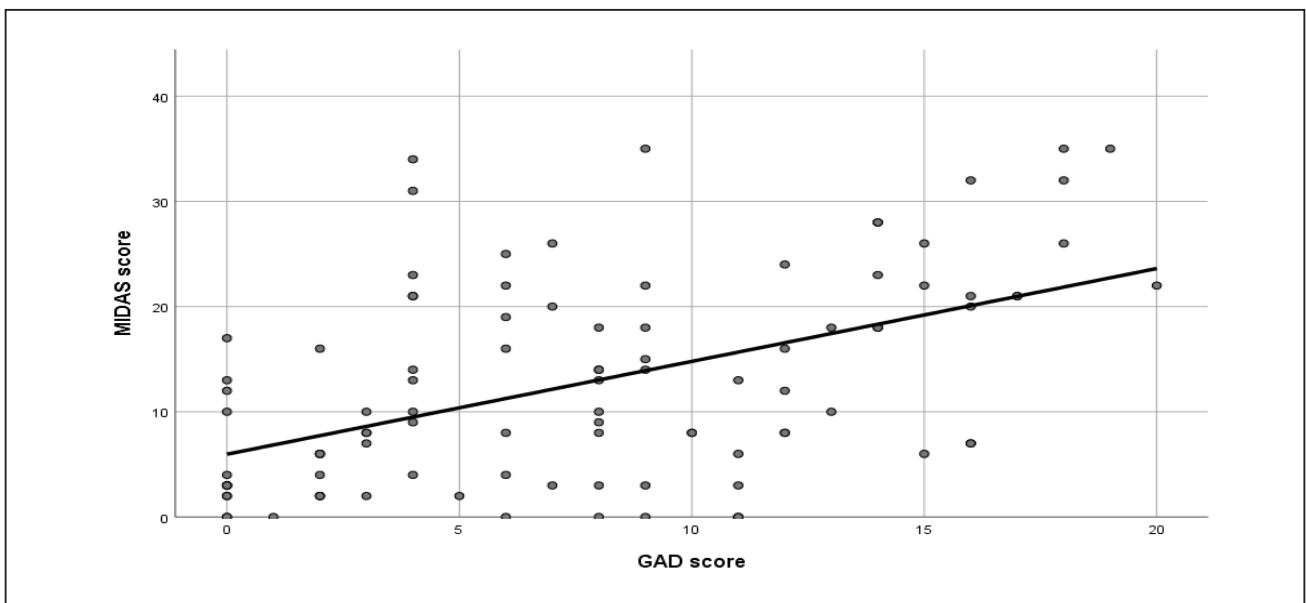


Figure 8: Correlation between GAD 7 score and MIDAS score

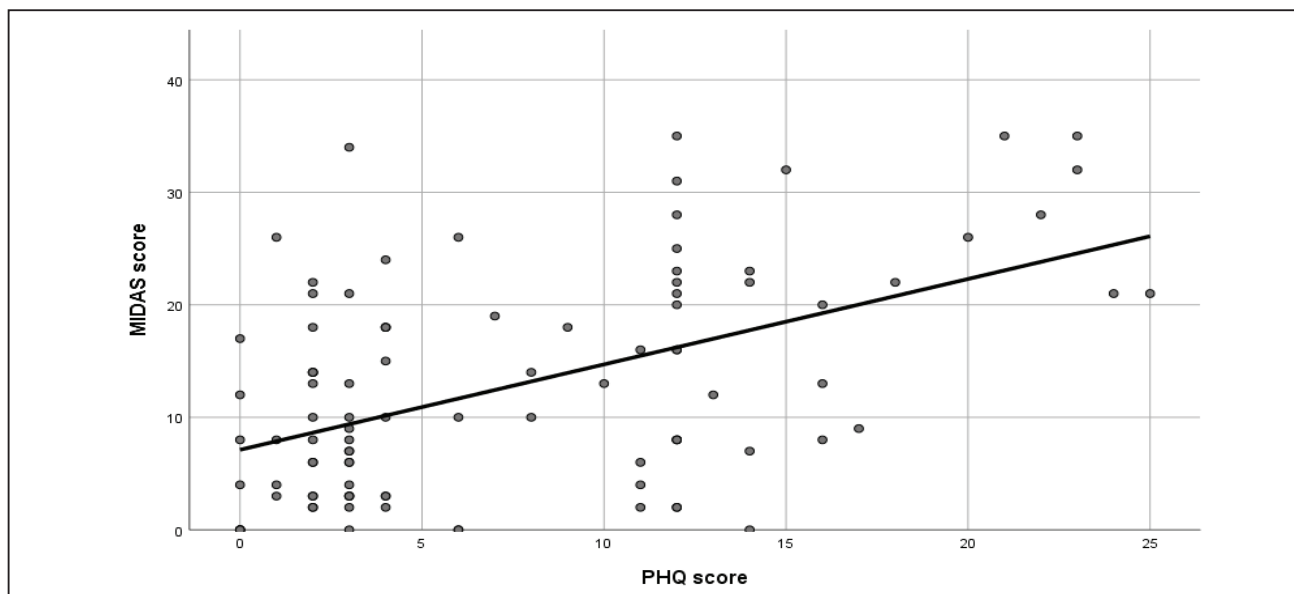


Figure 9: Correlation between PHQ 9 score and MIDAS score

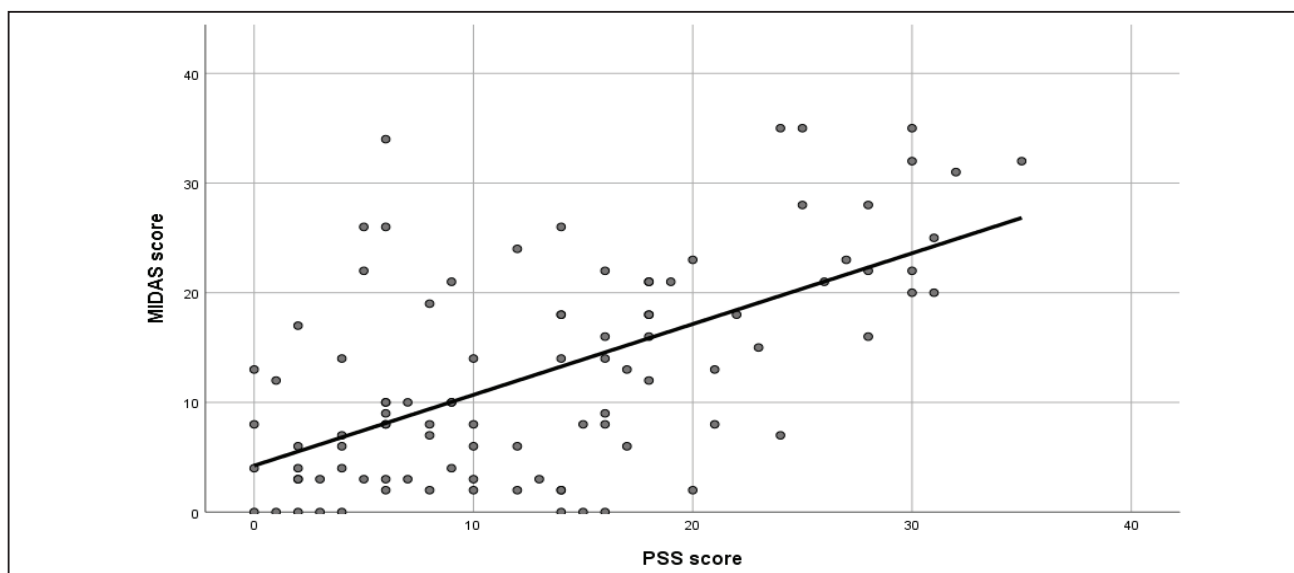


Figure 10: Correlation between PSS score and MIDAS score

Table 1: Comparison of age sex and family history

	Present study	Vishnu Renjith <i>etal</i> ⁷	Balakrishnan <i>etal</i> ⁶	Peres <i>etal</i> ⁸
Age group 18-30	40.8%	NA	34.7%	
% of Female	74.5%	70%	76.1%	73%
Family history	33.7%	28.3%	14.8%	-

Table 2: Comparison of associated symptoms

	Present study	Rasmussen <i>etal</i> ⁹	Wascogen <i>etal</i> ¹⁰
Photophobia	83.7%	89.3%	93.6%
Phonophobia	51%	92.7%	95.3%
Vomiting	55.1%	55.95%	23.4%
Nausea	78.6%	87.5%	86.4%
Menstrual worsening	20.5%	30.7%	71.6%

Table 3: Comparison of triggers

	Present study	Balakrishnan <i>et al</i> ⁶
Sun exposure	70.4%	48.3%
Sleep deprivation	69.4%	37.4%
Skipping of meal	40.8	22.1%
Loud sound	17.3 %	-
Mental stress	42.9	37.8%

Discussion

In our study, majority of the patients belonged to the 18-30 years age group (40.8 %), which was comparable with the study done by Balakrishnan *et al*⁶ which also had a majority of patients belonging to the age group of 18-29 years (34.7%). There were 25.5% males and 74.5% females which was comparable to the study done by Vishnu Renjith *et al*⁷ in which there were 70% female patients, Balakrishnan *et al*⁶ with a total of 76.1% females, and Peres *et al*⁸ with 73%. Family history of migraine was noted in 33.7% of the participants in present study, compared to 28.3% in the study by Vishnu Renjith *et al*⁷ and 14.8 % in the study by Balakrishnan *et al*⁶. However, Balakrishnan *et al*⁶ did not include 22.8% of subjects whose family history was not known, thus accounting for the reduced value (Table 1).

In the present study, aura was present in 40.8% of the subjects; the most common aura was visual aura, constituting 85% of the cases with aura. The most common visual aura reported was scotoma, which constituted 47.5%, followed by fortification spectra (25%) and flashes of light (12.5%). These findings are in contrast to those in the study done by Rasmussen *et al*⁹ which had far higher numbers of patients reporting scotomas (80.9%) and 76.6% with flashes. On the contrary, the study done by Balakrishnan *et al*⁶ showed a significantly lower proportion of patients with aura (11.7%).

In our study, 83.7% of subjects had photophobia, nausea in 78.6%, vomiting in 55.1%, and phonophobia in 51% of subjects. It was also noted that 20.5% of female subjects had worsening of migraine during menstrual time. Rasmussen *et al*⁹ reported the most common associated symptom as phonophobia (92.7%), followed by photophobia (89.2%), vomiting (54.95%), nausea (87.5%), and menstrual worsening (30.7%). In another study done by Wascogen *et al*¹⁰ photophobia was found in 93.6%, phonophobia in 95.3%, vomiting in 23.4%, nausea in 86.4%, and menstrual worsening in 71.6%. (Table 2)

In the present study, the most common trigger for migraine was sun exposure (70.4%), followed by sleep deprivation (69.4%), mental stress (42.9%), and skipping meals (40.8%). In the study done by Balakrishnan *et al*⁶ major trigger factor was sun exposure, but with a

Table 4: Comparison of MIDAS score

	Present study	Vishnu Renjith <i>et al</i> ⁷	Peres <i>et al</i> ⁸
Grade I	27.6	11.7	28
Grade II	23.5	15	15
Grade III	22.4	41.7	25
Grade IV	26.5	31.6	32

lesser percentage of 38.3%. They also found other triggers of migraine were hunger or skipping meals in 21%, stress in 37.8%, and sleep deprivation in 37.4% (Table 3).

Regarding disability, our study revealed that the proportion of patients was fairly evenly divided among the four grades of the MIDAS scale. While in the study by Vishnu Renjith *et al*⁷ had the maximum proportion of patients in grade III (41.7%). (Table 4).

In the present study, we found that the majority of migraineurs had anxiety (62.2%) and depression (48%), thus emphasising the high psychiatric comorbidity of migraine, which has been brought out in various studies^{8,10-13}. The majority of patients had moderate or high stress (53.1%), as demonstrated by the PSS score. Those who were on alternative medicine (31%) had significantly associated severe migraine (P value = 0.002), which implies the importance of standard care of treatment.

Stress, anxiety, and depression were strongly associated with severe migraine, with a P value of 0.001, 0.004, and 0.012, respectively, which was in concordance with our hypothesis. Correlation analysis shows depression, anxiety, and stress were positively correlated with severe migraine with R values of 0.509, 0.506, and 0.604, respectively (P value <0.001). The maximum correlation was seen with the stress score (R value = 0.604). This might be the reason why those with mental stress triggering migraine were significantly associated with severe migraine (p value 0.002) in the present study. A multiple linear regression model was performed to assess the predictive model of the MIDASS score, GAD7, PSS, and PHQ9 has R² value of 0.431, which implies that 43.1% of the variation in MIDAS was explained by the predictors. Stress, which shows the maximum correlation, may be considered as an independent risk factor for severe migraine.

In the study done by Wacogne *et al*¹¹ it was found that stress and anxiety were higher in the migraine group than in the control group, while depression scores (HAD score 5+/-3.3) were clinically not significant, but this could be explained by the fact that they had used the HAD score (Hospital Anxiety Depression Score), as the PHQ-9 score used in our study may categorise a greater proportion of patients with moderate or severe depression than HAD score¹¹. Peres *et al*⁸ also suggest that anxiety has a stronger

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association with migraine than depression. However, similar to the findings of our study, Yavuz *et al*¹² found that depression scores were significantly higher in migraineurs with moderate or severe disability than in patients with minimal or mild disability using a scoring system called DASS (Depression Anxiety Stress Score). MIDAS scores were also significantly correlated with the depression scores in this study. Regarding studies from India, Rammohan *et al*¹³ using the HAD score in a south Indian population, found a prevalence of 16.54% of anxiety and 9.02% of depression in migraineurs, a rate comparable to or less than many studies in international literature and a significantly increased disability in individuals with comorbid mood disorders and migraine. 19% and 7% of comorbid anxiety and depression in migraineurs were found in the Eurolight project¹⁴.

Stress acts as a factor in the triggering and perpetuation of migraine. Stress, anxiety, and depression cause the worsening of migraine both in severity and recurrence. Severe headache and its recurrence will increase stress, thus perpetuating a vicious cycle. The patient's quality of life depends on the severity of the disease, which depends on the way one handles psychological and environmental stress. Migraine is now considered to cause dysfunctional activation of the neurolimbic system in which there is altered functional connectivity between the brainstem modulating circuits and the limbic centers¹⁵. Hence, these psychological factors should be considered the backbone of migraine management. The management of migraine should be much more comprehensive through the screening and management of psychological factors, particularly stress. The inclusion of strategies like behavioural therapy, relaxation therapy, and other psychosocial approaches can thus provide better control of migraine. Avoidable migraine triggers like sun exposure, maintaining proper sleep hygiene, and mental and physical stress should be controlled or avoided to obtain good control of migraine and a better quality of life.

The limitations of our study are that it was done as a hospital based cross-sectional study, thus, the study might have preferentially included subjects with more severe symptoms who are likely to come to the hospital. The scoring systems used for assessing stress, anxiety, and depression were more screening in nature than diagnostic tests.

Conclusion

Our study has revealed the presence of comorbid anxiety, depression, and stress in a significant proportion of migraineurs, higher than reported in previous national and international literature. Disparity may be due to varying scales used in the assessment of depression, anxiety, and stress, as well as variations in baseline characteristics

in different populations. This calls for further detailed larger studies for elucidation. Stress may be considered as an independent risk factor for severe migraine. Stress, anxiety, and depression can act as factors that trigger and perpetuate migraines, with stress showing the highest correlation. The present study suggests the need for more comprehensive care in migraine, including screening for psychological factors like depression, anxiety, and stress in all patients with migraine, which will provide a better quality of life along with migraine control.

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