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Perception of university students about the use of painkillers, other remedies and lifestyle modifications for primary dysmenorrhea; a cross-sectional study at KEMU

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Abstract

Introduction and objectives Dysmenorrhea is a common gynecological complaint, affecting a significant percentage of menstruating women. The mainstay for the treatment of dysmenorrhea is NSAIDs and hormonal contraceptives while complementary and alternative therapies (CATs) are adjunct to it. This study investigates the perception of female medical students with dysmenorrhea towards the use of painkillers and CATs.

Methods We conducted this cross-sectional study among female medical students of Lahore by circulating the Google Forms-based questionnaire. Correlation analysis and logistic regression were applied using SPSS and descriptive statistics were given in frequencies and percentages.

Results Out of 202 participants, 76.7% ($n = 155$) experienced dysmenorrhea. 46% ($n = 93$) of the respondents reported using painkillers; paracetamol being the most common. 68.8% ($n = 139$) used CATs; bed rest and hot compresses were most used. The most common reason for using painkillers was their effectiveness (61.6%), followed by availability (42.5%). For CATs, the reason of choice included to reduce the need for analgesic (58%) and safety (38.3%). About 40.1% of respondents believed CATs were less effective than painkillers. 84.1% agreed that long-term consumption of painkillers causes stomach ulcers or kidney damage. The factors that led to CATs not being preferred over painkillers included less information about them (33.7%), time-consuming (25.7%), and the concept of non-effectiveness (20.3%). Uni-variate logistic regression analysis showed that students with severe dysmenorrhea had higher odds of using painkillers as compared to the students who had mild dysmenorrhea. (OR: 6.319, 95% CI: 3.244–12.309, $P = 0.000$).

Conclusions The prevalence of the use of CATs is high among female students as compared to painkillers and hormonal contraceptives (first-line). The reason for choosing CATs included reducing the need for analgesics, safety, and availability. Females should be encouraged to use the first-line therapies after consultation with doctors; for the effective management of dysmenorrhea and improvement of their quality of life.

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Keywords: dysmenorrhea, oral contraceptive pills, painkillers, complementary and alternative therapies, perception

Background

Menstruation, being a natural phenomenon, is a part of each women's life that usually starts in between 10 and 16 years of age; which affects the women life routinely every month in various way like mood swings, nausea, vomiting, bloating and very commonly pain. Mild pain, in lower abdomen, occurs in many women and is normal, but excessive, throbbing, cramping pain [1] that even abstains women and young girls from their daily chores like schooling, office work, housework etc. is known as dysmenorrhea. About 88.9% of the Pakistani females ranging from 12 to 16 years of age experience menstrual pain; and 44% of the females experience severe abdominal pain [2]. And globally 50 to 90% of women suffer from dysmenorrhea throughout their reproductive years [3]. Given its prevalence and potential effects on women's everyday functioning and well-being, it is extremely important for public health.

Dysmenorrhea is considered primary if no underlying pathology is diagnosed. Onset is typically six to twelve months after onset of menarche [4]. It occurs due to release of unfertilized ovum that causes a decrease in progesterone level [1] which leads to an increased amount of prostaglandins that results in increased contraction of uterus that restrict blood flow to uterus resulting in the formation of anaerobic metabolites that increase the sensitivity of pain receptors [5, 6]. Secondary dysmenorrhea is pain associated with conditions like endometriosis, uterine fibroids, adenomyosis, pelvic inflammatory disease, cervical stenosis etc.

Various ways are used to treat dysmenorrhea according to one's preference and common knowledge. NSAIDs and OCPs are commonly used as first-line treatments to reduce menstrual pain [4] and its use has been documented in previous studies [7, 8]. In current era, with educational advancement, the use of NSAIDs among females of developing countries has been rising [9]. NSAIDs act pharmacologically by reducing the synthesis of prostaglandins. Some side effects may be seen with their chronic use including GI irritation, salicylism, hypersensitivity, exacerbation of asthma and peptic ulcers [10]. Oral contraceptives are added to NSAIDs to treat dysmenorrhea [11]. OCPs inhibit ovulation, by creating an environment of reduced prostaglandins, hence reducing the pain of dysmenorrhea [10]. Many other complementary and alternative therapies referred to as CATs have also been proposed to treat dysmenorrhea and their use for dysmenorrhea is substantial worldwide [12]. Most common of these are bed rest, heating pad for increasing the circulation to the muscles and massaging

the pressure points; usage of herbs including chamomile, ginger [13], fennel [14], cinnamon, and aloe vera and five common non-herbal supplements (fish oil, melatonin, vitamins B1 and E, and zinc sulphate) [15], most of them act as anti-inflammatory. The review of trials found some evidence that Vitamin B1 and magnesium help reduce pain, but more research is needed in this regard [16]. Rose tea, fish oil, krill oil, a low-fat vegetarian diet and dates have also been used to relieve pain of dysmenorrhea [17]. Acupuncture may also reduce pain [18]. A review showed that exercise performed for 45 to 60 min each time; three or more times a week, increasing blood circulation, may prove to be beneficial in reducing menstrual pain intensity [19]. Physiotherapy can also relieve menstrual pain [20]. The data is still limited and conflicting, regarding OCPs' effectiveness as compared to first line therapies. However, they might be helpful as supplemental treatments or for individuals who are resistant to or uninterested in pharmaceuticals. [7].

The disease is often neglected and inadequately treated, and despite its high prevalence and impact on daily activities; given the fact that many young females prefer to suffer silently without seeking medical advice and this can be attributed to insufficient community healthcare clinics and an inadequate concept among the women in how to approach a community healthcare provider. Even in the 21st century, in some parts of Pakistan, there are some reservations among women regarding the use and side effects of NSAIDs/medications, as most of the knowledge is commonly being passed by mothers or sisters according to their own reasoning and understanding. So, it is necessary for the women to know what a myth is and what is a fact, using scientific and reliable ways, because it quite heavily affects the routine activities and hinders the productivity of the females [21, 22]; but this area is still lacking data, and a very small literary pool is present due to a lack of scientific studies at a national or community level. But health of the women should be prioritized. So, the objectives of this study are to find the prevalence of primary dysmenorrhea and perception about the efficacy and side effects of usage of NSAIDs, oral contraceptives and CATs for the treatment of dysmenorrhea among female students of KEMU so female students can be educated on the importance of seeking medical help for it to improve their quality of life.

Methods

Study design

A cross-sectional observational study was conducted in central east area of Pakistan among the undergraduate

female students at King Edward Medical University, Lahore, from August to October 2023, using an authenticated questionnaire. The university offers medical degrees and various allied health degrees.

Study population and sample

All female undergraduate students of the university, irrespective of their year of study, were invited to participate in this study. Students aged between 17 and 25 years and willing to participate were included; and those who did not provide consent or suffering from other gynecological issues were excluded. The sample size was calculated by following formula

$$N = Z^2_{1-\alpha/2} p \cdot q / d^2$$

Using the following assumptions; $Z^2_{1-\alpha/2} = 95\%$ confidence interval = 1.96, 5% absolute precision and 56.1% expected percentage of prevalence of dysmenorrhea [21]. The minimum sample needed to achieve was of 193 female undergraduate students and participants were recruited using a snowball sampling technique.

Study instrument

A questionnaire, in English language, was formulated on the basis of previous literature [23] with few changes according to the study on dysmenorrhea and the use and perception of usage of analgesics and complementary and alternative therapies. The questionnaire consisted of 29 variables were divided into 6 sections as follows: Sect. 1 included biodata of volunteers (3 questions), Sect. 2 included data about menstrual pattern (3 questions), Sect. 3 involved information about menstrual cramps and its effects on daily life (6 questions including WaLIDD score), Sects. 4 and 5 collected data about use of pain killers and other complementary and alternative therapies or homemade remedies (5 questions each) respectively and lastly, Sect. 6 assessed the perception about the use of pain killers and homemade remedies for treating dysmenorrhea (7 questions). The severity of dysmenorrhea was assessed using WaLLID score which ranges from 0 to 12, representing 0 as no, 1–4 as mild, 5–7 as moderate and 8–12 as severe dysmenorrhea. The CATs users included in this study involved those who used or are currently using natural herbs/supplements (green tea, ginger tea, fennel tea, fish oil, figs, date), yoga, bed rest, heating pads, hydrotherapy and massage for treating dysmenorrhea.

Data collection

An online questionnaire, with a front page explaining the objectives of the study and asking for consent to volunteer, was distributed among students to collect the data, from August to October 2023. Participants were well

informed that participation was completely voluntary, and the consent of all participants was required before completing the questionnaire. The questionnaire was repeatedly sent to the classes' main what's-app group so any remaining volunteer could be included.

Data analysis

The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23. Frequency and percentage were used for presenting categorical data; and mean (standard deviation) for continuous data. Associations among biodata, menstrual pattern, perceptions with usage of pain killers and CATs /homemade remedies for dysmenorrhea were assessed using uni-variate and multi-variate logistic regression analyses. The variables having $p < 0.05$ in uni-variate regression analyses were involved in multivariate regression analyses. A value of $p < 0.05$ was considered to be statistically significant.

Results

Demographics and menstrual characteristics of participants

As in Table 1 and 202 female students participated in the study via an online survey. All responses were included in the analysis. 67.3% of the participants ranged in age between 21 and 23 years, 31.2% in between 18 and 20 years and less than 1% were younger than 18 years. 79.2% of the participants had regular menses during last 1 year and 20.8% had irregular menses.

Prevalence of dysmenorrhea among respondents

Out of 202 respondents, 76.7% ($n = 155$) indicated that they experience menstrual pain (dysmenorrhea). 44.6% experienced menstrual pain during every menarche. 35.1% experienced pain at intervals. The severity of dysmenorrhea assessed via WaLIDD scale showed that 28.2%, 53.0 and 15.85% had mild, moderate and severe dysmenorrhea respectively (Table 2).

Use of painkillers and complementary and alternative therapies (CATs) for the treatment of dysmenorrhea

46% of the respondents used painkillers; 65.06% took paracetamol and 20.5% used ponston forte. About two-thirds (68.8%) of the respondents had used complementary and alternative therapies. Bed rest (68%), hot compressors (53.6%), natural herbs/supplements (36.5%) and massage (17.7%) were the most commonly used complementary and alternative therapies. Among natural herbs/supplements, green tea (29.5%), dates (20.9%), and chocolate (14.7%) were commonly taken. Hydrotherapy (12.7%) and yoga/exercise (5.5%) were the least commonly used CATs. The most common reason stated for the use of painkillers was their effectiveness (61.6%), followed by availability (42.5%), and recommendation from

Table 1 Demographics and menstrual characteristics of students who participated in the study

Variable	Frequency (N= 202)	Per-cent-age (%)
Age (years)		
< 18	2	1
18–20	63	31.2
21–23	136	67.3
> 24	1	0.5
Year of study		
1st	43	21.3
2nd	13	6.4
3rd	40	19.8
4th	90	44.6
5th	16	7.9
Marital status		
Single	4	98
Married	198	2
Length of menstrual period (days)		
< 5	45	22.3
5–7	143	70.8
≥ 8	14	6.9
Regularity of menses in last 1 year		
Irregular	42	20.8
Regular	160	79.2
Amount of Menstrual flow		
scanty	34	16.8
normal	125	61.9
heavy	34	16.8
very heavy	9	4.5

Table 2 Prevalence and severity of dysmenorrhea among participants

Variable	Frequency(N= 202)	Percentage (%)
Prevalence of dysmenorrhea	155	76.7
Severity of dysmenorrhea		
Mild	57	28.2
Moderate	107	53
severe	32	15.8

others (35.6%); the least common being their safety (26%) and price (4.1%). Among CATs, the reason of choice included to reduce the need for analgesic (58%), safety (38.3%) and availability (29.6%) with the least common reasons being recommendation from others (25.3%) and price (3.7%). About 40.1% of respondents believed CATs were less effective than painkillers and, 21% and 10.9% believed painkillers were equally and more effective than painkillers, respectively; shown in Table 3.

Table 3 Use of painkillers and cats for the treatment of dysmenorrhea

Variable	Frequency	Per-cent-age (%)
Use of painkillers	N=146	72.2
User of painkillers	93	46
Types of painkillers		
Paracetamol	95	65.1
Naproxen	8	5.5
Ibuprofen	13	8.9
Ponston forte	30	20.5
Reason for using Painkillers		
Safety	39	26.7
Effectiveness	90	61.6
Price	6	4.1
Availability	62	42.5
Recommendation from others	52	35.6
Use of CATs	N= 181	89.6
Users of CATs	139	68.8
Types of CATs		
Natural herbs/supplements/remedies	66	36.5
Exercise/yoga/meditation	10	5.5
Hydrotherapy	23	12.7
Using hot compressor	97	53.6
Bed rest	123	68
Massage	32	17.7
others	14	7.7
Reason for using CATs		
Safety	62	38.3
Efficacy	42	25.9
Reduced need of analgesic	94	58
Price	6	3.7
Recommendation from others	41	23.5
Availability	48	29.6
Effectiveness of CATs compared to painkillers		
Less effective	81	40.1
Equally effective	43	21
More effective	22	10.9

Perception towards the use of pain killers, complementary and alternative therapies for the treatment of dysmenorrhea

Table 4 shows, about 51.5% and 18.3%, agreed and strongly agreed that painkillers were effective for the treatment of dysmenorrhea while 25.2% showed neutrality about the effectiveness of painkillers for dysmenorrhea. Similarly, 57.9% and 11.9% agreed and strongly agreed for the effectiveness of complementary and alternative therapy for dysmenorrhea and 26.2% expressed neutrality regarding the use of CATs. 31.7% and 13.4% agreed and strongly agreed that CATs are better than painkillers and 36.6% were neutral about this. 57.4% and 26.7%, agreed and strongly agreed that long term

Table 4 Perceptions towards use of painkillers and cats for treatment of dysmenorrhea

Variables	Frequency (%)				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Painkillers are effective in relieving menstrual pain	37(18.3%)	104(51.5%)	51(25.2%)	8(4%)	2(1%)
CATs are effective in relieving menstrual pain	24(11.9%)	117(57.9%)	53(26.2%)	5(2.5%)	3(1.5%)
CATs are better than painkillers	27(13.4%)	64(31.7%)	74(36.6%)	34(16.85)	3(1.5%)
Long-term consumption of painkillers causes stomach ulcer or kidney damage	54(26.7%)	116(57.4%)	29(14.4%)	3(1.5%)	0
Long-term consumption of painkillers causes sterility	7(3.5%)	31(15.3%)	97(58%)	58(28.7%)	9(4.5%)

Table 5 Correlation analysis

	WaLIDD Score	Pain Killer Usage	Complementary Alternative Therapy Usage
WaLIDD Score (Dysmenorrhea Severity)	1	0.454**	0.253**
Pain Killer Usage	0.454**	1	0.099
Complementary Alternative Therapy Usage	0.253**	0.099	1

**means correlation at significance level of 0.01 (two tailed)

*means correlation at significance level of 0.05 (two tailed)

consumption of painkillers causes stomach ulcers or kidney damage and 14.4% were neutral; 15.3% and 3.5%, agreed and strongly agreed that long term consumption of painkillers leads to sterility and 48% were neither agreeing nor denying it. The factors that led CATs not being preferred over painkillers included less information about them (33.7%), time consuming (25.7%), concept of non-effectiveness (20.3%) and any misconception (14.4%).

Correlation analysis

The data was quantitative and variables were normally distributed. Pearsons correlation was used to find out the association between severity of dysmenorrhea, use of painkillers, and use of complementary alternative therapy. Null hypothesis formulated was that there was no significant association between severity of dysmenorrhea, use of painkillers, and use of complementary alternative therapies.

Pearson's correlation of severity of dysmenorrhea (WaLIDD score) and pain killer usage was found to be positive and statistically significant ($r=0.454$, $p<0.001$). It can be concluded that there is a statistically significant association between severity of dysmenorrhea and intake of pain killer frequency. Pearson's correlation of severity of dysmenorrhea and usage of complementary alternative therapy was also positive and statistically significant ($r=0.253$, $p<0.01$). Hence we can say there is significant association between severity of dysmenorrhea and usage of complementary alternative therapy (Table 5). The null hypothesis of no significant association between severity

of dysmenorrhoea, use of painkillers, and use of complementary and alternative therapies was rejected.

Logistic regression

For odds of using pain killers

As depicted earlier the measure of severity of dysmenorrhea is by WaLIDD score. The WaLIDD score, ranging from mild to severe, was dichotomized for analysis. Those participants who had WaLIDD score less than 6 were designated as '0' and those participants who had score more than 6 were denoted by '1'. Uni-variate logistic regression analysis showed that students with severe dysmenorrhea had higher odds of using painkillers as compared to the students who had mild dysmenorrhea. (OR: 6.319, 95% confidence interval (CI): 3.244–12.309, $P=0.000$). Omnibus, Hosmer and Lemeshow test showed the model was significant with classification table describing approximately 70% improvement in dependent variables because of the independent variable.

Multinomial Logistic Regression in SPSS was used for adjusting the factors of age, marital status, regularity of menses, amount of flow and timing of pain. It was found that people who had severe dysmenorrhea had still higher odds of using pain killers as compared to the participants with the mild dysmenorrhea (AOR: 5.388, confidence interval (CI): 2.636–10.812). Odds of using pain killers also increased (AOR=2.206, CI: 0.915–5.320) in the participants who suffered from extreme pain during menstruation in last three months. There was no significant association between demographics and other menstrual characteristics with intake of painkillers.

For odds of using complementary alternative therapy

Applying uni-variate logistic regression analysis it was also shown that students with severe dysmenorrhea had also higher odds of using complimentary alternative therapy as compared to the students who had mild dysmenorrhea. (OR: 1.833, 95% confidence interval (CI): 0.945–3.641, $P=0.04$). Omnibus, Hosmer and Lemeshow test showed the model was significant. There was no significant association between demographics and other menstrual characteristics with intake of painkillers.

Multinomial Logistic Regression in SPSS was used for adjusting the factors of age, marital status, regularity of menses, amount of flow and timing of pain. It was found that people who had severe dysmenorrhea had still higher odds of using complementary alternative therapy as compared to the participants with the mild dysmenorrhea (AOR: 2.091, confidence interval (CI): 1.011–4.324 $P=0.04$). Odds of using complementary alternative therapy also increased (AOR=1.937, CI: 0.996–3.765 $P=0.05$) as the age range of participants increased. There was no significant association between other demographics and menstrual characteristics with use of complementary alternative therapy.

Discussion

We conducted this cross-sectional study at King Edward Medical University, Pakistan to assess the perception of female university students about the use of painkillers and complementary and alternative therapies (CATs) for the treatment of dysmenorrhea.

The current research found that about three-fourth of female undergraduates in Lahore had dysmenorrhea. This supports the findings of previous studies conducted in Pakistan [24, 25], Malaysia [23], Saudi Arabia [26], Australia [27] and Iran [28]. However, similar studies from India [29] and China [30] have reported lower prevalence of dysmenorrhea. Among those with primary dysmenorrhea, moderate dysmenorrhea was reported in about half of the cases followed by mild dysmenorrhea while severe dysmenorrhea was least prevalent in our study population. This finding is in contrary to studies carried out in Saudi Arabia [26], Australia [27] and Iran [28] where severe dysmenorrhea was found to be more common than the mild one. These variations can be attributed to genetic and ethnic factors, nutritional and dietary habits, access to health care, sociocultural and lifestyle factors, reproductive and gynecological health of different populations.

About two-thirds (68%) of the respondents had used complementary and alternative therapies, and this is consistent with findings of previous studies conducted in Malaysia [23] and Saudi Arabia [26]. About 46% of the respondents used painkillers, of which the majority were using paracetamol; consistent with the findings of previous studies [23, 31]. Among complementary and alternative therapies, bed rest was the most common. The use of bed rest as the most common non-pharmacological approach towards pain management was consistent with previous researches [23, 26, 32, 33]. The reason for this is that sleeping distracts one from dysmenorrhea related pain. It was followed by usage of hot compressors. Heat application reduces menstrual pain by improving blood flow and causing relaxation of the muscles of the uterus [34, 35]. Natural herbs/supplements and massage were

less used CATs, consistent with the findings of a previous studies [23, 32]. The reason for this finding is unclear and further investigations should be made for the low usage of these therapies.

The study revealed that the majority of women used CATs because they considered them safer than painkillers. These findings are consistent with the findings of a previous study conducted in Saudi Arabia [26]. This may be due to the need to avoid side effects, including gastric ulcers and kidney damage, associated with painkillers especially non-steroidal anti-inflammatory drugs (NSAIDs); as indicated by some participants. The use of NSAIDs can cause peptic ulcer disease and other GI symptoms. However, this can be avoided by using NSAIDs for a short duration or in combination with proton pump inhibitors and/or selective COX-2 inhibitors, after consultation from a doctor [36]. Many women in the study also believed that the use of analgesics for dysmenorrhea may cause infertility, which is consistent with the findings of a previous study [37].

Despite limited research on CATs' efficacy for relieving menstrual pain, patients regularly employ CATs. The majority of these treatments carry little risk, but they have the potential to help relieve the pain of only mild dysmenorrhea [7]. Exercise, topical heat, physiotherapy, acupuncture and high-frequency trans-cutaneous electrical nerve stimulation have been shown to be effective in managing dysmenorrhea symptoms. Still, there is no scientific evidence suggesting their efficacy in managing the symptoms of moderate and severe dysmenorrhea [3, 38]. Also, there is insufficient data to substantiate the efficacy of any dietary supplement in treating dysmenorrhea, nor is there sufficient evidence to support its safety. There is some low quality evidence on the effectiveness of some supplements, so more studies are necessary in this regard [15]. These alternatives are unlikely to provide patients with symptom relief equivalent to that of NSAIDs or hormone therapy, but they might be helpful as supplemental treatments or for patients who are unable to take medication or who are not interested in it. So, public awareness campaigns should be launched to emphasize the importance of seeking medical attention for severe menstrual pain. Health care providers should address any potential worries or concerns regarding the side effects of first-line therapies and educate the patients that first-line agents are recommended by medical guidelines and have a strong evidence base for treating dysmenorrhea and improving their quality of life.

The results also showed that there was an increase in the frequency of use of painkillers and CATs with the increase in severity of dysmenorrhea. The severity of symptoms (WaLIDD score) showed a significant association ($p<0.01$) with an increased use of analgesics and CATs. This shows that as the severity of menstrual

pain increases, the desire to relieve it also increases because it causes difficulty for women in doing daily chores and academic tasks. [39, 40, 41].

This study has some limitations also. Firstly, it was a small-scale study conducted in only one medical university, so the results may not be applicable to entire female population of Pakistan. Secondly, in this study, the respondents were required to recall information, so there might be recall bias. Thirdly the respondents self-reported the responses, so there might be social desirability bias. And lastly many women feel reluctant in speaking about their issues regarding dysmenorrhea, so this might also have influenced the response rate. However, despite all these limitations, this study has, for the first time, managed to provide valuable information regarding the prevalence of use of analgesics and CATs for the treatment of dysmenorrhea and the perception of Pakistani women regarding their usage. This information can be helpful in taking measures to promote health-care seeking behavior among the women regarding their reproductive health.

Conclusion

The current study showed that of the participants involved in the study, about two-thirds used CATs to relieve menstrual pain. The most commonly used CATs were bed rest, hot compresses and natural herbs. Of the participants using painkillers, paracetamol was the most commonly used analgesic. Majority of the participants involved in the study considered CATs to be safer than painkillers to relieve menstrual pain. Some participants even had the misconception that painkillers can cause sterility. Awareness should be created among the general public, by healthcare authorities, regarding proper use of NSAIDs and OCPs as they are the first line for effective management of dysmenorrhea. Women should be encouraged to use these appropriate first-line measures (NSAIDs and OCPs) to relieve dysmenorrhea after consultation from a healthcare professional.

Abbreviations

OCPs	Oral contraceptive use
NSAIDs	Non steroidal anti inflammatory drugs
CATs	Complementary and alternative therapies

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12905-025-03777-1>.

Supplementary Material 1

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Author contributions

A.T., B.N. and F.S. collected the data and wrote the main manuscript text. F.S. prepared the data collection method and A.T. and B.N. analysed the data and interpreted it and all authors reviewed the manuscript.

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Data availability

The data which was used and analysed in this study, is being provided in supplementary information files[dysmenorrhea data and material spreadsheet].

Declarations

Ethical approval and consent to participate

This study received ethical approval by Institutional Review Board (IRB) of King Edward Medical University, Lahore, Pakistan. And online questionnaire, with a front page explaining the objectives of the study and asking for the consent of the volunteers was given and those who didn't volunteer weren't included in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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