COMPARATIVE ASSESSMENT OF MENSTRUAL-RELATED AND UNRELATED MIGRAINE IN INDIAN FEMALES

Dr Tarunendra Kumar Mishra,[1] Dr Rakesh Kumar Sisodia[2] Dr. Deepika Sharma,[3] Dr Pratibha Dixit[4*]

[1]MBBS, MD, Assistant Professor, Department of General Medicine, Government Medical College and Hospital, Ratlam, Madhya Pradesh

[2]MBBS, MD, Associate Professor, Department of General Medicine, Government Medical College and Hospital, Ratlam, Madhya Pradesh

[3]MBBS, MS, Assistant Professor, Department of Obstetrics and Gynecology, LNCT Medical College and Sewakunj Hospital Indore, Madhya Pradesh

[4*]MBBS, MS, Associate Professor, Department of Obstetrics and Gynecology, Government Medical College and Hospital, Ratlam, Madhya Pradesh

Address for correspondence:Dr Pratibha Dixit

dr.pratibha.dixit@gmail.com

ABSTRACT

Background: Migraine is a disease that is considered among the top 10 diseases causing disability in humans with the highest involvement in middle-aged and young females. In females of menstrual age, a different variant of migraine is seen and is known as MM (menstrual migraine).

Aim: The present study aimed to comparatively assess the menstrual-related and menstrual unrelated migraine in Indian females.

Methods: The present study assessed females from the Department of Obstetrics and Gynecology having the primary headache of the migraine type. After screening, the subjects were divided into two groups where Group I had menstrual migraine subjects and Group II had MUM (menstrual unrelated migraine) subjects following the criteria by IHS (International Headache Society). The subjects were then compared for migraine attacks after questioning them for different symptoms.

Results: Among these 90 subjects, 70% (n=63) subjects were found to fit the inclusion criteria and had the primary headache. The results showed that phonophobia was seen in 41.93% (n=13) subjects with menstrual migraine and 25% (n=8) subjects with menstrual unrelated migraine which was significantly higher in the menstrual migraine group with p=0.02. Photophobia has seen in 67.74% (n=21) subjects from the menstrual migraine group and in 34.37% (n=11) subjects with MUM which was also significantly higher in the MM group with p=0.00007. Vomiting as a symptom was higher in the MM group with 64.51% (n=20) subjects and was seen in 53.12% (n=17) subjects from the MUM group with p=0.24. The nausea was significantly higher in 87.09% (n=27) subjects compared to 62.5% (n=20) subjects in the MUM group with

p=0.002. In the menstrual migraine group, the unilateral headache was seen in 77.41% (n=24) study subjects and bilateral in 22.58% (n=7) study subjects respectively.

Conclusion: The present study, considering its limitations, concludes that more features of migraine headaches are observed in females with menstrual-related migraine including the longer attack duration and overall worse migraine experience.

Keywords: Headache, migraine, menstruation, menstrual migraine, menstrual unrelated migraine.

INTRODUCTION

Migraine is a disease that is considered among the top 10 diseases causing disability in humans with the highest involvement in middle-aged and young females. Migraine negatively affects the quality of life (QOL), decreases productivity, and leaves school. MM (menstrual migraine) signifies an attack that is mainly seen two days before or three days following the menstruation onset in a minimum of two to three menstrual cycles. Menstrual migraine is divided into two subcategories namely PMM (pure menstrual migraine) and MRM (menstrually related migraine).[1]

MRM (menstrual-related migraine) signifies the attack seen in the pre-menstrual period. However, it can also be seen at other periods of the menstrual cycle. Pure menstrual migraine is assessed when the migraine attacks are limited to only pre-menstrual time. Estrogen withdrawal is mainly linked to the pathogenesis of menstrual migraine. In comparison to the MUM (menstrual-unrelated migraine), the menstrual migraine is more resistant to treatment, long-lasting in duration, and is a more severe form of the migraine.[2]

For the pathophysiology of migraine in females, exogenous and endogenous female sex hormones are considered vital contributors. The prevalence of migraine is significantly higher in females after menarche which has high frequency during menopause and pregnancy which are considered the hormonal milestones in female life.[3] In females, menstruation is considered the most common factor in a female life triggering migraine attacks. The pathophysiology of this trigger can be attributed to decreased levels of estrogen before menstruation which can trigger the trigeminovascular system and increase the excitability of the brain. The estrogen decline rates seem vital in the provocation of migraine attacks.[4] The previous literature data report a longer duration of migraine attacks in the perimenstrual period causing high disability compared to non-perimenstrual attacks. However, controversial results are reported for associated symptoms, pain intensity, and acute therapy efficacy.[5]

Majority of subjects having migraine present prodromal symptoms before the headache. In the initiation of the migraine attack, diencephalic and subcortical brain activation is seen along with the basal ganglion thalamus, and hypothalamus which can cause the top-down effect on the structures of the brainstem involving the trigeminovascular nociception. Also, many similarities are seen between the prodromal migraine phase and the physical, behavioral, and affective symptoms of PMS (pre-menstrual syndrome). The risk of migraine attacks is increased by 60% in females during the PMS period.[6]

However, the prevalence of menstrual migraine shows a great variation in various data and the literature data concerning this is scarce in the literature. Also, previous data only assessed subjects with primary headache compliance which might be a contributor to the study bias, and the subjects not seeking medical care and having less severe symptoms were not assessed which can present less valid results.[7] Hence, the present study aimed to comparatively assess the menstrual-related and menstrual unrelated migraine in Indian females.

MATERIALS AND METHODS

The present cross-sectional study aimed to comparatively assess the menstrual-related and menstrual unrelated migraine in Indian females. The study was done after the clearance was taken from the concerned Ethical committee. The study population was comprised of subjects from the Department of Obstetrics and Gynecology of the Institute. After explaining the study design in detail, informed consent was taken from all the subjects in verbal and written format.

For the present study, all the subjects visiting the Department of Obstetrics and Gynecology were screened for the primary headache irrespective of the presenting symptoms. The study included subjects aged 18 years or above who were willing to participate in the study. All the study subjects underwent a detailed verbal questionnaire assessment by an expert doctor to assess if the headache reported by the subjects is a migraine if the headache met the criteria by IHCD-3 (International Classification of Headache disorders)[8] or if the subject had a previously confirmed diagnosis of migraine or was taking the prophylaxis for migraine.

All the subjects that met the inclusion criteria were given a preformed structured questionnaire to be filled by the subjects and followed the IHCD-3 criteria. The questionnaire was aimed to assess the prevalence of menstrual migraine. The exclusion criteria for the study were subjects that had a headache of non-migraine, did not give consent for study participation, and had amenorrhea.

The subjects after completion of the questionnaire were divided into 2 groups where Group I included subjects having the menstrual migraine following the IHCD-3 criteria definition for menstrual migraine and Group II included all the subjects with migraine having headache episodes at times not related to the menstrual cycle and were considered as MUM or migraine unrelated migraine.

After the detailed recording of the history for all the subjects, the features considered for headache were drug history, gynecological history including menarche age and dysmenorrhea, migraine symptoms, demographic data, headache site whether bilateral or unilateral, associated symptom occurrence including phonophobia, photophobia, vomiting, and/or nausea, average attack days, and attack duration.

The gathered data was assessed using the SPSS software version 25.0 (IBM Corp., Armonk, NY) for the two study groups. Mean and standard deviation was used to present the continuous data and demographic characteristics. The study utilized a two-tailed t-test and chi-square test to compare different means. The confidence interval was 95% and the level of significance was taken at $p<0.05$.

RESULTS

The present cross-sectional study aimed to comparatively assess the menstrual-related and menstrual unrelated migraine in Indian females. For the present study, 90 subjects visiting the Department of Obstetrics and Gynecology were screened for primary headaches. Among these 90 subjects, 70% (n=63) subjects were found to fit the inclusion criteria and had the primary headache. These 63 subjects were then divided into two groups where Group I included 49.20% (n=31) of the subject which were diagnosed with menstrual migraine following the criteria by HIS, whereas, Group II included 50.79% (n=32) subjects with menstrual unrelated headaches. All the study subjects were in the age range of 12 years to 56 years. The mean age of the study subjects was 31.97±7.03 years.

On the comparison of the demographic characteristics of the two groups of the study subjects, it was seen that the mean age in the menstrual migraine was significantly higher with 34.42±9.45 years compared to the menstrual unrelated migraine, where the mean age was 29.61±5.48 years with p=0.0006. The age of the study subjects at menarche was 12.58±1.23 years in the menstrual migraine group and 12.3±1.16 years in the menstrual-unrelated migraine group. The difference between the two groups for menarche age with p=0.67. The mean attack days duration was 2.69±1.24 days which was significantly higher for menstrual migraine compared to menstrual unrelated migraine where it was 1.79±0.97 days with p=0.00001 as shown in Table 1.

Concerning the comparison of the symptoms of the MM and MUM in the study subjects, the results are summarized in Table 2. The results showed that phonophobia was seen in 41.93% (n=13) subjects with menstrual migraine and 25% (n=8) subjects with menstrual unrelated migraine which was significantly higher in the menstrual migraine group with p=0.02. Photophobia has seen in 67.74% (n=21) subjects from the menstrual migraine group and in 34.37% (n=11) subjects with MUM which was also significantly higher in the MM group with p=0.00007. Vomiting as a symptom was higher in the MM group with 64.51% (n=20) subjects and was seen in 53.12% (n=17) subjects from the MUM group with p=0.24. The nausea was significantly higher in 87.09% (n=27) subjects compared to 62.5% (n=20) subjects in the MUM group with p=0.002. In the menstrual migraine group, the unilateral headache was seen in 77.41% (n=24) study subjects and bilateral in 22.58% (n=7) study subjects respectively. In the menstrual unelated migraine group, the unilateral and bilateral headache was seen in 75% (n=24) subjects and 25% (n=8) subjects respectively. This was comparable between the two groups with p=0.58 (Table 2).

DISCUSSION

The present cross-sectional study aimed to comparatively assess the menstrual-related and menstrual unrelated migraine in Indian females. For the present study, 90 subjects visiting the Department of Obstetrics and Gynecology were screened for primary headaches. Among these 90 subjects, 70% (n=63) subjects were found to fit the inclusion criteria and had the primary headache. These 63 subjects were then divided into two groups where Group I included 49.20% (n=31) of the subject which were diagnosed with menstrual migraine following the criteria by HIS, whereas, Group II included 50.79% (n=32) subjects with menstrual unrelated headaches. All the study subjects were in the age range of 12 years to 56 years. The mean age of the study

subjects was 31.97±7.03 years. These results were similar to the previous studies of Vetvik KG et al[9] in 2018 and Koverach A et al[10] in 2019 where authors reported a prevalence of migraine in menstrual females with a prevalence comparable to the present study.

The study results showed that the demographic characteristics of the two groups of study subjects, it was seen that the mean age in the menstrual migraine was significantly higher at 34.42±9.45 years compared to the menstrual unrelated migraine, where the mean age was 29.61±5.48 years with p=0.0006. The age of the study subjects at menarche was 12.58±1.23 years in the menstrual migraine group and 12.3±1.16 years in the menstrual-unrelated migraine group. The difference between the two groups for menarche age with p=0.67. The mean attack days duration was 2.69±1.24 days which was significantly higher for menstrual migraine compared to menstrual unrelated migraine where it was 1.79±0.97 days with p=0.00001. These demographics were consistent with the previous studies of Barra M et al[11] in 2019 and Allais A et al[12] in 2011 where authors assessed subjects with demographics comparable to the present study.

It was seen that for the comparison of the symptoms of the MM and MUM in the study subjects, the results are summarized in Table 2. The results showed that phonophobia was seen in 41.93% (n=13) subjects with menstrual migraine and 25% (n=8) subjects with menstrual unrelated migraine which was significantly higher in the menstrual migraine group with p=0.02. Photophobia has seen in 67.74% (n=21) subjects from the menstrual migraine group and in 34.37% (n=11) subjects with MUM which was also significantly higher in the MM group with p=0.00007. These findings were in agreement with the previous findings of Macgregor EA et al[13] in 2004 and Macgregor EA et al[14] in 2006 where authors suggested the symptoms of menstrual migraine as phonophobia and photophobia which were less common in menstrual unrelated migraine as seen in the present study.

Vomiting as a symptom was higher in the MM group with 64.51% (n=20) subjects and was seen in 53.12% (n=17) subjects from the MUM group with p=0.24. The nausea was significantly higher in 87.09% (n=27) subjects compared to 62.5% (n=20) subjects in the MUM group with p=0.002. In the menstrual migraine group, the unilateral headache was seen in 77.41% (n=24) study subjects and bilateral in 22.58% (n=7) study subjects respectively. In the menstrual unelated migraine group, the unilateral and bilateral headache was seen in 75% (n=24) subjects and 25% (n=8) subjects respectively. This was comparable between the two groups with p=0.58. These findings were in line with the studies of Pinkeman B[15] in 2010 and Pavlovic JM et al[16] in 2015 where authors suggested more prevalence of nausea and more prevalence of unilateral headache in the menstrual headache group as in the present study.

CONCLUSION

Considering its limitations, the present study concludes that more features of migraine headaches are observed in females with menstrual-related migraine including the longer attack duration and overall worse migraine experience. However, further long-term studies are needed with a large sample size to reach a definitive conclusion

REFERENCES

1. van Casteren DS, Verhagen IE, Onderwater GLJ, MaassenVanDenBrink A, Terwindt GM. Sex differences in the prevalence of migraine trigger factors: a cross-sectional study. *Cephalalgia.* 2021;41:643-8.
2. MacGregor EA. Migraine headache in perimenopausal and menopausal women. *Curr Pain Headache Rep.* 2009;13:399-403.
3. Macgregor EA. Headache in pregnancy. *Continuum.* 2014;20:128-47.
4. Stewart WF, Lipton RB, Chee E, Sawyer J, Silberstein SD. Menstrual cycle and headache in a population sample of migraineurs. *Neurology.* 2000;55:1517-23.
5. Karsan N, Goadsby PJ. Imaging the premonitory phase of migraine. *Front Neurol.* 2020;11:140.
6. Mattsson P. Hormonal factors in migraine: a population-based study of women aged 40 to 74 years. *Headache.* 2003;43:27-35.
7. Facchinetti F, Neri I, Martignoni E, Fioroni L, Nappi G, Genazzani AR. The association of menstrual migraine with premenstrual syndrome. *Cephalalgia.* 1993;13:422-5.
8. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia.* 2018;38:1-211.
9. Vetvik KG, MacGregor EA, Lundqvist C, Russell MB. Symptoms of premenstrual syndrome in female migraineurs with and without menstrual migraine. *J Headache Pain.* 2018;19:97.
10. Koverech A, Cicione C, Lionetto L, et al.. Migraine and cluster headaches show impaired neurosteroid patterns. *J Headache Pain.* 2019;20:61.
11. Barra M, Dahl FA, MacGregor EA, Vetvik KG. Identifying menstrual migraine: improving the diagnostic criteria using a statistical method. *J Headache Pain.* 2019;20:95.
12. Allais G, Sanchez del Rio M, Diener HC, et al. Perimenstrual migraines and their response to preventive therapy with topiramate. *Cephalalgia.* 2011;31:152-60.
13. MacGregor EA, Hackshaw A: Prevalence of migraine on each day of the natural menstrual cycle. Neurology. 2004;63:351-3.
14. MacGregor EA, Frith A, Ellis J, Aspinall L, Hackshaw A: Incidence of migraine relative to menstrual cycle phases of rising and falling estrogen. Neurology. 2006;67:2154-8.
15. Pinkerman B, Holroyd K: Menstrual and nonmenstrual migraines differ in women with menstrually-related migraine. Cephalalgia. 2010;30:1187-94.
16. Pavlović JM, Stewart WF, Bruce CA, Gorman JA, Sun H, Buse DC, Lipton RB: Burden of migraine related to menses: results from the AMPP study. J Headache Pain. 2015;16:24.

TABLES

Characteristics	**Menstrual migraine (Mean± S.D)**	**Menstrual unrelated migraine (Mean± S.D)**	**p-value**
Age (years)	34.42±9.45	29.61±5.48	0.0006

Menarche age (years)	12.58±1.23	12.3±1.16	0.67
Mean attack days	2.69±1.24	1.79±0.97	0.00001

Table 1: Demographic feature comparison in two groups of study subjects

Parameters	**Menstrual migraine (n=31)**		**Menstrual unrelated migraine (n=32)**		**p-value**
	%	**N**	**%**	**N**	
Phonophobia	41.93	13	25	8	0.02
Photophobia	67.74	21	34.37	11	0.00007
Vomiting	64.51	20	53.12	17	0.24
Nausea	87.09	27	62.5	20	0.002
Site					
Unilateral	77.41	24	75	24	0.58
Bilateral	22.58	7	25	8	

Table 2: Comparison of symptoms concerning MM and MUM in study subjects