Migraine in Premenstrual Syndrome; Frequency and Associated Factor

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ABSTRACT

Background: The prevalence of migraine headaches significantly increased in girls after menarche. This indicated that there is a closely relation between hormonal changes especially the estrogen level with migraine headaches.

Objectives: The aim of this work was to determine the frequency of migraine and its associated factors in medical students affected with premenstrual syndrome (PMS).

Materials and Methods: This cross-sectional study was done on 218 of medical students (between 18 to 30 years old) in Mashhad in the North-East of Iran from March 2015 to March 2016. Premenstrual syndrome was confirmed by Premenstrual Symptoms Screening Tool (PSST). Migraine headache was determined according to International Headache Society (HIS) criteria. The frequency of menstrual migraine and its associated factors including educational degree, life style, marital status, menstrual regularity, family history and type of migraine were determined among the participants with PMS. Data analyze was performed by SPSS 21 and STATISTICA 10.

Results: Of 218 students with premenstrual syndrome, 32 persons (14.7%) had migraine headache. 84.4% of migraines were without aura and the mean attacks per months were 4.34±1.93. The most prevalence of migraine observed in students with 22.09±2.44 years old, intern students (16.1%), Mariel students (20%), students with irregular menstruation (26.3%), students with positive family history (36.5%) and students which lived in dorm (26.1%).

Conclusion: According to our results, the prevalence of migraine in students with PMS is in the range of 14.7%. Therefore, it is recommended that women suffering from PMS be evaluated for migraine based on diagnostic criteria of HIS.

Keywords: Premenstrual Syndrome; Headache; Migraine Disorders

Introduction

Premenstrual syndrome (PMS) is one of the major diseases that most women of childbearing age are engaged with [1].

By definition, PMS is a set of unpleasant physical, psychological or behavioral symptoms observed repeatedly during luteal

phase of the menstrual cycle whose intensity can adversely affect women's relationship with other people or interfere with their normal activities [2]. In a study conducted in Spain (2008), the prevalence of PMS was reported 73.3% [3]. According to some studies, the frequency of migraine headaches in PMS considerably increased, while other similar studies reported no relationship between these two conditions [4-7]. In addition, there is disagreement about migraine prophylaxis medications for these patients [7].

There are several biological theories about the cause of PMS [8-11]. It seems that there is a consensus that natural fluctuations in gonadal hormones (estrogen and progesterone) in women who are vulnerable to developing migraines can lead to the biochemical changes in the brain which are responsible for PMS symptoms. Fluctuations in estrogen levels lead to increased cerebrovascular stimulation and cause headache [7-12]. It seems that among all neurotransmitters studied until now, serotonin is more related to PMS than others. Serotonin levels may decrease in most women before menstruation and varying degrees of psychiatric symptoms can be observed in women who are vulnerable to developing migraine. During or immediately after menstruation, many women feel psychological pleasure (sometimes as euphoria) that could indicate sudden return of normal serotonin activity. The possible effects of gonadal hormones on serotonin activity are the base of many current treatments of PMS [8,13]. In addition, serotonin is known as the primary cause and trigger for all headaches [10,14,15].

The prevalence of migraine is more or equal in the boys than/by in the girls before

puberty, but is clearly increased in girls after menarche. This shows a close relationship between hormonal changes, particularly estrogen and migraine headaches. However, women's migraine headaches vary in different stages of life. So that such headaches are increased at the time of menarche, at the beginning of each menstrual cycle, taking contraceptive pills, early pregnancy, postpartum period, before the onset of menopause, after menopause and at the time of taking estrogen and progesterone [10,14,15].

Overall, headache occurs more frequently before or during menstruation in 60% of women with migraine. These headaches are longer, more severe and hard to treat [10,14,15].

Given the high prevalence of PMS among women, a high prevalence of migraine headaches, and hormonal disturbance as a triggering factor for migraine headaches and lack of studies on the relationship between the two conditions in Iran, and a limited number of similar studies, we decided to examine the relationship between the two conditions with evaluating the frequency of migraine headaches among people with PMS.

Materials and Methods

This cross-sectional study recruited female medical students in a faculty medicine in Mashhad in the North-East of Iran, diagnosed with PMS in 2015. Inclusion criteria included students who consented to participate in the study and had moderate to severe PMS and exclusion criteria included those who did not consent to participate in the study. A total of 445 female medical students selected from all stages of education by stratified sampling based on the number of students per level.

First, the researcher delivered premenstrual symptoms screening tool (PSST) to students with PMS. Then students were examined in terms of premenstrual migraine headaches.

PSST consists of 19 items in two parts (part I contains 14 items on psychological, physical and behavioral symptoms and the second part includes 5 items in which the effect of these symptoms is evaluated on subjects' lives). Each item was scored based on a four-point Likert scale of never, mild, moderate and severe. The following three conditions should be together to detect moderate or severe PMS: at least one item from 1 to 4 should be moderate or severe, at least four items from 1 to 14 should be moderate or severe and in the last five items, there should be one moderate or severe item; the reliability and validity of the questionnaire have been confirmed in Iran [16]. In PSST, Cronbach's alpha for symptoms is 0.90, for interference of symptoms with daily activities was 0.91 and for whole scale was 0.93. The intra-class correlation between the two sections was 0.8. In the quantitative content analysis, the necessary changes were made in the questionnaire according to experts' views [16]. For qualitative content validity content validity ratio and content validity index were reported as 0.7 and 0.8, respectively. These values are higher than acceptable level indicating that this questionnaire has content validity.

If PMS was determined moderate or severe according to PSST, the subjects were referred to a neurologist for the diagnosis of migraine. Criteria for diagnosis of migraine headache were based on International Headache Society Criteria [17].

Finally, if the students with PMS had migraine, they were referred to a neurologist for confirmation of their migraine, and the neurologist collected information according to a checklist. The content of the checklist was previously approved by the Department of Neurology at Islamic Azad University and included individual characteristics such as age, educational level, marital status, type of residence (independent, in dormitory or with families), family history of migraine, the presence or absence of migraine with aura, migraine attacks per month and menstrual regularity.

The rest of subjects who did not suffer PMS according to PSST were also evaluated by a neurologist in terms of migraine headaches. Data integrity was considered at all stages of this study to prevent misleading and unrealistic results. Any prejudgment or data manipulation was strictly avoided. Demographic data included name and last name, which were strictly confidential. Students were completely free to collaborate in the study and their acceptance or refusal had no effect on the follow-up treatment.

Appropriate statistical indicators such as mean, standard deviations and the range of changes were used to describe the quantitative data and frequency and percent frequency were used to describe qualitative data. SPSS 21 and STATISTICA 10 were used in this study.

In this study initially, 445 female students were assessed by PSST for PMS, 15 students did not complete the questionnaire, and 218 students were diagnosed by PMS. All of them were examined for the presence or absence of migraine by a neurologist based on the diagnostic criteria of the International Headache Society.

The frequency of migraine associated with PMS was 14.7% (n=32) among all subjects,

while the frequency of migraine was observed in 12% of students without PMS.

The mean age of the students was 22.11±2.57 years and the frequency of migraine associated with PMS was not significantly related to age (*p*=0.943).

From a total of 218 students with PMS in this study, 54 students (24.8%) were in basic stage of education, 54 students (24.8%) in intermediate stage, 54 students (24.8%) in externship and 56 students (25.6%) in internship course. The findings show that the distribution of educational stage had no significant difference in students with and without migraine in terms of PMS (*p*=0.975) (Table 1).

Table 1. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to Educational degree

Educational degree	With migraine frequency (%)	Without Migraine frequency (%)	Total frequency (%)	*p-value*
Basic science	8 (14.8)	46 (85.2)	54 (100)	
Physiopathology	8 (14.8)	46 (85.2)	54 (100)	0.975
Apprenticeship	7 (13)	47 (87)	54 (100)	
Internship	9 (16.1)	47 (83.9)	56 (100)	

The frequency of migraine among students with PMS who were staying in the dormitory was more than others (26.1%). Then, the most frequency of migraine was reported in students who lived away from the family in private residence (21.1%). The frequency of migraine was reported 7.7% in students with PMS who lived with their families. Given the probability value of chi-square test, it is concluded that there is a significant relationship between the type of residence and migraine (*p*=0.002). The prevalence of migraine was significantly higher in students who were living in the dormitory and those who were away from their family than those who lived with their family (Table 2).

Table 2. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to life style

Life style	With migraine frequency (%)	Without migraine frequency (%)	Total frequency (%)	*p-value*
With family	10 (7.7)	120 (92.3)	130 (100)	
Dorm	18 (26.1)	51 (73.9)	69 (100)	0.002**
Independent home	4 (21.1)	15 (78.9)	19 (100)	

From a total of 163 students with PMS, 21 students (12.1%) had migraine. In addition, among 55 married students, 11 students (20%) had migraine symptoms. According to the probability value of chi-square test, it is concluded that there is no significant relationship between marital status and migraine (*p*=0.197) (Table 3).

Table 3. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to marital status

Marital status	With migraine frequency (%)	Without migraine frequency (%)	Total frequency (%)	*p-value*
Single	21 (12.9)	142 (87.1)	163 (100)	0.197
Married	11 (20)	44 (80)	55 (100)	

A total of 142 students with PMS had regular menstrual cycles and the frequency of migraine among them was 8.5% (n=12). But a higher percentage of students with migraine were in a group who had irregular menstrual cycles. The frequency of migraine among 76 students with irregular menstrual was 26.3% (n=20). According to the probability value of

chi-square test, it is concluded that there is a significant relationship between menstrual regularity and having migraine; in other

words, the frequency of migraine in students who had irregular menstrual cycles was significantly more than those with regular menstrual cycles (*p*<0.0001) (Table 4).

Table 4. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to menstrual regularity

Menstrual regularity	With migraine frequency (%)	Without migraine frequency (%)	Total frequency (%)	*p-value*
Regular	12 (8.5)	130 (91.5)	142 (100)	<0.0001**
Irregular	20 (26.3)	56 (73.7)	76 (100)	

From a total of 218 students with PMS, 52 students had a family history of migraine among them the frequency of migraine was 36.5% (n=19). Among 166 students without family history of migraine, the frequency of migraine was also 7.8% (n=13). According to the probability value of chi-square test, it is

concluded that there is a statistically significant relationship between the family history of migraine and having migraine; in other words, the frequency of migraine in students who had a positive family history of migraine was significantly higher than other students (*p*<0.0001) (Table 5).

Table 5. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to family history

Family history	With migraine frequency (%)	Without migraine frequency (%)	Total frequency (%)	*p-value*
Yes	19 (36.5)	33 (63.5)	52 (100)	<0.0001**
No	13 (7.8)	153 (92.2)	166 (100)	

The mean number of migraine attacks in all students was 3.34±1.93 times a month, in students with PMS who had migraine with aura was 7±1.72 times a month and in those with migraine without aura was 3.85±1.54 times a month. The number of migraine attacks was evaluated in both groups and as it was normal, t-test was used to compare the

two groups. According to the probability value of t-test, it is concluded that there is a significant difference between the mean number of migraine attacks in students with migraine with aura and without aura (*p*<0.05).

According to the results, 15.6% of the migraine reported was migraine with aura and 84.4% was migraine without aura (Table 6).

Table 6. The frequency of migraine in patients with Premenstrual syndrome (PMS) according to type of migraine

Type of migraine	Frequency (%)
With urea	5 (15.6)
Without urea	27 (84.4)
Total	32 (100)

Discussion

Overall, the prevalence of migraine in students without PMS was 12% and the frequency of migraine in students with PMS

was 14.7%, most of them had the type of migraine without aura and the number of attacks was between 2 and 8 times a month.

The highest prevalence of migraine was in the age group 20 to 25 years old, in internship course and in married students. In addition, migraine was observed more in students with irregular menstrual cycles, with a family history of migraine, and also in students who lived in the dormitory. The findings of this study show that the prevalence of migraine is increased in cases of PMS. Migraine headaches which are thought to result from consecutive contractions in cerebral vessels are influenced by hormonal cycles and change [2]. These headaches are 2 to 3 times more common in women than in men. The disorder is improved in about 80% of patients during pregnancy, but relapses afterward [10]. Typically, migraine headaches are improved after the onset of menopause. According to 60% of women who suffer from migraine, the start of attacks is related to menstrual cycle and 7% of them have migraine headache two days before and two days after the onset of menstruation [14,15]. It is thought that the relationship between migraine headaches and hormonal changes of the menstrual cycle is related to estrogen reduction. Evidence on this issue is obtained from many studies, first, a small proportion of women with menstrual migraine have an increase in the frequency of headache after an increase in estrogen before ovulation; second, sometimes oral estrogen reduces the prevalence of migraine, and third, oral progesterone may delay the onset of menstruation without preventing migraine attacks. Several mechanisms have been used to explain why the decline in estrogen may cause migraine headaches. These mechanisms include abnormal platelet aggregation, impaired regulation of opioids on the central nervous system and stimulating increased production of prostaglandins in the central nervous system [14,18,19].

PMS associated with menstrual migraine has been evaluated and increased symptoms of PMS associated with menstrual migraine were observed [18-25]. It is therefore suggested that all women with PMS be examined for the presence of menstrual migraine using IHS criteria (International headache society) as medical and social consequences of menstrual headache affect not only the women but also their family [25]. Therefore, the diagnosis and determination of the type of headache can help use an appropriate treatment and largely solve this problem.

From a total of 218 students whose PMS was approved by PSST, 32 students (14.7%) had migraine according to IHS criteria, and some of these headaches were severe and even resulted in the absenteeism from the class or the hospital and interfered with their function.

The study of Naderi *et al.* (2000) is the only similar study in Iran in which the prevalence of migraine was measured in 700 female students suffering from PMS. In their study, the prevalence of migraine was 8.6% and menstrual migraine was 5%, which is less than the value obtained in our study [23]. In the study of Vetvik, from a total of 237 students with PMS, 7.6% had menstrual migraine [20]. In the study of Fragoso, the most common type of headache was migraine without aura with a prevalence of 60% among 45 women with PMS [22]. In the study of McGregor, 7.2% of 55 women with PMS had migraine without aura [24].

The prevalence of migraine was higher among interns than other students (16.1%). In addition, a higher prevalence of migraine was observed in married women (20%), students living in the dormitory (26.1%), those with irregular menstruation (26.3%) and those with

a family history of migraine (36.5%) which was consistent with a similar study by Naderi *et al.* [23]. Comparing many different studies shows an apparent increase in the frequency of migraine in women with PMS in this study.

Conclusion

Given that the prevalence of migraine in women with PMS is in the range of 14.7% and headaches can negatively affect the performance of individuals, it is recommended that women suffering from PMS be evaluated for migraine based on diagnostic criteria of IHS and in the case of having migraine, the preventive treatments are considered more. It is suggested that further studies with larger sample size and more widely be conducted among different women and the significant relationship between migraine and the related factors be measured. It is better to evaluate them according to the true menstrual migraine (attacks only during menstruation), menstrual related migraine (increasing number of attacks during menstruation) and non-menstrual migraine (attacks regardless of the time of menstruation). In addition, after further studies, the screening of women in terms of premenstrual syndrome, migraine and menstrual migraine can be on the agenda for appropriate treatments.

Conflict of Interest

The authors have no conflict of interest.

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