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REVIEW ARTICLE

Menstrual Cycle and Headache in Teenagers

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Abstract

Objective This population-based study on school-aged girls aimed to estimate the rate of peri-menstrual headache, evaluate headache pain pattern during the menstrual cycle, and verify its relationships with physical, psychosocial and life-style factors.

Methods The students ($n = 4973$) fulfilled a self-administered questionnaire on demographic and behavioral characteristics, menarche, menstrual pattern and features including headache and dysmenorrhea. The prevalence of headache and the mean pain intensity score at the three menstrual cycle phases (premenstrual, menstrual, in-between period) were estimated, both overall and by gynecological year. Furthermore, the prevalence of three different patterns of headache (peri menstrual/mid-cycle/acyclic) was evaluated, together with the mean pain intensity score.

Results The overall prevalence of headache at least once at any time during the menstrual cycle was 64.4%. At multivariable logistic analysis, gynecological age (OR 1.07; 95%CI 1.03–1.12), middle social level (1.24; 1.01–1.55, compared to high social level), physical activity (0.67; 0.51–0.89), oral contraceptive use (1.34; 1.04–1.73) and dysmenorrhea (2.30; 1.54–3.42) were significantly associated with headache. Among girls with headache, 83.4% had peri-menstrual headache (44.6% premenstrual, 38.8% menstrual), 3.5% mid-cycle headache and 13.2% acyclic headache. The gynaecological age and dysmenorrhea were significantly associated with the headache pattern ($p = 0.03$ and $p < 0.0001$, respectively).

Conclusions This study suggests that peri-menstrual headache is highly prevalent among adolescents. In girls, the headache rate linearly raises with higher gynecological age; menses-related painful syndromes, such as headache and dysmenorrhea, are strongly interrelated. The anamnesis and monitoring of menstrual health should be mandatory when taking care of girls with headache.

Keywords Adolescents. Menstrual headache · Headache pattern · Pain · Gynecological age · Dysmenorrhea

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Introduction

The overall lifetime prevalence of headache is estimated at 60%–80%, and the prevalence of the main types (migraine, tension-type and chronic headache) is greater in women than in men. Particularly elevated female to male ratios have been reported for migraine, peaking in midlife (3 or 4 to 1) [1]. Sensitivity to sexual hormone fluctuation has been invoked to explain this gender-related difference [2]. It is still unclear how gonadal hormones may trigger headache, but their effects on pain perception have been confirmed [3]. The Appendix of the third edition of the International Classification of Headache Disorders (ICHD) defined different patterns of menstrual migraine depending on the timing of attacks during the menstrual cycle [4]. Only in recent years some of the implicated processes have begun to be elucidated [5–7]. The ICHD does not include specific criteria for adolescents; furthermore, no clear and fully established information about menstrual headache among adolescent girls is available yet [8].

In children and adolescents, primary headache is the most frequent neurological symptom and pain complaint [9, 10]. It may likely develop into a chronic condition, and complex, often bidirectional, relationships between headache and comorbid neurological, psychiatric, cardiovascular diseases have been suggested [11]. Furthermore, in children, headache was proved to be associated with other medical conditions (anxiety, depression, fever, *etc.*) and, regarding girls, an association was found between age at menarche and frequent headache episodes [12, 13]. In adolescents, the burden of headache substantially threatens the quality of life and school attendance and performance [14]. In an extensive review of 64 cross-sectional studies on primary headache in children and adolescents [15], Wöber-Bingöl showed that the prevalence of headache in childhood varies considerably (10%–90%), depending on the diagnostic criteria applied, the setting, the data collection methodology and the period used for reporting on headache attacks. Data suggest that tension-type headache may be atleast 2–3 times more common in children (as in adults) than migraine [15, 16].

Until puberty, headache is only slightly more prevalent in boys than in girls, while with age older than 12 y headache prevalence increases in females [17]. It has been suggested that this disproportion depends on the different timing in pubertal development of boys and girls [6, 18, 19], with a hormonal status after puberty characterized by estrogen level fluctuations that can predict headache among girls [20, 21]. Evidence from the studies suggests that in adolescents also the clinical phenomenology of primary headache of any type is affected by menstruation. This population-based study on school-aged girls aimed to estimate the rate of peri-menstrual headache, evaluate the headache pain pattern during the menstrual cycle, and verify its relationships with physical, psychosocial and life-style factors.

Material and Methods

This observational cross-sectional study was carried out on a large sample of Italian secondary school girls from the most geographical areas in Italy. The study was designed in accordance with the Declaration of Helsinki. All participants were informed about the nature, purpose and procedures of the study, and gave informed written consent directly or by means of their legal guardians. Sampling strategies have been described elsewhere [22]. The girls were contacted at school and only those who had reached menarche were recruited. A self-administered anonymous questionnaire was given to the girls to fill in at school and, for some information (regarding mother and/or sisters), at home. At school, the science teachers, trained by the researchers, explained and handed out the questionnaire to their students.

The questionnaire, designed for this research by a group of pediatric endocrinologists and child psychiatrists of the University of Padua, is described in previously published papers [22–24]. It included three shares. A general section listed questions on demography, anthropometry, date of menarche, behavioral habits - smoking, alcohol, and illicit drug consumption - and physical activity, parents' socio-demographic data, mothers' and sisters' age at menarche. A second section explored menstrual pattern and characteristics, including many somatic and psychological symptoms pertaining to premenstrual syndrome and other painful syndromes (dysmenorrhea and headache). Finally, a third section investigated girls' perceptions and beliefs about menstruation.

For the purposes of this work, the first and the second sections, including questions about headache were considered.

Headache was explored by means of questions about its presence during three menstrual cycle phases (a few days before menses, during menstruation, in-between menses period) with pain intensity graded on a seven-point scale (0 = absent, 6 = intolerable). The girls were asked to answer referring to the overall experience during the last three menstrual cycles. Those subjects who reported pain intensity different from zero during at least one menstrual cycle phase were considered as having suffered from headache.

As proposed in the literature [25], in the present study the adolescents were grouped by different headache patterns over the menstrual cycle by using retrospective information collected at individual level. The headache patterns were defined using the intensity of headache pain at the 3 cycle phases. The pain intensity peak (maximum declared pain intensity) during the menstrual cycle was the grouping criterion. The adolescents were classified as suffering from peri-menstrual

headache when the highest pain intensity was before (premenstrual) or during (menstrual) menses. Mid-cycle headache was defined as a peak in headache intensity outside of menstrual onset ± 5 d, while acyclic headache was conceptualized as headache that was reported with comparable pain intensity during the menstrual cycle phases.

Other questions explored duration of pain (less than 1 d, 1, 2, 3 or more days); need to take medication, to limit daily activities and/or to stay in bed (no, sometimes, often, always).

Abdominal pain was ranked on four levels: (i) no or mild/moderate abdominal pain; (ii) severe abdominal pain without any use of medication, or sufficient to limit the girl's activities; (iii) severe abdominal pain treated with medication, and/or activity limitations during bleeding days; (iv) severe abdominal pain treated with medication and/or activity limitations before bleeding days (dysmenorrhea).

Chronological, menarche and gynecological age (in years) were calculated. High-intensity-physical activity was classified as > 6h/wk, while alcohol consumption was recorded for alcoholic beverages consumed more than twice a week.

Data were analyzed by means of SAS statistical software rel. 9.3 (SAS Institute, Cary, NC, USA). Significance level was set at 0.05 and all tests were two-tailed. Descriptive analyses were performed on quantitative and qualitative variables for the entire sample and for specific subgroups. Normality of distribution of quantitative variables was verified by means of the Shapiro-Wilk test. As appropriate, parametric or non-parametric one-way analysis of variance was used to test differences between mean/median values, while the chi-square test was applied to compare rates. Unadjusted/age-adjusted OR (and respective 95% CI) for having headache were obtained by means of separate simple logistic models where general and menses-specific features were included as explanatory variables. To evaluate independent associations, multiple logistic regression (forward stepwise selection) models were used including the following covariates: menarche and gynecological age, social level, family size, alcohol drinking, physical activity, current use of oral contraceptives, dysmenorrhea. Goodness of fit was tested by means of the Hosmer and Lemeshow test. The prevalence of headache and the mean pain intensity score at the three menstrual cycle phases were computed in girls suffering from headache, both overall and by gynecological year. Moreover, the prevalence of the different patterns of headache (premenstrual/menstrual/mid-cycle/acyclic) was evaluated, together with the mean pain intensity score. The difference between the headache patterns in terms of length of attacks, consequences on the use of medication and daily life habits was verified by using the chi-square test.

Results

Four thousand nine hundred ninety two questionnaires were collected out of 6924 distributed (71%) and quite all had complete information (99.6%).

The school-aged population was thus composed by 4973 girls aged 13-21y (mean = 17.2y, SD = 1.4y). The overall prevalence of headache (at least once at any time during the menstrual-cycle) was 64.4% (3207/4973).

The general characteristics and the menstrual features in adolescents with or without headache are shown in Table 1. Girls suffering from headache were significantly older (17.3y *vs.* 17.1y; $p = 0.0006$), had menarche at a younger age (12.4y *vs.* 12.5y; $p = 0.02$) and, consequently, had a higher gynecological age (4.8y *vs.* 4.6; $p = 0.0006$). They performed less high-intensity-physical activity (6.4% *vs.* 9.5%; $p < 0.0001$) and more likely drank alcoholic beverages (41.1 *vs.* 44.5%; $p = 0.02$). Among girls with headache, the prevalence of those taking oral contraceptives was significantly higher than among the ones without headache (13.8% *vs.* 10.8%; $p = 0.002$). No difference was found in menstrual pattern (cycle and bleeding length), while dysmenorrhea was more prevalent among the girls declaring headache (7.0% *vs.* 2.9%; $p < 0.0001$).

The prevalence of headache and the median intensity of pain were evaluated by gynecological age. As shown in Fig. 1A, as gynecological age increased, the headache rate also significantly increased from 60% to 73% ($p = 0.004$), while the mean pain intensity score rose from 1.6 to 1.9 ($p = 0.03$).

At multivariable logistic analysis, only gynecological age (OR = 1.07; 95% CI 1.03–1.12), middle social level (1.24; 1.01–1.55, compared to high social level), high-intensity-physical activity (0.67; 0.51–0.89), oral contraceptive use (1.34; 1.04–1.73) and dysmenorrhea (2.30; 1.54–3.42) were significantly associated with headache.

Considering the entire sample at each phase of the menstrual cycle, the overall prevalence of headache during the main 3 cycle phases (categorized as premenstrual, menstrual and in- between periods) was 43%, 58%, and 24%, respectively. Out of the 3207 girls with headache, 66% indicated headache attacks before menstruation, 90% during menses and 38% in the in-between-period. Corresponding mean headache pain scores were 1.7 ± 1.7, 2.6 ± 1.6 and 0.8 ± 1.3, respectively.

The proportion of girls reporting headache attacks in the premenstrual phase increased significantly with gynecological age (from 64% to 74%, p for trend = 0.0002), while no such trend was observed for the headache prevalence during the other two phases (Fig.1B). In addition, among girls reporting headache, the pain intensity significantly increased with gynecological age in the peri-menstrual phases ($p = 0.0006$ and 0.03 in the premenstrual and menstrual phase, respectively).

Table 1 General characteristics and menstrual features in adolescents with and without headache

	Whole sample ($N = 4973$)	Headache ($N = 3207$)	No Headache ($N = 1766$)	Unadjusted p	Age-adjusted p	Age-adjusted OR (95%CI)	Multiple* p	Multiple* OR (95%CI)
Chronological age, y *(Mean ± SD)*	17.2 ± 1.4	17.3 ± 1.5	17.1 ± 1.5	0.0006	–	1.08 (1.03–1.12)		
Menarcheal age, y *(Mean ± SD)*	12.4 ± 1.3	12.4 ± 1.3	12.5 ± 1.3	0.02	0.007	0.93 (0.88–0.98)		
Gynecological age, y *(Mean ± SD)*	4.7 ± 1.8	4.8 ± 1.8	4.6 ± 1.8	<0.0001	0.008	1.07 (1.02–1.13)	0.002	1.07 (1.03–1.12)
Body mass index, kg/m^2 *(Mean ± SD)*	20.3 ± 2.5	20.3 ± 2.5	20.2 ± 2.4	0.12				
Social level (%)	%	%	%					
Low	5.1	5.0	5.2	0.07	0.06	0.94 (0.69–1.27)	0.01	0.96 (0.66–1.41)
Middle	34.0	35.3	31.6			1.13 (0.95–1.36)		1.24 (1.01–1.55)
High	42.3	41.0	44.6			0.93 (0.79–1.11)		0.93 (0.75–1.14)
Very High	18.7	18.7	18.7			ref		ref
Family size (%)								
≤ 3 persons	26.0	26.7	24.7	0.005	0.008	1.27 (1.07–1.51)	–	–
4	52.6	53.2	51.4			1.13 (1.07–1.44)		
≥ 5	21.4	20.0	23.9			ref		
Smoking habit (%)	32.7	33.6	31.0	0.06	0.13	1.10 (0.97–1.35)		
Alcohol drinking (%)	43.3	41.1	44.5	0.02	0.04	1.14 (1.01–1.28)	–	–
Physical activity (%)	7.5	6.4	9.5	<0.0001	0.0004	0.68 (0.55–0.84)	0.005	0.67 (0.51–0.89)
Current use of oral contraceptives (%)	12.7	13.8	10.8	0.002	0.02	1.25 (1.04–1.51)	0.02	1.34 (1.04–1.73)
Current cycle length (%)								
< 21 d	2.9	3.1	2.7	0.74	0.70	1.18 (0.81–1.72)		
21–29	85.1	85.1	85.1			ref		
29–35	3.4	3.5	3.2			1.12 (0.79–1.58)		
> 35	8.6	8.3	9.0			0.95 (0.76–1.18)		
Current bleeding length (%)								
< 4 d	3.2	3.1	3.5	0.71	0.60	0.92 (0.66–1.28)		
4–6	19.0	19.2	18.6			ref		
> 6	77.8	77.7	77.9			1.07 (0.92–1.24)		
Dysmenorrhea (%)	5.6	7.0	2.9	<0.0001	<0.0001	2.53 (1.18–3.55)	<0.0001	2.30 (1.54–3.42)

* significance level and ORs (95%CI) from a multiple logistic regression model (forward stepwise application) including the following independent variables: menarcheal and gynecological age, social level, family size, alcohol drinking, physical activity, current use of oral contraceptives, dysmenorrhea

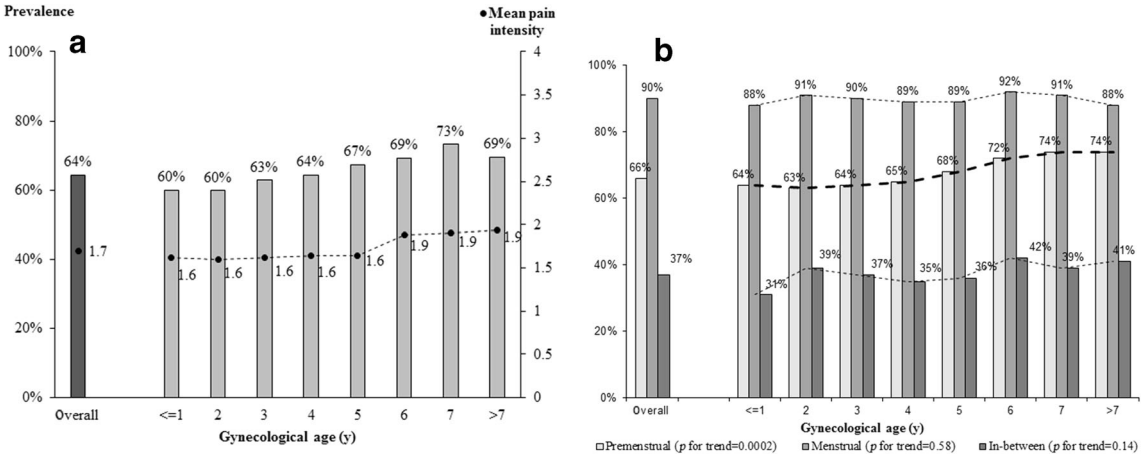

Fig. 1 Prevalence of headache, overall and related to menstrual cycle phases. **a**. Prevalence of headache in the whole sample, overall and by gynecological age (p for trend < 0.0001), during the menstrual cycle (atleast at one phase). Mean pain intensity score is shown in the secondary vertical axis ($p = 0.03$). **b** Prevalence of headache at each menstrual cycle phase, among girls declaring headache in at least at one phase ($n = 3207$), by gynecological age

No significant increase in pain intensity was shown in the in-between-period.

Among girls with headache, 68 (2.1%) were excluded because their headache pain patterns did not fit any of the four defined headache patterns. In the remaining cohort, the prevalence of the patterns was 28.1% (premenstrual), 24.5% (menstrual), 8.3% (acyclic) and 2.2% (mid-cycle). Among girls with headache, the percentages were 83.4% peri-menstrual headache (44.6% premenstrual, 38.8% menstrual), 3.5% mid-cycle headache and 13.2% acyclic headache.

As shown in Table 2, the results suggest that the prevalence of acyclic and mid-cycle headache likely did not significantly change with gynecological age, while a significant increasing trend of the proportion of premenstrual headache was shown (41.4% up to 50%), corresponding to a decreasing trend of menstrual headache (from 43.0% to 33.3%) (p for trend = 0.02).

Figure 2 illustrates the trend of the intensity of pain during the menstrual cycle of the four different patterns, as derived from a model that assumed the pattern was unchanged in three consecutive cycles. As shown, the peak of pain intensity was highest for the premenstrual pattern (mean score about 3), while the lowest intensity of pain was observed for menstrual and mid-cycle patterns in the descending part of the curve. Conversely, acyclic headache showed pain of the same intensity (mean level about 3) over the entire menstrual period (comparable pain intensity over all 3 cycle phases).

At statistical analysis verifying the association between the headache patterns and potential covariates, only dysmenorrhea was shown to be significantly related. Its prevalence was significantly higher among acyclic (9.0%), and premenstrual (10.7%) and mid-cycle (8.0%) headaches than among menstrual (2.3%) headaches ($p < 0.0001$).

The comparison of the general characteristics and menstrual features in adolescents with different patterns of headache pain is shown in Table 3. The gynaecological age and the presence of dysmenorrhea were significantly associated with the headache pattern ($p = 0.03$ and < 0.0001, respectively). The girls with premenstrual and acyclic pattern had an older gynaecological age, and dysmenorrhea was definitely infrequent (2.3%) among the girls with menstrual headache.

The headache patterns were shown (Table 3) to be significantly associated with the length of the headache attacks ($p < 0.0001$). The menstrual pattern had a greater prevalence of attack lasting more than 3 d (20.8%), followed by acyclic (20.8%) premenstrual (13.9%) and mid-cycle (12.8%) headache ($p < 0.0001$). Moreover, the length of pain attack was significantly associated with the length of abdominal pain ($p < 0.0001$). The prevalence of headache attacks lasting more than 3 d rose from about 5%, if abdominal pain lasted 1 d, up to 33% if abdominal pain lasted more days (data not shown).

The frequent use of medication was more common among girls with *acyclic* headache (35.1%; $p < 0.0001$) than among girls with other headache patterns (*premenstrual* 26.6%; *menstrual* 21.4%, *mid-cycle* 24.0%). The prevalence of limitation in daily activities and being bedridden was higher among acyclic headaches (both about 10%) even though not significantly.

Discussion

Headache is one of the painful conditions that could reach clinical significance during the menstrual periods in adult women. Evaluation, diagnosis and treatment are crucial, because correct management could help to prevent serious consequences, such as overuse of medication [26] and withdrawal from daily activities, and could ameliorate the health-related quality of life. Evidence on the burden of menstrual headache in adolescence is still limited and it has not yet been included in the headache diagnostic classifying criteria [4].

Table 2 Headache patterns among adolescents stating headache attacks; prevalence of patterns, overall and by gynecological age

	Premenstrual	Menstrual	Mid-cycle	Acyclic	p^*
Overall	44.6	38.8	3.5	13.2	
Gynecological age					
≤1 *y*	41.4	43.0	2.3	13.3	0.02
2 y	40.3	40.3	5.1	14.5	
3 y	43.8	41.2	3.0	12.0	
4 y	46.7	37.2	5.4	10.7	
5 y	47.7	37.4	3.0	11.9	
6 y	49.4	36.1	2.0	12.5	
7 y	49.3	34.8	2.2	13.8	
≥8 y	50.0	33.3	3.6	13.1	

* significance level obtained by applying the Cochran-Armitage trend test to premenstrual and menstrual headache patterns with Bonferroni correction

The present study analyzed a large population-based dataset to provide some insights into adolescents' experience of headache attacks in relation to menstrual cycle phases. Moreover, the research aimed to substantiate the presence of menstrual headache patterns in adolescents, as previously described for adult women.

The findings of the study confirmed the high prevalence (64%) of headache during the menstrual cycle among adolescent girls. This overall figure is comparable with published data on similar target populations [15, 27–29]. In this cross-sectional study, girls self-reported data on headache attacks referring to the last three menstrual cycles; consequently, the picture obtained is a simplified compendium of intra-individual heterogeneity. In adolescents, not only primary headache features may differ from those in adult women, and may vary with age, but also one subtype of primary headache (migraine and tension-type headache) may change, in the same subject, over time towards other subtypes [30]. Consequently, a diagnostic classification of pediatric subjects is particularly problematic. At present, diagnosis in childhood and adolescence is difficult due to the lack of a specific system to classify headache in children [31]. Moreover, in childhood, the presence of symptoms recognized as potential precursors (such as abdominal pain, cyclical vomiting, motion sickness, but also stress, anxiety, and sleep difficulty) may be suggestive of developing primary headaches and many believe they share the same pathophysiologic spectrum [30]. Given that puberty and sexual maturation affect the onset and the features of both migraine and non-migraine primary headache, methodological guidelines should suggest the use of data on pubertal growth and menstrual characteristics in longitudinal studies on headache in childhood. In future research, detailed data about frequency, timing of onset, duration, accompanying symptoms, use of medications and their effectiveness collected with a menstrual and symptom chart may add further and more detailed information for studying headache in children and adolescents.

Recently, some authors described a new pattern of menstrual cycle-related headache in adult women, known as mid-cycle headache [32]. The real existence of this

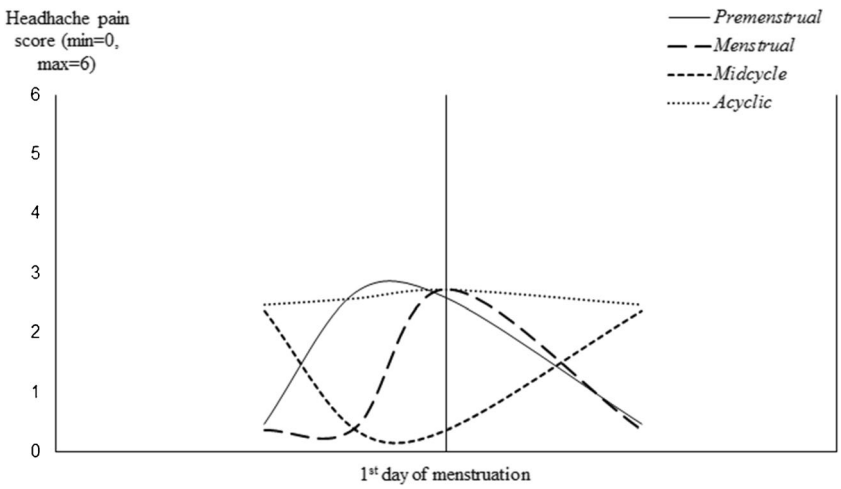

Fig. 2 Trajectories of the intensity of headache pain of the four different headache patterns, over the menstrual cycle

Table 3 Comparison of the general characteristics, menstrual features and length and severity of headache attacks, by headache pattern in adolescents with different patterns of headache pain

	Premenstrual	Menstrual	Mid-cycle	Acyclic	*p*
Chronological Age (years) (Mean ± SD)	17.3 ± 1.4	17.2 ± 1.4	17.1 ± 1.5	17.3 ± 1.4	0.03
Menarcheal Age (years) (Mean ± SD)	12.3 ± 1.3	12.4 ± 1.3	12.6 ± 1.5	12.4 ± 1.2	0.17
Gynecological Age (years) (Mean ± SD)	4.4 ± 1.7	4.2 ± 1.7	4.1 ± 1.6	4.3 ± 1.7	0.03
Body Mass Index, kg/m^2 (Mean ± SD)	20.3 ± 2.6	20.3 ± 2.6	20.3 ± 2.6	20.3 ± 2.6	0.77
Social level (%)					
Low	4.8	5.4	4.1	5.0	0.36
Middle	36.4	32.9	32.7	39.7	
High	41.3	42.1	41.8	36.0	
Very High	17.5	19.7	21.4	19.3	
Family size (%)					
≤ 3 persons	26.1	28.1	20.6	27.5	0.55
4	52.8	53.2	57.9	52.7	
≥ 5	21.1	18.7	21.5	19.8	
Smoking habit (%)	35.4	31.4	27.5	35.9	0.08
Alcohol drinking (%)	44.8	43.6	38.5	48.2	0.23
Physical activity (%)	6.7	6.3	6.4	5.6	0.89
Current use of oral contraceptives (%)	14.2	13.2	17.4	13.8	0.64
Current cycle length (%)					
< 21 d	3.3	2.4	5.2	3.0	0.56
21–29 d	84.5	86.0	86.6	84.6	
29–35 d	4.0	3.3	1.0	3.0	
> 35 d	8.1	8.4	7.2	9.4	
Current bleeding length (%)					
< 4 d	3.4	2.5	2.8	4.0	0.30
4–6 d	76.1	79.4	82.4	77.3	
> 6 d	20.5	18.3	14.8	18.8	
Dysmenorrhea	10.7	2.3	8.1	9.0	<0.0001
Length of headache attack (%)					
< 1 d	23.0	34.5	50.0	26.7	<0.0001
1d	35.7	37.1	26.9	36.5	
2 d	27.4	19.9	10.3	20.0	
≥ 3d	13.9	26.4	12.8	20.8	
Use of medication (%)	26.6	21.4	24.0	35.1	<0.0001
Limitation in daily activities (often, always) (%)	7.6	6.3	6.0	10.1	0.11
Bedridden (often, always) (%)	7.3	7.3	8.7	10.3	0.26

entity is still debated, and data are sometimes conflicting [25, 33–37]. The results from the present study suggest that the menstrual headache patterns described for adult women [25] adequately fit the pain trajectories also in adolescents, given that only in 2% of girls the headache did not correspond to any pattern. Actually, in our adolescent girls the proportion of the peri menstrual pattern seemed considerably higher than in young women aged 17–25 y (83% *vs.* 51%), and, conversely, the acyclic pattern rate was lower in present sample (13% *vs.* 33%), as was the mid-cycle pattern (3.5% *vs.* 16%). The methodological dissimilarities of the studies make it problematic to provide a clinical interpretation of such different rates and this issue deserves further investigation.

An original finding of this study relies on the independent statistical association between gynecological age and the prevalence of headache and its different patterns. In the present sample, the rate of headache was 59% for girls having menarche within the previous year and about 70% in the girls with gynecological age of 7 y or more. Furthermore, the proportion of premenstrual headache grew linearly with increasing gynecological age. Moreover, pain intensity and duration significantly worsened during premenstrual headache attacks. At multivariate analyses, only gynecological age was

independently associated with headache occurrence and pattern. Published literature suggests that the headache rate rises during the pubertal period, but conflicting results have been reported on the association with menarche. In their study [6], Kröner-Herwig B and Vath N. reported that in girls 11–16 y the risk for recurrent headache is increased when compared with girls without menarche, but they also stated that intraindividual longitudinal analyses do not support the hypothesis that headaches become more frequent after the onset of menarche. In their study including adolescents (aged 12–19 y) and women (aged ≥ 20y), Aegidius and colleagues reported lower headache rates with increasing age at menarche [7]. Further, they commented that several population-based studies found that menarche coincides with migraine onset in 10–23% of girls/women with migraine and that those subjects are most likely to suffer from menstrual-related headaches. Actually, none of those studies considered the role of gynecological age. Especially in cross-sectional studies on adolescents, the association between early menarche and headache onset and frequency could be biased by the fact that, at the same chronological age, girls with early menarche have longer exposure to gonadal hormones. In a study on adolescents, embracing a theory of genetic polymorphism in estrogen receptors [38], Hershey stated that the effect of sexual hormones on headache starts at puberty, but becomes stable after menarche, with a plateau in the prevalence of menstrual migraine after menarche [8]. Crawford and colleagues in a retrospective analysis of close to 900 girls aged 9–18 y found a gradual increase in migraine frequency that may start as young as age 9, with over 20% of girls starting to have a monthly pattern [5]. They reported a prevalence peak at age 13y, when over 60% of girls had such a monthly pattern, a figure similar to that found in adult women. Their study suggested that girls with a tendency to have monthly headaches may start suffering from headache even before menarche and they will often develop menstrual-related migraine.

In the present study, the linear growth of headache rate and the progression of the premenstrual headache rate with gynecological age seem likely to challenge the conclusion about a plateau in peri menstrual headache rate after menarche. On the other hand, the constant rates of acyclic headache seem to confirm the presence of girls suffering from headache not sensitive to hormonal fluctuations.

A number of constraints might reduce the strength of present results. The research project was not designed for diagnosis of headache, consequently, authors could not discriminate previous diagnosis of secondary headache, between tension-type headache and migraine, nor could they identify the different medications used to alleviate headache and comment on their appropriateness. In authors' opinion, these data are necessary to optimize the use of analgesics (with or without hormonal medication) and prophylactic therapies, and to identify lifestyle factors that could be modified. Moreover, retrospective self-reporting on headache timing and pain may have led to overestimation of prevalence rates of headache.

In conclusion, this study showed that a high overall proportion (64%) of adolescent girls (13-21y) suffered from headache. Four menstrual headache patterns made it possible to classify 98% of the headache pain trajectories in adolescents as seemingly comparable to those previously described for adult women. Overall, 44.6%, 38.8%, 3.5% and 13.2% of the girls suffered from premenstrual, menstrual, far from menses (mid-cycle) and acyclic (pain levels independent from the menstrual phases) headache, respectively. Headache rate was significantly and positively associated with dysmenorrhea and gynecological age, with occurrence and pain intensity linearly growing with longer time since menarche.

Menstrual headache in adolescence is often neglected in clinical setting; despite this, its anamnesis might be relevant for the development of headache in adulthood. This study found a close relationship between headache pain attacks and menstrual cycle phases in teenagers. Pediatricians and pediatric nurses who take care of adolescent girls suffering from headache attacks should be concerned about menstrual migraine. In girls, as well as in adult women, the anamnesis of menstrual health should be mandatory for headache diagnosis and treatment.

Contributions DSC: Conception and design of the study, acquisition of data, revision of the paper; DSV: Conception and design of the study, acquisition of data, interpretation of data, revision of the paper; PE: Conception of the scientific question and design of the study, analysis and interpretation of data, draft and revision of the paper; RG: Conception and design of the study, acquisition of data, interpretation of data, revision of the paper; RF: conception and design of the study, acquisition of data, interpretation of data, revision of the paper.

BL: Conception of the scientific question and design of the study, analysis and interpretation of data, draft and revision of the paper; BM: Conception and design of the study, acquisition of data, interpretation of data, revision of the paper; BPA: Conception of the scientific question, revision of the paper; BS, BG, BF and TG: Conception and design of the study, acquisition of data, interpretation of data and revision of the paper. PE will act as guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

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