

Prevalence and predictors of migraine among medical students in Karachi

Farah Anwar¹, Anum Bilal Sheikh^{1*}, Tasneem Taher¹, Minaam Iqbal Khan¹, Aisha Masoom¹, Ashna Khursheed¹, Sidra Saeed¹, Mazia Nasim¹, Hassan Sohail¹, Syeda Haya Fatima¹, Kehkashan Noor¹, Mir Mahnoor Ellahi¹, Mahnoor Azam¹, Kaneez Fatima²

1. Medical Student, Dow University of Health Sciences, Karachi, Pakistan
2. Internal Medicine, Dow Medical College and Civil Hospital, Karachi, Pakistan

***Corresponding author:** Tel: +92 213312397027 Fax: +92 21 35149577
Address: F-F-2, Block 33, Sea view Apartments, D.H.A-V, Karachi-75500, Pakistan
E-mail: anumbilalsheikh@gmail.com
Received; 6/01/2020 Revised; 26/04/2020 Accepted; 12/05/2020

Abstract

Introduction: Migraine is a chronic health issue having a global prevalence of more than one billion people. Migraine impairs daily activities of sufferers and hence the academic performance of medical students as well. This study aimed to investigate the migraine prevalence among a sample of university medical students and to examine the predictors, trigger factors and impact of migraine among these students.

Materials and Methods: A cross-sectional study was conducted in three months, among the medical students of Karachi, Pakistan. Responses were collected using a self-administered questionnaire employing convenience sampling technique. The frequency, duration of attacks, severity, trigger factors, predictors and impact were measured for migraine cases. Independent t-test and chi-square test were used as the primary statistical tests. IBM Statistical Package for the Social Sciences (SPSS) Statistics (version 24) was used for all the analyses.

Results: The overall migraine prevalence among students was 52.3% with the majority of migraines occurring in females. Year of study, age of onset, frequency and pain intensity were significantly associated with migraine in ($P < 0.05$) whereas age and gender were not ($P > 0.05$). Stress (96.4%) and lack of sleep (92.8%) were the most frequent trigger factors of migraine while family history was the most common predictor (32.1%).

Conclusion: Almost half of the medical students suffered from migraine with the majority being females. Reducing stress and improving sleep quality might be helpful in decreasing the migraine attacks in this population.

Keywords: Migraine, Prevalence, Predictors, Triggers, Impacts, Medical students, Pakistan

Introduction

Migraine is a neurological condition characterized by a recurrent, pulsating headache usually affecting one side of the head and often being accompanied by nausea, vomiting, photophobia and phonophobia. It is a chronic health issue having a global prevalence of more than one billion people

(14.7% of the world's population) (1) with a preponderance of women among the migraineurs (2). Migraine impairs daily activities of sufferers and is ranked by the Global Burden of Disease as the 3rd principle cause of disability in people under 50 years of age (3).

Previous studies have linked this condition to certain predictors like GI disorders and

Copyright © 2021 Journal of Basic Research in Medical Science. This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits copy and redistribute the material, in any medium or format, provided that the original work is properly cited.

family history of migraine (4). Studies have also assessed triggering factors of this disorder and medical students appear to be at risk; these students have a heavy study load, demanding schedules and clinical responsibilities which may result in stress (5), sleep deprivation and irregular dietary habits. All of these are common triggers that can increase the frequency of migraine (6) (7). Considering that studies have shown a decline in academic output (8) and an increase in absence from academic institutes among the affected (9) a worrisome situation arises for the society given the future role of medical students as health professionals. Migraine has been studied broadly among the general population and medical students however few studies have been conducted on migraine among medical students of Karachi.

Taking into account the variation of prevalence of migraine among countries (10), the serious effects of migraine on the productivity of students and the paucity of data in Karachi, our research aimed to determine the prevalence and predictors of migraine among medical students of Karachi. Our study also focused on academic impacts, triggers and preferred method of alleviating the pain as secondary objectives.

Materials and Methods

A cross-sectional study was conducted from the month of August to October, in the year 2018 among medical students in Karachi, Pakistan. The respondents comprised MBBS (Bachelor of Medicine and Bachelor of Surgery) students only, from first to final year. Non-MBBS students and those who declined to fill the questionnaire were excluded from this research. A sample size of 375 was calculated with a 95% confidence interval using openepi.com. However, expecting a low response rate, a higher number of questionnaires were distributed

and the research was concluded at 439 forms. Google forms were used to gather 221 of these responses. Using a convenience sampling method, 218 responses were gathered manually by approaching students with a printed form, these forms were collected back on spot. The online and printed forms were identical to maintain reliability of results. Attempts to reduce non-response bias were made by ensuring that the questionnaire was coherent. No interviewer was employed as the questionnaire was self-explanatory and the target population was educated in the English language, nonetheless authors were within reach during the administration of the forms. All participants were willing, assured of confidentiality of information and given the choice to withdraw their responses if they felt like doing so. 22 students declined to fill the questionnaire resulting in the response rate for the self-distributed forms to be 90.8%. There were 64 incomplete forms in this research which were discarded. The Declaration of Helsinki was abided by. The research was exempted from Institutional Review Board (IRB) approval since it was a questionnaire based population survey with no intervention performed on human subjects.

The questionnaire comprised 25 questions which covered five main areas i.e. demographics, prevalence, triggers, predictors and impact of migraine on daily life of an individual. The first few questions targeted basic information about headaches such as their frequency, duration and characteristics. Pain intensity felt by the person was measured using numeric pain rating scale (NPRS) (11). This was followed by questions designed on the basis of the IHS criteria of diagnosing migraine (12) to manually classify the participants as migraine sufferers and non-migraine sufferers. A list of 14 common triggers of migraine was then provided which participants could choose

from along with an option to write their own personal trigger. Family history of migraine, presence of Gastrointestinal disorders or Cardiovascular disorders (CVD), head and neck trauma and other predictors were asked about in order to establish a possible reason as to the appearance of migraine. MIDAS (Migraine disability assessment test) (13) a brief, standardized questionnaire was used to assess the severity of impact on day to day life. In conclusion, the individual was asked about their efforts to shorten or alleviate the pain caused by the headache; taking medicine, reducing stress etc.

Statistical analysis

Analysis of data was performed using IBM Statistical Package for the Social Sciences (SPSS) Statistics (version 24). Simple statistical tests (mean, median, mode, standard deviation) were used to present numerical values, whereas number and percentages were used to describe categorical data. Independent t-test was used to present comparisons between numerical variables. Comparison between non-numerical variables was performed using chi-square (χ^2) test. Differences between groups were regarded as significant if p value was less than 0.05.

Results

From a total of 375 students that were approached, 99.5% of them had headaches. According to the IHS criteria, 196 of them had migraine. The mean age for eligible subjects were 20.5 ± 1.26 years while the mean age for the onset of migraine was 14.6 ± 3.2 years. For most participants, headache lasted for 30 minutes to 4 hours when they did not take medicine while the duration decreased to less than 30 minutes if they did. Nearly one tenth of them had headaches that lasted for greater than 20 days. The pain intensity ranged from 1-10 (Mode = 6) of

which 17.3% had severe pain (>7); amongst whom 37.7% consulted a doctor.

Table 1. Characteristics of migraineurs and migraine. The table shows biodata of individuals and whether they experience migraine. It signifies the relationships by calculation of P value.

	Migraine		P value
	Yes	No	
Total number	196 (52.3)	179(47.7)	
Gender			0.058
Male	28 (14.3)	39 (21.8)	
Female	168 (85.7)	140 (78.2)	
Year of study			0.024
First year	37	36	
Second year	106	80	
Third year	21	26	
Fourth year	20	11	
Fifth year	12	26	
Age	20.5 ± 1.26	20.7 ± 1.59	0.253
Age of onset*	14.6 ± 3.20	15.6 ± 3.43	0.006
Frequency**			0.00001
1 to 3 days	61 (31.1)	131 (73.2)	
4 to 6 days	50 (25.5)	20 (11.2)	
7 to 12 days	45 (23.0)	8 (4.5)	
13 to 20 days	19 (9.70)	5 (2.8)	
> 20 days	17 (8.70)	3 (1.7)	
Pain intensity			0.047
Mild (1-3)	34 (17.3)	90 (50.3)	
Moderate (4-6)	99 (50.5)	65 (36.3)	
Severe (>7)	63 (32.1)	24 (13.4)	

Data are shown as mean \pm SD or number (percent).

*44 people didn't know their age of onset of migraine.

**16 people failed to answer it.

Table 1 shows year of study, age of onset, frequency and pain intensity were significantly associated with migraine in the study ($P < 0.05$). The highest occurrence of migraine was in second year medical students. Moreover, age and gender did not differ significantly between the groups.

As shown in Table 2, stress (96.4%) and lack of sleep (92.8%) were the most frequent triggering factors of students' migraine. Other reported triggers were change in routine (79.1%), exposure to sun/weather changes (68.9%) and sleeping too long (59.7%). The most common trigger in male and female students was stress ($P=0.00$) while the least

common was smoking ($P=0.796$) however this was found to be insignificant. Moreover

almost 50% of females chose menstrual cycle as a potential trigger.

Table 2. Triggers and their frequencies (%). The table lists potential triggers of migraines and their frequency among sufferers in the population.

Triggers	Frequency		
	No headache	Some headaches	All headaches
Stress levels you experienced	7 (3.6)	126 (64.3)	63 (32.1)
Excessive caffeine containing drinks e.g. coffee, tea, cola	159 (81.1)	31 (15.8)	6 (3.1)
Lack of caffeine containing drinks e.g. coffee, tea, cola	97 (49.5)	81 (41.3)	18 (9.2)
Sleeping too long	79 (40.3)	108 (55.1)	9 (4.6)
Lack of sleep	14 (7.10)	142 (72.4)	40 (20.4)
Smoking	189 (96.4)	5 (2.6)	2 (1.00)
Missing meals	85 (43.4)	92 (46.9)	19 (9.7)
Change in routine	41 (20.9)	133 (67.9)	22 (11.2)
Certain food/smells	125 (63.8)	60 (30.6)	11 (5.6)
Exposure to sun/ weather changes	61 (31.1)	115 (58.7)	20 (10.2)
Bright lights and sounds	76 (38.8)	92 (46.9)	28 (14.3)
Your menstrual cycle	108 (55.1)	76 (38.8)	12 (6.10)
Too much exercise	157 (80.1)	36 (18.4)	3 (1.50)
Onset of headache during sleep	132 (67.3)	60 (30.6)	4 (2.00)

Data are shown as number (percent).

Table 3 shows the most frequent predictor for migraine was family history (32.1%) followed by gastrointestinal disorders (30.6%) and mental health disorders (22.4%).

Table 3. Predictors of Migraine and their Significance. The table lists potential predictors of migraine among migraineurs and non-sufferers. P value is calculated for sufferers only.

Predictors	Migraine		P
	Yes	No	
Family history	63 (32.1)	34 (19.0)	0.004
Gastrointestinal disorders	60 (30.6)	26 (14.5)	0.001
Cardiovascular diseases	10 (5.10)	5 (2.79)	0.254
Mental health disorders	44 (22.4)	23 (12.8)	0.015
Head and neck injuries	13 (6.63)	3 (1.68)	0.018
Asthma	17 (8.67)	16 (8.94)	0.928
Hypertension	18 (9.18)	10 (5.59)	0.186

Data are shown as number (percent).

Among 196 students who had migraines, only 23% had consulted a physician for their headache with a greater percentage being males (39.2%) than females (20.8%, $P=0.033$). Shifting to a calmer environment was mostly adapted by eligible subjects to relieve their symptoms. The table 4 shows

that most people had little or no disability (107 -54.6%) while least number of people had moderate disability (15-7.65%). Females had greater disability of all grades and this association was significant ($P=0.047$). More than half of the students having severe disability (grade 4) were second year students.

Table 4. MIDAS grades. This table shows the number and percentage of migraineurs against the level of impact that the disorder has on their lives.

MIDAS grade	N	Female	Male
Grade I	107 (54.6)	88 (44.9)	19 (9.69)
Grade II	17 (8.67)	14 (7.14)	3 (1.53)
Grade III	15 (7.65)	15 (7.65)	0 (0.00)
Grade IV	57 (29.1)	51 (26.0)	6 (3.06)

Data are shown as number (percent).

Discussion

The primary objective of this study was to assess the prevalence and predictors of migraine among medical students, with triggers and impacts as the secondary objective. Our study found that migraine was common among the medical students of Karachi, with a high prevalence of 52.3%. The prevalence was particularly higher

among second year MBBS students with a female preponderance.

Our figure is comparable with those in India and Brazil, where the prevalence of migraine in medical students was also found to be high (42% and 40.2% respectively) with a similar female preponderance (14) (15). However, the prevalence of migraine in our study is significantly higher than in students in China (7.9%) (16), and also differs from that in Iran, where most of the 16.3% affected by migraine were men (17). The trend seen in our study does not correspond with previous epidemiological studies that suggest a significantly lower prevalence in Asia as compared to Europe and North America (18). However, these studies were mostly population-based and thus their results may not be at par with the results of this study. Another reason for this disparity could be differences in diagnostic criteria. Nonetheless, other studies have suggested that people from a particular race have a certain genetic susceptibility to migraine (19).

In this study, the female participants were six times more prone to migraine than their male counterparts; a substantially high prevalence as compared to that seen in other studies (14) (15). This unusually high ratio may be because there were generally more female participants than males in this study sample. The pre-pubertal prevalence in migraine is almost the same in both genders, however after puberty; migraine tends to be more common in females than males, signifying a role of hormonal changes that take place at menarche and during sexual cycles in causing migraine (20). Around half of the female migraineurs reported menstrual cycle as a potential trigger. Estrogen is known to play its role in perpetuating migraine attacks in females with an increased duration, functional disability and treatment resistance (21). A comparatively larger number of female migraineurs in the study

were seen to have greater disability of all grades. Another reason could be the difference in the pattern of pain perception and processing which differs greatly in men and women for biological and psychological reasons (20) (22).

The high prevalence seen in second year MBBS students is comparable with a study conducted in Southeast China which suggests that tough curriculum and adapting to a new environment might be possible reasons (16). Peer pressure could be another reason as the threshold for entry in medical schools, particularly DUHS, is unusually high; hence, the competition is cut-throat amongst the brilliant masses enrolled in the MBBS programme here. Also, the study was conducted in the latter half of the year, which is close to the time of the semester examinations.

Similar to a study conducted in Kuwait (23), most students in our study had moderate-to-severe migraine. Most participants reported frequent episodes of migraine attacks, but despite that, very few consulted a physician and of those who did, most were males. Duration of migraine was significantly short in people who took any medication for it whereas it persisted for a couple of hours in those who did not. Headache is mostly considered a nuisance in our part of the world where most people resort to self-treatment or home remedies. This clearly indicates inadequate knowledge about migraine and attitude towards its management which in this study group was very unusual as medical students are expected to know better. Also, the university has a teaching hospital attached to it which ideally means an easier access to health facilities. Self-medication, however, is a very common phenomenon in this country, with the use of analgesics and non-steroidal anti-inflammatory drugs being widespread for treating migraine pain (24). Another reason could be the sale of drugs without prescription in a lot of places in

Karachi; the sale of only a few medicines is strictly under prescription. Previous work also showed that despite high prevalence of migraine headache, very few university students sought medical advice (14) (15) (24).

Apart from medical treatment, most students reported moving to a peaceful environment to alleviate their symptoms. Since 'lack of sleep' and 'stress' were the most frequent trigger factors reported, with 'change in routine' being another popular choice for migraine triggers in this study, retiring to peaceful surroundings and resting, either with or without medication, may have proven to be a successful strategy which thus makes a medical visit somewhat inconsequential. Since 'stress', 'lack of sleep' and 'disrupted routine' are rampant among medical students, as seen in existing literature (23), there is a dire need for stress management programmes to help students in dealing with its undesirable consequences, promptly. 'Weather changes' and 'exposure to bright light and sounds' were also responsible for migraine in a large number of people. Karachi experiences a tropical climate with warm winters and hot summers and humidity levels remain high for most of the year. Fluctuating patterns of temperature change, high humidity and sun glares are factors that contribute to migraine.

Family history of migraine was reported by 63% of the population, with results showing a positive relation between family history and migraine. Previous studies have documented an incidence as high as 80% (15). The high sensitivity in this population could be misleading owing to the fact that the participants might have wrongly classified any headache as migraine, considering that its manifestations may not be very obvious each time. Also, the data was collected from medical students who are not professional doctors yet; hence their diagnosis may lack credibility. Lateef TM et al in their study also

established the lack of reliability of family history of migraine based on misclassification by the study participants (25). In contrast to our findings, lower family history for migraine has been reported with the need for more population based studies to identify any racial or genetic link (24).

A significant number of participants (i.e. 60%) were seen to record gastrointestinal (GI) disorders as a comorbidity. In line with the findings of Huerta-Franco MR et al, whereby a positive relation was established between occupational stress and GI disturbances (26), the high levels of stress that were reported, particularly make medical students a high risk group for physiological consequences of stress, GI alteration being a major one. This justifies the statistically significant association of GI disturbances with migraine found in this study.

Other predictors for migraine were mental health disorder, as notified by a fair number in the study, hypertension, asthma, head and neck injury and cardiovascular disorders. However, no correlation was found between these predictors and migraine. A population-based study would be a better approach in establishing any link amongst these. This sample population was small and does not adequately represent the community at large. It is noted that migraine causes functional disability resulting in physical, psychological and social consequences, thereby adversely affecting family, academic and occupational responsibilities (27). In this study, MIDAS questionnaire was used to assess disability and approximately half the population (i.e. 54.6%) reported little or no disability but with a significant number (57 out of 196) reporting severe disability as well. However, a higher proportion of female participants suffered from disability of all grades. Of those suffering from severe disability, a large number were second year MBBS students.

This is essentially because of the higher migraine prevalence in this group.

This study has some limitations which include its cross-sectional nature, the small sample size and the sample population which is highly selective and does not represent the community at large. Also, migraine subtypes were not investigated, like menstrual migraine, subtypes such as migraine with or without aura and episodic or chronic migraine, thus limiting the understanding of migraine features among different subtypes. The cross-sectional nature of the study may have resulted in recall bias to an extent though attempts were made to reduce it.

Conclusion

Concluding this, migraine is common among medical students in Karachi and is prevalent in female and second year students, with family history of migraine documented as the most important predictor, and stress and lack of sleep the most common trigger factors in this population. Future studies should focus on identifying migraine subtypes and more studies should be conducted with a prime focus on the general population for a better understanding of the disorder. An educational program for increasing migraine awareness among medical students is also suggested.

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2010; 380(9859):2163-96. doi: 10.1016/S0140-6736(12)61729-2.
2. Launer LJ, Terwindt GM, Ferrari MD. The prevalence and characteristics of migraine in a population- based cohort: the GEM study. *Neurology*. 1999;

Conflict of interest

The authors of this research have no affiliations with or involvement in any organization with any financial or non-financial interest in the subject matter discussed in this research.

Author contributions

Kaneez Fatima served as a mentor for this research only. The other authors all agreed with the topic of the research once it was put forward by Sidra Saeed. Sidra Saeed, Hassan Sohail and Mahnoor Azam were involved with the introductions for this research article which were then compiled by Anum Bilal Sheikh. Planning and methodology of the research were the responsibility of Anum Bilal Sheikh, Syeda Haya Fatima and Mir Mahnoor Ellahi. All the authors were involved in data collection from the sample population. Minaam Khan, served as the group leader, and along with Aisha Masoom and Ashna Khursheed contributed to the results and conclusion of the research article. They were responsible for analyzing the entire data set and all statistical calculations and tables. Farah Anwar, Tasneem Taher, Mazia Nasim and Kehkashan Noor wrote discussions for the article which were compiled into one by Farah. At the end, Tasneem Taher wrote the abstract.

53(3):537-42. doi: 10.1212/WNL.53.3.537.

3. Steiner TJ, Stovner LJ, Vos T. GBD 2015: migraine is the third cause of disability in under 50s. *J Headache Pain*. 2016; 17(1):104. doi: 10.1186/s10194-016-0699-5.
4. Ibrahim NK, Alotaibi AK, Alhazmi AM, Alshehri RZ, Saimaldaher RN, Murad MA. Prevalence, predictors and triggers of migraine headache among medical students and interns in King Abdul Aziz

- university, Jeddah, Saudi Arabia. *Pak J Med Sci.* 2017; 33(2):270-75. doi: 10.12669/pjms.332.12139.
5. Dyrbye LN, Thomas MR, Shanafelt TD. Systematic review of depression, anxiety, and other indicators of psychological distress among U.S. and Canadian medical students. *Acad Med.* 2006; 81:354-73. doi: 10.1097/00001888-200604000-00009.
 6. Marmura MJ. Triggers, Protectors, and Predictors in Episodic Migraine. *Curr Pain Headache Rep.* 2018; 22(12):81. doi: 10.1007/s11916-018-0734-0.
 7. Andress-Rothrock D1, King W, Rothrock J. An analysis of migraine triggers in a clinic-based population. *Headache.* 2010; 50(8):1366-70. doi: 10.1111/j.1526-4610.2010.01753.x.
 8. Bigal ME, Bigal JM, Betti M, Bordini CA, Speciali JG. Evaluation of the impact of migraine and episodic tension-type headache on the quality of life and performance of a university student population. *Headache.* 2007; 15(7):710-9. doi: 10.1046/j.1526-4610.2001.041007710.x.
 9. Smitherman TA, McDermott MJ, Buchanan EM. Negative impact of episodic migraine on a university population: Quality of life, functional impairment, and comorbid psychiatric symptoms. *Headache.* 2011; 51:581-9. doi: 10.1111/j.1526-4610.2011.01857.x.
 10. MacGregor EA, Brandes J, Eikermann A. Migraine prevalence and treatment patterns: the global Migraine and Zolmitriptan Evaluation survey. *Headache.* 2003 Jan; 43(1):19-26. doi: 10.1046/j.1526-4610.2003.03004.x.
 11. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage.* 2011; 41:1073-93. doi: 10.1016/j.jpainsymman.2010.08.016.
 12. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia.* 2013; 33(9):629-808. doi: 10.1177/0333102413485658.
 13. Stewart WF, Lipton RB, Kolodner K, Liberman J, Sawyer J. Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. *Cephalalgia.* 1999; 19:107-14. doi: 10.1177/0333102413485658.
 14. Menon B, Kinerra N. Prevalence and characteristics of migraine in medical students and its impact on their daily activities. *Ann Indian Acad Neurol.* 2013; 16(2):221-5. doi: 10.4103/0972-2327.112472.
 15. Sanvito WL, Monzillo PH, Peres MF, Martinelli MO, Fera MP, Gouveia DA, et al. The epidemiology of migraine in medical students. *Headache.* 1996; 36:316-9. doi: 10.1046/j.1526-4610.1996.3605316.x.
 16. Xiao Gu, Yaojie Xie. Migraine attacks among medical students in Soochow University, Southeast China: a cross-sectional study. *J Pain Res.* 2018; 11:771-81. doi: 10.2147/JPR.S156227.
 17. Yazdanparast M, Abrishamizadeh AA, Mahboobi H, Omrani A, Ghasemi M, Ghorashi M, et al. Prevalence of and factors associated with migraine in medical students at Bandar Abbas Southern Iran, in 2012. *Electron Physician.* 2013; 5(3):679-84. doi: 10.14661/2013.679-684.
 18. Merikangas KR. Contributions of epidemiology to our understanding of migraine. *Headache.* 2013; 53(2):230-46. doi: 10.1111/head.12038.
 19. Stewart WF, Lipton RB, Liberman J. Variation in migraine prevalence by

- race. *Neurology*. 1996; 47:52-9. doi: 10.1212/wnl.47.1.52.
20. Delaruelle Z, Ivanova TA, Khan S, Negro A, Ornello R, Raffaelli B, et al. Male and female sex hormones in primary headaches. *J Headache Pain*. 2018; 19(1):117. doi: 10.1186/s10194-018-0922-7.
21. Brandes JL. The influence of estrogen on migraine: a systematic review. *JAMA*. 2006; 295:1824-30. doi: 10.1001/jama.295.15.1824.
22. Loewendorf AI, Matynia A, Saribekyan H, Gross N, Csete M, Harrington M, et al. Roads less traveled: sexual dimorphism and mast cell contributions to migraine pathology. *Front Immunol*. 2016; 7:140. doi: 10.3389/fimmu.2016.00140.
23. Al-Hashel JY, Ahmed SF, Alroughani R, Goadsby PJ. Migraine among medical students in Kuwait University. *J Headache Pain*. 2014; 15:26. doi: 10.1186/1129-2377-15-26.
24. Ojini FI, Okubadejo NU, Danesi MA. Prevalence and clinical characteristics of headache in medical students of the University of Lagos, Nigeria. *Cephalalgia*. 2009; 29:472-7. doi: 10.1111/j.1468-2982.2008.01766.x.
25. Lateef TM, Cui L, Nakamura E, Dozier J, Merikangas K. Accuracy of family history reports of migraine in a community-based family study of migraine. *Headache*. 2015; 55(3):407-12. doi: 10.1111/head.12501.
26. Huerta-Franco MR, Vargas-Luna M, Tienda P, Delgadillo-Holtfort I, Balleza-Ordaz M, Flores-Hernandez C. Effects of occupational stress on the gastrointestinal tract. *World J Gastrointest Pathophysiol*. 2013; 4(4):108-18. doi: 10.4291/wjgp.v4.i4.108.
27. Renjith V, Pai MS, Castelino F, Pai A, George A. Clinical profile and functional disability of patients with migraine. *J Neurosci Rural Pract*. 2016; 7(2):250-6. doi: 10.4103/0976-3147.176188.