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ARTICLE

Headache classification and aspects of reproductive life in young women

Classificação das cefaleias e aspectos da vida reprodutiva em mulheres jovens

Eliana M. Melhado[1], Marcelo E. Bigal[2], Andressa R. Galego[3], João P. Galdezzani[3], Luiz P. Queiroz[4]

ABSTRACT

Objective: To classify headaches as a function of the menstrual cycle and to contrast aspects relating to the reproductive cycle as a function of headache type. **Method:** Participants responded to a structured questionnaire consisting of 44 questions. Detailed headache information, enabling the classification of headaches, and questions relating to the menstrual cycle were obtained. **Results:** The sample consisted of 422 students. Menstrual headaches were experiencedby 31.8%. Migraine without aura (MO) occurred in 13.3%, migraine with aura (MA) in 7.8%, and probable migraine in 6.4%. Women with MA were significantly more likely to have reached menarche at earlier ages than women without headaches (p=0.03). Use of a hormonal contraceptive was related to the function of having MA headaches or not. **Conclusion:** Most female college students are affected by menstrualheadaches. Although the vast majority experience MO, other headaches also occur. Women with MA are equally likely to receive hormonal contraceptives as others.

Keywords: migraine, menarche, menstrual, reproductive, pregnancy.

RESUMO

Objetivo: Classificar cefaleias em relação ao ciclo menstrual e contrastar aspectos relacionados ao ciclo reprodutivo de acordo com o tipo de cefaleia. **Método:** Participantes responderam um questionário estruturado de 44 perguntas. Foi obtida informação detalhada das cefaleias, permitindo sua classificação e perguntas relativas ao ciclo menstrual. **Resultados:** A amostra foi constituída de 422 estudantes. Cefaleias menstruais foram constatadas em 31,8%. Migrânea sem aura (MO) ocorreu em 13,3% delas, migrânea com aura (MA) em 7,8%, provável migrânea em 6,4%. Mulheres com MA apresentaram probabilidade significativamente maior de ter sua menarca em idades mais precoces do que mulheres sem cefaleia (p=0,03). O uso de contraceptivos apresentou frequência semelhante independentemente da mulher ter ou não migrânea com aura. **Conclusão:** A maioria das mulheres estudantes universitárias apresenta cefaleia menstrual. Apesar da MO representar a maioria, outras cefaleias também ocorrem. Mulheres com MA podem receber contraceptivos hormonais com probabilidade de desenvolver cefaleia igual às mulheres com outros tipos de cefaleia.

Palavras-chave: migrânea, menarca, menstrual, reprodutivo, gravidez.

Migraine and several other primary headaches affect women disproportionately[1], and hormonal influences may be of importance in at least partially explaining this gender-related differential prevalence[1]. Several hypotheses have been considered to justify these gender-related differences. The influence of sexual hormones, mainly estrogen, on migraine pain, has been well explored[2-4]. Other putative mechanisms have also been proposed[5].

Beyond the differential gender-related prevalence, some women also experience headaches that are more severe when they are related to menstruation, or exclusively related to menstruation[6]. A proper description of such headaches relies on an accurate classification system[7]. Of the headaches associated with the menstrual period, menstrual migraine is by far the most studied. The Third Edition of the International Classification of Headache Disorders (ICHD-III)[6] offers appendix criteria for menstrual migraine. According to the criteria, pure menstrual migraine (PMM) occurs when migraine arises solely in relation to the menstrual period, while associated menstrual migraine (AMM) refers to women whose migraines are worse close to or during menstruation, relative to other times of the month. PMM affects 3.5–12% of

[1]PhD., Professor of Neurology, Departamento de Neurologia, Faculdades Integradas Padre Albino, Catanduva SP, Brazil;

[2]M.D., Ph.D. Chief Medical Officer, Labrys Biologics, San Mateo CA, USA;

[3]College Students, Departamento de Neurologia, Faculdades Integradas Padre Albino, Catanduva SP, Brazil;

[4]PhD., Professor of Neurology, Departamento de Neurologia, Universidade Federal de Santa Catarina, Florianopolis, Brazil.

Correspondence: Eliana M Melhado; Rua Belém 61/Apto. 15; 15800-280 Catanduva SP - Brasil; E-mail: neuroeliana@hotmail.com

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women with migraine, while AMM affects as many as 50%[8]. Although menstrual migraine seems to be the most common form of menstrual-related headache, clinicians often see patients with menstrually related non-migraine headaches[9]. Accordingly, the classification of non-migraine headaches as a function of the menstrual cycle needs to be further explored. It is clear therefore that some women with migraine are more susceptible to hormonal fluctuations than others. It is still unknown, however, whether women with menstrual headaches differ from other women regarding other aspects of their reproductive life. For example, it is not yet known whether age at menarche, duration of menstrual cycles, and other characteristics are different as a function of menstrual headaches. It is also unclear whether the use of hormonal contraceptivescoupled with number of pregnancies varies as a function of headache type.

Accordingly, we conducted a study with the following aims: (1) to classify headaches according to the ICHD-III[6] as a function of the menstrual cycle, in college students,and (2) to contrast aspects relating to women's reproductive cycle (age at menarche, menstrual cycle, duration of periods, use of contraceptive pills, number of pregnancies, headaches during pregnancy) as a function of headache status and headache type.

METHOD

Overview and sample

In order to conduct this study, female college students (Faculdades Integradas Padre Albino, Brazil) were invited to respond to a structured questionnaire inone sitting. They were selected among students from all courses offered by the college (business, law, physical education, nursing and medicine).

For convenience, the sample comprised whole classes of students from the same study year. All were invited to participate and signed the consent form, with no random selection involved.

We invited students ranging in age from 18 to 45 years in order to include adult fertile women. Weight and height were measured and the body mass index (BMI) calculated.

Women both with and without headache were enrolled. We excluded women with confirmed or suspected pregnancy from the interview.

Questionnaires and procedures

Data collection was conducted in May 2010 and February 2011. Volunteers were asked to complete a structured questionnaire consisting of 42 questions divided intothree parts. In part one (10 questions), demographic variables were captured. In part two (22 questions), detailed headache information was gathered, enabling classification of the headaches according to the ICHD-III[6].

Although the questionnaire had been validated for the assessment of headaches in the population, it had not been specifically validated for identifying menstrual headaches.

Finally, in part three (10 questions) we explored the temporality of headache relative to the menstrual cycle, and aspects relating to fertility and reproductive life.

Classification of headaches

As a function of headache type, patients were divided into the following groups: migraine with aura (MA), migraine without aura (MO), probable migraine (PM) and Chronic daily headache (CDH such as Chronic migraine + chronic tension type headache + migraine and 8.2- medication-overuse headache).

Other headache types (tension-type headache (TTH), probable tension-type headache, idiopathic stabbing headache, unclassified headache) were classified. Controls experienced no headaches. Participants with more than one headache type were asked to focus on the most severe headache type[10].

Assessment of headache relative to the menstrual cycle

Menstrual headache was defined as a headache occurring from two days before the first day of menstruation until the third day of menstruation, as per the ICHD-III[6]. It was further divided into pure menstrual headache (not happening at other times) and associated menstrual headache. We emphasize that, as one of our aims was to assess whether different headache phenotypes were related to the menstrual period, herein we did not restrict our assessments to migraine headaches only.

In the ICHD, menstrual headaches are listedonly in the appendix and the classification only describes pure menstrual migraine and menstrually related migraine. We propose the use of a classification for other types of headaches that occur during menstruation.

We did not assess the occurrence of menstrual cramps/dysmenorrhea.

Variables and analysis

Women were classified as a function of headache type and grouped according to the following variables:

1) Duration of the menstrual cycle, which was divided into short (21 days or fewer), regular (21–32 days) and long (32 days or more);
2) Duration of menstruation, which was divided into short (1–4 days), intermediate (5–6 days) and long (7 days or more);
3) Age of menarche (in years);
4) Number of past pregnancies, headaches during pregnancy, headaches before pregnancy, and whether pregnancy was associated with improvement, worsening, or no change relative to prior headaches (in those with prior headaches).

Summary tables were presented and statistics calculated. Proportions were compared with the chi-squared test and the significance level was established at 5%.

The study was approved by an academically affiliated Investigation Review Board (no. 33/10 – *Comitê de Ética em Pesquisa-FIPA ofício* no. 38/10 of 14 June 2010), and signed consent forms were collected.

RESULTS

Of 555 students invited to participate, 422 (76%) consented and responded to the questionnaire. Their median age was 22 years. Of the total participants, 20% were aged 18–20 years and 59.0% were aged 21–25 years. Only 3.2% were aged 36–45 years. Furthermore, most participants (88.4%) were white, 7.1% were of Africandescent, 3.1% were of Asiandescent, and 1.4% did not disclose their race. Most (85.8%) were single and of normal weight.

Headache classification

Of the participants, 334/422 (79.1%) reported that they had experienced headaches over the last year. The headache classification is summarized in Table 1. Most women with headaches had a migraine subtype (62.3%). MO (27.8%) was the most common form of headache. A significant proportion of participants had chronic daily headaches (CDHs,6.8%).

Headache and the menstrual cycle

Pure or associated menstrual headaches were experienced by 134 women (31.8%). Of these, most (30.8%) were associated menstrual headaches (happened also outside the menstruation period, as defined by the ICHD-III) and only four (1%) had pure menstrual headache. Of the pure menstrual headache cases, three (0.7%) fulfilled the criteria for MO and one case (0.3%) for probable migraine without aura. There were no reports of other headaches purely associated with menstruation.

Regarding menstrually related headaches, most could be classified as migraine (27.5%); 13.3% were MO, 7.8% were MA and 6.4% were PM. Menstrually related tension-type headache occurred in 3.1% of the sample; menstrually related idiopathic stabbing headache occurred in 0.5%; and unclassified menstrual headaches occurred in 0.7% (Table 1). We did not classify the CDHs as a function of the menstrual cycle, as they occurred on more days than not.

Menstrual characteristics as a function of headache type

Duration of menstruation and the menstrual cycle

Duration of menstruation as a function of headache type is presented in Table 2. When comparing the number of days per period as a function of headache types, we found no significant differences, although women with MA and CDH had non-significant longer periods. However, when we compared the proportion of women with periods lasting more than seven days, women with CDH (13.9%) and MA (13.3%) were significantly different from women with episodic migraine (6.1%) or with no headaches (9.3%) ($p<0.05$). As shown in Table 2, most women (78.2%) had a menstrual cycle ranging from 21 to 32 days, and no differences were observed as a function of headache type.

Menarche

Age at menarche ranged between 9 and 17 years, but was most commonly (81.7%) between the ages of 11 and 14. Median age at menarche was 12.3 years.

Age of menarche as a function of current headache status is presented in Figure 1. Women with MA were significantly more likely to have had their menarche at an earlier age than women without headaches ($p=0.03$) (Figure 1). Similarly, women with MO were also more likely to have had their menarche at a younger age ($p=0.05$).

Table 1. Prevalence and classification of headaches in our study sample.

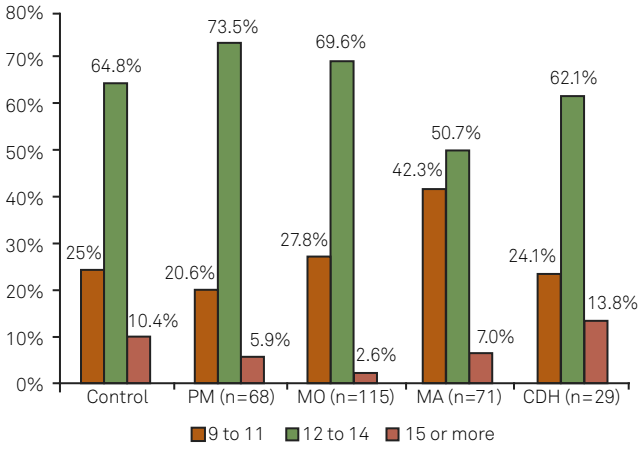
Classification	Number of cases	Overall prevalence (%)	Menstrual classification (related and pure)	Prevalence (%)
Unclassified headache	8	1.9	3	0.7
Chronic headaches (All)	29	6.8	0	
Idiopathic stabbing headache	6	1.4	2	0.5
Probable TTH	14	3.3	6	1.4
TTH	13	3.1	7	1.7
PM	71	16.9	27	6.4
MA	75	17.8	33	7.8
MO	118	27.9	56	13.3
Total	334	79.1	134	31.8

CM: chronic migraine; TTH: tension-type headache; PM: probable migraine; MA: migraine with aura; MO: migraine without aura; All: CM+MO.

Table 2. Duration of menstruation and of menstrual cycle as function of headache type.

	Duration of period (days)					Menstrual cycle (days)				
	Short (1–4)	Intermediate (5–6)	Long (>7)	No Answer	Total	Regular (21–32)	Long (>32)	Short (<21)	No answer	Total
Controls	47 (36.4%)	62 (48.1%)	12 (9.3%)	8 (6.2%)	129	102 (79.1%)	6 (4.7%)	15 (11.6%)	6	129
All migraine	120 (45.5%)	117 (44.3%)	16 (6.1%)	11 (4.2%)	264	208 (78.8%)	10 (3.8%)	36 (13.6%)	10	264
PM	34 (47.9%)	34 (47.9%)	2 (2.8%)	1 (1.4%)	71	51 (71.83%)	3 (4.2%)	14 (19.7%)	3	71
MA	29 (38.7%)	32 (42.7%)	10 (13.3%)	4 (5.3%)	75	54 (72%)	5 (6.7%)	12 (16%)	4	75
MO	57 (48.4%)	51 (43.2%)	8 (6.8%)	2 (1.7%)	118	103 (89.83%)	2 (1.7%)	10 (8.5%)	3	118
CDH	11 (37.9%)	12 (41.4%)	4 (13.9%)*	2 (7%)	29	22 (75.86%)	1 (3.4%)	3 (10.3%)	3	29
	p≤0.05					p>0.05				

PM: probable migraine; MA: migraine with aura; MO: migraine without aura; CDH: chronic daily headache; All migraine: PM+MA+MO.



MA: migraine with aura; MO: migraine without aura; PM: probable migraine; CDH: chronic daily headache.

Figure 1. Age (years) at menarche as a function of headache type. Significant difference (p=0.03) for MA vs controls.

Use of contraceptives

Of the participating sample, 73.1% used contraceptive pills, 25.8% did not, and 1.1% declined to respond.

Use of hormonal contraceptives was strikingly similar as a function of having or not having migraine headaches, having or not having aura, and as a function of the number of headache days per month (Table 3). No differences as a function of body mass index were observed.

Headache and pregnancy

Past pregnancy was reported by 10.4% of the sample. Of these, 25% had MO, 22.7% had MA, 15.9% had PM, 15.9% had CDH and 20.5% had no headaches (Table 4). Women with current CDH and MA were more likely to report headache during pregnancies than women with other headache types (Figure 2).

Pregnancy modified the phenotype of the headache quite considerably. The relative frequency of CDH and MA was significantly increased during pregnancy relative to outside pregnancy (p<0.01) (Figure 2).

DISCUSSION

In this sample we found that most women within a fertile age range have menstruallyrelated headaches, while a minority have pure menstrual headaches. More interestingly, we found evidence that other aspects of reproductive life, including age at menarche and duration of menstruation, vary as a function of headache type. We found that pregnancy not only modify the phenotype of headaches during pregnancy, but also after it. Finally, we found that the proportion of women using a contraceptive pill was virtually identical to the proportion that experienced headaches, regardless of the headache type.

The high prevalence of headaches in female college students has previously been reported[7,11,12]. It has been suggested that menstrual headaches often do not fulfill the criteria[6] for migraine. Because menstrual migraine is common and debilitating[13], non-migraine headaches that occur in relation to the menstrual cycle are often neglected or misdiagnosed. Our data suggest that, for pure menstrual headaches, migraine without aura is the most common form, as previously reported. Migraine with aura was very common (in associated menstrual headaches), but was not seen strictly related to the menstrual cycle.

Other forms of headache, including tension-type headaches[4,14] and idiopathic stabbing headache, may occur during menstruation, although not strictly so, and this should come as no surprise, since menstruation is unlikely to protect against other forms of pain. A Brazilian study suggested that, in up to 10% of women with migraine plus aura, the migraine worsens around the menstrual cycle[12]. A study conducted in Turkey found that, of women with menstrual headaches, 35.6% had migraine and 24.5% had tension-type headache, but no differentiation was made between strict and associated forms[9]. In a Spanish study, however, 4.5% of women suffered from pure menstrual tension-type headache and 7.5% from menstrual-related tension-type headache[15]. Among pure menstrual headaches, we found only migraine subtypes.

Table 3. Use of contraceptives as a function of headache type and body mass index (BMI).

	No contraceptives	Contraceptives	No answer	Total
Control	35 (27.1%)	92 (71.3%)	2 (1.6%)	129
MA	18 (24%)	56 (74.7%)	1 (1.3%)	75
MO	29 (24.6%)	89 (75.4%)	0 (0%)	118
PM	21(29.6%)	49 (69%)	1 (1.4%)	71
CDH	8 (27.6%)	19 (65.5%)	2 (7%)	29
Underweight	0 (0%)	4 (100%)	0 (0%)	4
Normal weight	13 (25.5%)	37 (72.5%)	1 (2%)	51
Overweight+all obese	**4 (26.7%)**	**11 (73.3%)**	**0 (0%)**	**15**
No answer	1 (20%)	4 (80%)	0 (0%)	5
	18	56		75
MO				
Underweight	3 (33.3%)	6 (66.7%)		9
Normal weight	19 (23.5%)	62 (76.5%)		81
Overweight+all obese	5 (20.8%)	19 (79.2%)		24
No answer	2 (50%)	2 (50%)		4
	29	89		118
PM				
Underweight	3 (25%)	9 (75%)	0	12
Normal weight	11 (24.5%)	33 (73.3%)	1 (2.2%)	45
Overweight+all obese	**4 (44.5%)**	**5 (55.5%)**	**0**	**9**
No answer	3 (60%)	2 (40%)	0	5
	21	49	1	71
CDH				
Underweight	1 (50%)	1 (50%)	0	2
Normal weight	4 (20%)	15 (75%)	1 (5%)	20
Overweight+all obese	**2 (50%)**	**1 (25%)**	**1 (25%)**	**4**
No answer	1 (33.3%)	2 (66.7%)	0	3
	8	19	2	29

PM: probable migraine; MA: migraine with aura; MO: migraine without aura; CDH: chronic daily headache; underweight: BMI<18; normal weight: BMI 18.5–24.9; overweight: BMI 25.0–29.9; all obese: BMI>30.0.

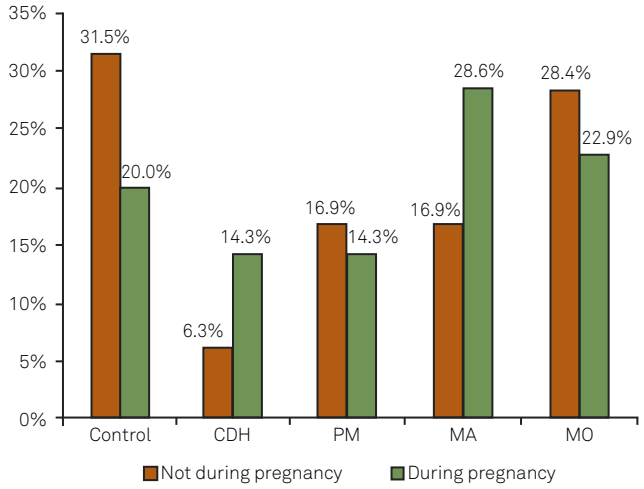
Table 4. Headache type before and during pregnancy.

Headache	Before pregnancy			During pregnancy			
	Not pregnant	Pregnant woman	Total	No headache in pregnancy	Headache during pregnancy	No answer	Total
Control	120 (31.7%)	9 (20.5%)	129	**121 (31.5%)**	**7 (20.0%)**	1	129
CDH	22 (5.8%)	7 (15.9%)	29	**24 (6.3%)**	**5 (14.3%)**	0	29
PM	64 (16.9%)	7 (15.9%)	71	**65 (16.9%)**	**5 (4.3%)**	1	71
MA	65 (17.2%)	10 (22.7%)	75	**65 (16.9%)**	**10 (28.6%)**	0	75
MO	107 (28.3%)	11 (25.0%)	118	**109 (28.4%)**	**8 (22.9%)**	1	118
% column	378	44	422	384	35	3	422

PM: probable migraine; MA: migraine with aura; MO: migraine without aura; CDH: chronic daily headache.

Accordingly, our findings suggest that the ICHD-III[6] criteria, which state that menstrual migraine can only be classified in women without aura, is sufficient to classify pure menstrual migraine, but is too restrictive for menstrually related headaches. For menstruallyrelated migraine, we suggest that criteria be either eliminated (acknowledging that women with headaches outside of their period may experience headaches related to the period as well) or revised to be more inclusive.

Women with CDH were significantly more likely to have longer periods, raising the suspicion that hormonal fluctuations relate not only to the prevalence of migraine, but also to the frequency of headaches. Since our study was cross-sectional, causality was not addressed, but the finding is intriguing enough to suggest further studies. The influence of hormones related to the menstrual cycle on the chronicity of pain has not been formally demonstrated, although their influence on pain thresholds has been demonstrated. For



ICHD-III: International Classification of Headache Disorders; MA: migraine with aura; CDH: chronic daily headache; PM: probable migraine; MO: migraine without aura.

Figure 2. Headache diagnoses according to ICHD-III as a function of pregnancy. Significant difference ($p<0.01$) for MA and CDH during pregnancy vs outside of pregnancy.

example, women with fibromyalgia consistently have cyclical fluctuationsin their pain threshold during the menstrual cycle, relative to women without chronic pain, although it seems that the hormonal influence on the over-representation of fibromyalgia in women has been ruled out[16]. Furthermore, it has been suggested that women with migraine are more likely to have menorrhagia and painful endometriosis than women without migraine[17].

Menarche happened earlier in women with MA than in the others. To the best of our knowledge, similar findings have not been reported; therefore, caution is necessary until they are replicated. Mechanisms of exploring this relationship should also be considered, as our study was cross-sectional. It would be of interest to define whether earlier menarche age is associated with an increased risk of MA, whether the opposite is true, or whether an unidentified association or predisposition would explain the finding.

A significant proportion of our participants used oral contraceptives, as expected[12,18], and the proportion was strikingly similar as a function of headache type. Migraine with aura seems to be a risk factor for cerebrovascular disease[19-21], and the risk is magnified in the presence of other risk factors, such as the use of contraceptive pills and smoking. Accordingly, guidelines suggest caution before prescribing contraceptive pills for women with migraine plus aura[20,21]. Accordingly, the fact that women with MA are just as likely to be taking hormonal contraceptives as women without headaches, or with other headache types, raises the question as to whether providers are properly assessing the risk of cardiovascular outcomes in certain cases. As we did not assess body mass index or tobacco addiction tabagism, we cannot comment on adequacy of care. We did, however, expect a lower proportion of women with MA to be using hormonal medications.

Although headaches often improve during pregnancy[11,12,22,23], the relative frequency of aura or frequent headaches (MA and CDH) increased during pregnancy relative to outside pregnancy. Other studies have suggested that migraine with aura is less likely to improve during pregnancy than migraine without aura[12,24]. The reasons for this need to be further explored. Studies should also focus on whether or not these headache types are associated with complications during pregnancy.

Our study had limitations. First, although the questionnaire had been validated for the assessment of headaches in the population[25,26], it had not been specifically validated for identifying menstrual headaches. Second, we did not confirm the number of pregnancies or assessed abortions. Third, and most important, our information concerningthe phenotype of headache during pregnancy was retrospective and limited to the last pregnancy when women had had more than one headache. Recall bias cannot be ruled out, and data in this regard should be considered as exploratory, to be confirmed by prospective studies.

Most female college students were affected by menstrual headaches. Although the vast majority of participants reported migraine without aura, other headaches also occurred. Women with MA are just as likely to be taking hormonal contraceptives as others. The finding that the menstrual cycle may vary as a function of headache frequency also raises the suspicion that hormonal fluctuations[23] relate not only to the prevalence of migraine but also to the frequency of headaches.

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