

## Endocrine Abnormalities in Adolescents with Menstrual Disorders

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### Abstract

**Purpose** To look for endocrine abnormalities like thyroid disorders, hyperprolactinemia, hyperandrogenism and PCOS among adolescents with menstrual disorders and to compare the above endocrine status with those without menstrual disorders.

**Methods** This was a case–control study carried out in adolescent girls aged 10–19 years in gynecology outpatient

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department of a tertiary care hospital. Sample of venous blood (5 ml) was taken for hormonal studies as clinically indicated—thyroid function test, serum prolactin, total testosterone, which were analyzed by chemiluminescence system.

**Results** Oligomenorrhea was the most common menstrual abnormality in our study, the prevalence being 61.0% in cases followed by primary amenorrhea (16.4%). Thyroid dysfunction was found in 13.6% girls with menstrual disorders compared to 3.5% in those without menstrual disorders, and this was statistically significant ( $p = 0.006$ ). Biochemical hyperandrogenism was seen in 9.04% cases compared to 0.7% controls ( $p = 0.001$ ). The overall prevalence of hyperprolactinemia was 0.94%, and there was no statistically significant difference in girls with and without menstrual disorders. The prevalence of PCOS was 12.4% in the study population and 22.6% cases. Oligomenorrhea and PCOS were the most prevalent phenotypes in 52.5% of PCOS girls. No endocrine abnormality was detected in cases of polymenorrhea, hypomenorrhea and intermenstrual bleeding.

**Conclusions** Although immaturity of hypothalamic pituitary ovarian axis is considered to be the most common cause of menstrual irregularities in adolescent girls, endocrine abnormalities, namely thyroid dysfunction and hyperandrogenism, may be responsible in some cases, thus warranting further evaluation.

**Keywords** Thyroid disorders · Hyperprolactinemia · Hyperandrogenism · PCOS · Adolescents

## Introduction

Adolescence is a period when enormous physical and psychological changes take place marking transition from childhood to puberty. Although serious gynecological pathology is not common in this age group, menstrual disturbances are not uncommon. Menstrual problems are very common in adolescents. Seventy-five percentage of adolescents will have them sometime. Menstrual disorders during adolescence can often be a source of anxiety and confusion in young girls and their parents. A study conducted on 1051 Australian teenagers had found that 26% adolescents had menstrual disorders to an extent to interfere with their life or schooling [1]. Anovulation due to immaturity of hypothalamic pituitary ovarian (HPO) axis is the most common cause of menstrual problems during the initial few years following menarche. Other hormonal abnormalities that cause anovulation and prolonged menstrual bleeding include thyroid disorders, hyperprolactinemia, excess androgen production and polycystic ovary syndrome (PCOS).

Most studies on endocrine disorders leading to menstrual dysfunction are in older women aged 20–45 years. Although thyroid disorders can cause menstrual abnormalities [2], data are lacking on the prevalence of thyroid dysfunction in adolescents with menstrual problems. Hyperprolactinemia is not rare in young women with menstruation-related problems; its prevalence ranges from 5.5% in secondary amenorrhea to 2.6% in abnormal uterine bleeding [3]. Hyperandrogenism has been observed in up to 50% of adolescent girls with menstrual disorders. Regarding PCOS, one recent report from India found its prevalence to be 9.13% among 461 adolescents in the community [4].

There is a paucity of information on hormonal abnormalities in adolescent girls with menstruation disturbances. Therefore, this study was proposed to evaluate endocrine abnormalities like thyroid disorders, hyperprolactinemia, hyperandrogenism and PCOS in adolescent girls aged 10–19 years with menstrual disorders when compared to those without menstrual disorders. It is possible that identifying and treating these endocrine abnormalities may correct the menstrual disorders. This may decrease the need for treatment with estrogen and progesterone, which are most often used in menstrual disorders in adolescents.

## Methods

This case–control study was conducted in the Department of Obstetrics and Gynecology, JIPMER hospital, Puducherry, from September 2012 to August 2014. The Ethics Committee of JIPMER approved the study protocol. Adolescent girls aged 10–19 years were asked to participate. Patients fulfilling the inclusion criteria based on the menstrual history were recruited for the study after obtaining informed consent.

## Inclusion criteria

**Cases** Adolescent girls aged 10–19 years with the menstrual disorders, namely primary amenorrhea, secondary amenorrhea, oligomenorrhea, polymenorrhea, hypomenorrhea, menorrhagia, metropathia and irregular bleeding

**Controls** Adolescent girls aged 10–19 years without menstrual disorders

Primary amenorrhea was defined as the absence of menstruation by 14 years of age without secondary sexual characteristics or no menarche by 16 years of age with secondary sexual characteristics. Secondary amenorrhea was defined as the cessation of menstruation for >3 cycles or >6 months once they had begun. Oligomenorrhea was defined as infrequent menstruation that occurs at intervals of >45 days in adolescents. Polymenorrhea was defined as

frequent episodes of menstruation usually occurring at intervals of <21 days. Hypomenorrhea was defined as regularly timed but scanty episodes of bleeding. Menorrhagia was defined as regularly timed episodes of bleeding that are excessive in amount (>80 ml) and/or duration of flow (>5 days). Metropathia was defined as episodes of amenorrhea followed by excessive bleeding.

The participants of this study and their parents were given brief information about this study and its purpose. After obtaining an informed consent from participants/their parents, a detailed interview schedule containing sociodemographic details and medical/surgical/personal/family history was administered. After the questionnaire was completed, they were examined in the presence of a female staff nurse with privacy being maintained throughout. Physical examination including height, weight, BMI, acanthosis nigricans, thyromegaly, secondary sexual characteristics, hirsutism score and abdominal examination was then carried out. All participants were subjected to hormonal evaluation, namely serum T3, T4, TSH, serum prolactin and serum testosterone, on day 2nd of menstrual cycle. The girls were asked to follow up in the OPD with hormone test results. The procedure followed was in accordance with the ethical standards of the responsible committee on human experimentation or with the Declaration of Helsinki of 1975 as revised in 1983.

Hormone estimates, including free T3, free T4, free TSH, total testosterone (TT) and prolactin (PRL), were performed by fully automated bidirectionally interfaced chemiluminescent competitive immunoassay. Ultrasonography of abdomen and pelvis was performed for patients with oligomenorrhea for polycystic ovaries. 17(OH) progesterone, overnight dexamethasone suppression test (ONDST), coagulation profile, pregnancy test, MRI-brain, karyotyping, Mantoux and ESR were performed wherever clinically indicated. Thyroid function tests were interpreted according to standard reference range values: free T3—2.3–4.2 pg/ml, free T4—0.8–2.0 ng/dl, TSH—0.7–6.4  $\mu$ IU/ml. Hyperprolactinemia was defined as the presence of abnormally high levels of prolactin in the blood (>25 ng/ml). Clinical hyperandrogenism refers to modified Ferriman and Gallwey (mFG) score of 8 or higher and biochemical hyperandrogenism was defined as serum testosterone level of >82 ng/dl. PCOS was diagnosed according to the Rotterdam consensus criteria. The ultrasound criteria for polycystic ovaries are 12 or more subcapsular follicular cysts 2–9 mm in diameter and/or increased ovarian volume >10 mm<sup>3</sup>. If any abnormalities were detected, appropriate treatment was instituted.

Sample size was calculated to be 160 in each group in order to detect a difference of 5% exposure in controls (thyroid disorders in normal adolescent girls) and 15% exposure in cases (thyroid disorders in girls with

menstrual problems), and 1:1 ratio of cases to controls. Calculations were based on two-sided confidence levels of 95% and power of 80%, using Open EPI software. Allowing for 10% non-response or dropouts (no investigations, etc.), final sample size was calculated to be 176 in each group. All categorical variables such as age, menstrual complaints, education, duration of menstrual flow, cycle length, dysmenorrhea, hirsutism, presence of thyroid disorder, hyperprolactinemia, hyperandrogenism and PCOS were expressed as frequencies and percentages. Chi-square/Fisher's exact test was used to compare the categorical variables. After checking for normality in distribution, independent-samples t test was used to compare the means between groups. The normality of the continuous variables was tested, and mean with standard deviation was used to present normal variables such as age, BMI, hormone levels, i.e., serum T3, T4, TSH, serum testosterone and serum prolactin. Independent Student's t test and Mann–Whitney 'U' test were used to compare the continuous variables. Data were analyzed using SPSS version 16.0;  $p < 0.05$  was considered significant.

## Results

The mean age of girls among the cases and controls was  $17.36 \pm 1.85$  years and  $17.21 \pm 1.88$  years, respectively. Majority (75%) of girls in the study population had completed or were completing higher secondary school education. 74.5% of adolescents enrolled in this study hailed from Puducherry, while the remaining were from other districts. There was no statistical difference in the distribution of cases and controls according to their place of origin ( $p = 0.295$ ).

Most common complaint reported in the control group was white discharge per vaginum (36.8%) followed by pain in abdomen (27.7%), urinary tract infection 4.1%, dysmenorrhea 11.1, 4.2% fever and 2.8% pruritus. Nonspecific complaints included myalgia, body ache, coarse skin and not gaining weight. One girl had genital injury with paraurethral tear. The number of controls was lesser than that of cases, as the adolescent girls presenting to OPD without menstrual disturbances were limited within data collection period.

Majority of girls in the cases group (22.6%) had menarche at 13 years of age, while majority of controls (30.6%) had menarche at 12 years of age. There was a significant difference in the age at menarche among two groups ( $p < 0.001$ ). Among the cases, the most common abnormality was oligomenorrhea (61%) followed by primary amenorrhea (16.4%). Menorrhagia was seen in 9.6% cases, secondary amenorrhea in 7.3%, and metrorrhagia/

metropathia was seen in 1.1% each. Polymenorrhea and hypomenorrhea were found in 2.3 and 1.1% cases, respectively.

Out of 29 cases of primary amenorrhea, 4 had Mullerian agenesis, one had imperforate hymen, one had transverse vaginal septum, 2 had hypergonadotropic hypogonadism, 1 case had hypogonadotropic hypogonadism, 2 had hypopituitarism, 5 had hypothyroidism, 2 patients had cervical agenesis, 3 had hypoplastic uterus, while no definite cause was established in rest 8 cases and two subjects had cryptomenorrhea, due to imperforate hymen (1) and transverse vaginal septum (1).

Out of 17 cases of menorrhagia, three had bleeding disorders, six had thyroid dysfunction; in the remaining eight, no cause was found. Among the bleeding disorders, one had von Willebrand's disease, one had idiopathic thrombocytopenic purpura and one patient was on warfarin with deranged PT/INR. Out of the six thyroid disorders, one was a case of primary hypothyroidism, 4 cases were of subclinical hypothyroidism and one case of primary hyperthyroidism. Both cases with menorrhagia had thyroid dysfunction: one with subclinical hypothyroidism and the other with subclinical hyperthyroidism. In our study population, dysmenorrhea was prevalent in 22.6% adolescents. There was a higher prevalence of dysmenorrhea in cases compared to controls (27 vs. 18.1%).

Regarding anthropometrical parameters, mean height in case group was  $151.31 \pm 7.84$  cm compared to  $149.28 \pm 7.73$  cm in control group. Mean weight in both groups was  $50.27 \pm 13.89$  kg (cases) versus  $47.87 \pm 6.16$  kg (controls). Body mass index (BMI) showed mean values for case group as  $21.82 \pm 5.36$  kg/m<sup>2</sup> and for control group as  $21.59 \pm 2.24$  kg/m<sup>2</sup>. A higher proportion of cases when compared to the control group were found to be underweight (27 vs. 5.6%) and overweight or obese (23.2 vs. 6.3%). This difference was found to be statistically significant ( $p < 0.001$ ).

Five cases had breasts in Tanner I stage (poor development). Out of these 5, one case had no ovaries, whereas another had streak gonads (hypergonadotropic hypogonadism). Third was a case of pulmonary tuberculosis with panhypopituitarism, while the fourth was a case of pituitary hypofunction with non-cirrhotic portal fibrosis. Hypogonadotropic hypogonadism was detected in the fifth case with poor development of breast. With regard to pubic hair development, sixteen cases had under/no development of pubic hair. Out of these 16 cases, 5 had underdeveloped breasts as mentioned above. Among the other 11 cases, 4 cases had hypothyroidism and 1 case had hyperthyroidism. No apparent cause was found in the remaining six cases.

Mean level of serum free T3 in cases ( $2.81 \pm 0.78$  pg/ml) was lesser than that in controls ( $2.91 \pm 0.64$  pg/ml). This difference was not found to be statistically significant ( $p = 0.199$ ). Mean level of serum free T4 in cases was

$1.49 \pm 0.59$  pg/dl compared to  $1.45 \pm 0.65$  pg/dl in controls. No statistical significance was found ( $p = 0.134$ ). Mean level of serum TSH was higher in cases ( $6.59 \pm 19.05$   $\mu$ IU/ml) than in controls ( $2.96 \pm 1.74$   $\mu$ IU/ml). This was found to be statistically significant ( $p = 0.013$ ). Overall thyroid dysfunction was found in 29 out of 321 adolescent girls enrolled in the study, and as listed in Table 1, thyroid dysfunction was characteristically more prevalent in the adolescents with menstrual disorders (13.6%) compared to controls (3.5%). Unadjusted risk of menstrual abnormality was more among the subjects with abnormal thyroid function tests compared to normal thyroid status (OR 4.36, 95% CI 1.6–11.7).

The mean serum prolactin level was  $14.01 \pm 8.68$  ng/ml in the cases and  $12.99 \pm 4.33$  ng/ml in the controls. However, this difference in mean levels was not found to be statistically significant ( $p = 0.200$ ). Only in three cases serum prolactin was raised (1.7%). Out of three cases of hyperprolactinemia, one case had primary hypothyroidism with oligomenorrhea, while other two in addition to hyperandrogenism had secondary amenorrhea and oligomenorrhea, respectively. None of the girls in the control group had hyperprolactinemia.

Mean total testosterone level was  $43.74 \pm 22.56$  ng/dl in the cases and  $37.47 \pm 16.98$  ng/dl in the controls. There was a statistically significant difference regarding serum total testosterone levels in both groups ( $p = 0.004$ ). Table 2 shows 9.04% adolescents with menstrual abnormalities having biochemical hyperandrogenism in comparison with 0.7% in the control group. Unadjusted risk of menstrual abnormalities was more among the subjects with biochemical hyperandrogenism compared to normal testosterone levels (OR = 14.2, 95% CI 1.8–108.5). This association was found to be statistically significant. Of the 22 subjects with Hirsutism among cases, 16 had Ferriman–Gallwey score  $\geq 8$ , and thus, clinical hyperandrogenism was prevalent in 9.04% of cases. No girl with normal menstruation had clinical hyperandrogenism. The

**Table 1** Prevalence of thyroid dysfunction in the study groups

Thyroid status	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Total <i>n</i> (%)
Normal	153 (86.4%)	139 (96.5%)	292 (91.0%)
Hypothyroidism	21 (11.9%)	5 (3.5%)	26 (8.1%)
Primary	9 (37.5%)	2 (40%)	11 (37.9%)
Subclinical	9 (37.5%)	3 (60%)	12 (41.4%)
Secondary	3 (12.5%)	0 (0%)	3 (10.3%)
Hyperthyroidism	3 (1.7%)	0 (0%)	3 (0.9%)
Primary	2 (8.3%)	0 (0%)	2 (6.9%)
Subclinical	1 (4.2%)	0 (0%)	1 (3.4%)
Secondary	0 (0%)	0 (0%)	0 (0%)
Total	177 (100%)	144 (100%)	321 (100%)

$p = 0.006$

**Table 2** Prevalence of hyperandrogenism in the study population

	Cases ( <i>n</i> = 177)	Controls ( <i>n</i> = 144)	Total ( <i>n</i> = 321)
Biochemical hyperandrogenism			
Present	16 (9.04%)	1 (0.7%)	17 (5.3%)
Absent	161 (90.96%)	143 (99.3%)	304 (94.7%)
Clinical hyperandrogenism			
Absent	161 (90.96%)	144 (100%)	304 (95.02%)
Present	16 (9.04%)	0 (0%)	16 (4.98%)

*p* = 0.001

difference in the prevalence of hyperandrogenism (biochemical or clinical) between cases and controls was statistically significant (*p* = 0.004) in our study.

The prevalence of hormonal abnormalities in adolescents with menstrual disorders is summarized in Table 3.

Polycystic ovarian syndrome was seen in 40 girls amounting to 22.6% of all adolescent girls with menstrual disorders and was the most common endocrine abnormality in the case group. Oligomenorrhea with PCOS changes on ultrasound was the most common phenotype seen in 52.5% cases of PCOS, whereas oligomenorrhea with hyperandrogenism and ultrasonographic changes of PCOS were seen in 37.5% cases of PCOS. Oligomenorrhea along with hyperandrogenism was seen in 5 cases. Oligo/amenorrhea was present in 100% of cases with PCOS, 47.5% had hyperandrogenism and 90% the girls with PCOS had polycystic ovaries. Thirty percentage cases of PCOS had biochemical and 30% cases of PCOS had clinical hyperandrogenism.

## Discussion

During adolescence, there is a tendency of irregularity in menstrual cycles, and this is mostly due to immaturity of hypothalamic pituitary ovarian axis. Though irregular

menses during early menarche are usually physiological, occasionally they can be due to underlying endocrine disorders like polycystic ovary syndrome, hypo- or hyperthyroidism, hyperandrogenism and hyperprolactinemia. Studies evaluating endocrine abnormalities in adolescents with menstrual disorders are few [3–8]. In the present study, mean age was higher when compared to two other studies [9], which had a mean age ranging from 15.4 ± 1.8 to 16.9 ± 1 years but similar to another study [5]. Adolescents usually do not approach the gynecologist, probably because of embarrassment, undue fear of disease or ignorance about normality of menstruation. A large study in 2411 adolescents found that only 11.1% girls had consulted gynecologist for menstrual complaints. In our study, 54.1% adolescents presented with menstrual complaints and this incidence might be higher as ours in a tertiary hospital with a high referral of cases.

Regarding menstrual characteristics, the prevalence of polymenorrhea was lower in our study similar to another Italian study [5], but other studies from Malaysia and Africa [9] have shown higher prevalence. 9.6% of the adolescent cases had menses lasting >5 days in our study similar to other studies [9]. Other studies [5, 9] have not segregated extensively adolescents with various menstrual disorders like ours. The prevalence of dysmenorrhea was lower in our study (22.6%) when compared to other studies that have shown a higher prevalence of 67.3–72% [5, 9]. Low prevalence of dysmenorrhea in the present study may be probably because of more tolerance to the pain related to menstruation.

Menstruation is affected by general body habitus of the patient, genetic and nutritional factors. In the present study, although there was a significantly higher prevalence of underweight and overweight/obese girls in cases than in controls, another study found no consistent association between BMI (body mass index) and menstrual dysfunction.

**Table 3** Prevalence of hormonal abnormalities in adolescents with menstrual disorders

Menstrual abnormalities in the present study	No. of cases	Thyroid dysfunction		Hyperprolactinemia		Biochemical hyperandrogenism	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Primary amenorrhea	29	7	24.1	0	0.0	0	0.0
Secondary amenorrhea	13	3	23.1	1	7.7	1	7.7
Polymenorrhea	4	0	0.0	0	0.0	0	0.0
Oligomenorrhea	108	6	5.6	2	1.9	13	12.0
Hypomenorrhea	2	0	0.0	0	0.0	0	0.0
Menorrhagia	17	6	35.3	0	0.0	2	11.8
Metrorrhagia	2	2	100.0	0	0.0	0	0.0
Intermenstrual bleeding	2	0	0.0	0	0.0	0	0.0
Total	177	24	13.6	3	1.7	16	9.0



There is paucity of studies in the literature evaluating the prevalence of thyroid disorders in adolescents with menstrual abnormalities. The data available describe menstrual disturbances in patients with already existing thyroid dysfunction in women in the reproductive age group [2]. The evidence shows that the prevalence of menstrual disturbances in thyroid dysfunction was either not different from those in healthy controls or was less frequently associated with menstrual irregularities [2]. Our study has attempted to establish prevalence of thyroid disorders in adolescent girls with and without menstrual disorders. The prevalence of hypothyroidism and hyperthyroidism in girls with menstrual disorders was 11.9 and 1.7%, respectively. Another study from Puducherry, India, which had evaluated thyroid dysfunction in women in the age group of 20–80 years found that 84.2% women were euthyroid, 11.5% women hypothyroid and 1.8% women hyperthyroid [10]. This shows a comparable prevalence of thyroid dysfunction in Puducherry population in adolescent and adult women.

In the present study, 24 adolescents with menstrual disorders were found to have thyroid dysfunction. Out of them, 29.2% had primary amenorrhea, 12.5% had secondary amenorrhea, 25% were oligomenorrheic, 25% were menorrhagic and 8.3% had metrorrhagia. A study conducted in older women aged 20–45 years showed a higher prevalence of secondary amenorrhea (2.5%) and hypomenorrhea (3.7%) in patients with severe hyperthyroidism than those with mild or moderate hyperthyroidism (0.2% for secondary amenorrhea and 0.9% for hypomenorrhea). Also menstrual disturbances were found to be more common in patients with severe hypothyroidism (34.8%) compared to mild to moderate hypothyroidism (10.2%) [2].

The prevalence of hyperprolactinemia was 1.7% among the cases in our study. The prevalence varies from 0.4% in the normal adult population to as high as 9–17% in women with menstrual disorders [2]. In our study, hyperprolactinemia was seen in 7.7% cases of secondary amenorrhea and 1.9% of oligomenorrhea. Another study [3] found prevalence of hyperprolactinemia as 5.5% in cases with secondary amenorrhea and 2.6% in abnormal uterine bleeding in adolescent age group.

Clinical or biochemical hyperandrogenism is one of the Rotterdam's criteria for diagnosing PCOS. Hirsutism is uncommon in adolescents as compared to adults as it takes a longer time to develop in the presence of high levels of circulating androgens [4]. Hirsutism including various grades of F–G score was prevalent in 6.9% of all the adolescent girls in the present study. Another community-based study has found the prevalence of hirsutism to be 13.7% [11]. Overall, the prevalence of clinical hyperandrogenism (F–G score  $\geq 8$ ) was found to be 4.98% in the study

population and 9.04% in cases. Other studies have shown the prevalence of clinical hyperandrogenism ranging from 3.4 to 5.65% [10]. The latter prevalence is slightly higher possibly because a lower score cutoff was used (F–G score  $>6$ ). Overall, the prevalence of biochemical hyperandrogenism was found to be 5.3% in the study population and 9.04% in cases. Hyperandrogenism has been observed to be as high as 50% in adolescent girls with menstrual disorders in another study. But this was a small study in 24 girls with menstrual disorders out of which 21 had polycystic ovaries, resulting in higher prevalence of hyperandrogenism. Mean total testosterone level in our study was similar to another community-based study, which also found that the total testosterone levels in non-PCOS group ( $34 \pm 10$  ng/dl) were lower when compared to PCOS group ( $45 \pm 19$  ng/dl) [11]. Mean testosterone level in adolescents with PCOS was  $33.37 \pm 20.47$  ng/dl in another study [4]. Sixteen cases of biochemical hyperandrogenism were seen in adolescents with menstrual dysfunction, out of which 81.2% had oligomenorrhea, 12.5% had menorrhagia and 6.3% had secondary amenorrhea.

There is varied prevalence of polycystic ovary syndrome across various populations, ranging from 2.2 to 26% [12]. Varying prevalence is due to different diagnostic criteria, varying symptoms, varied age groups, subjective differences in ultrasound findings and different ethnicity of population. The prevalence of PCOS was 12.4% among all the 321 adolescent girls in our study which is slightly higher when compared to an Indian study carried out in Andhra Pradesh which found the prevalence to be 9.13% among 461 adolescents in the community [4]. In contrast, another recent study from Mumbai India, has shown the prevalence to be as high as 22.5% [11]. Among cases, the prevalence of PCOS was 22.6% similar to another study which showed it to be higher (16%) in adolescent girls with menstrual dysfunction [8].

The prevalence of clinical hyperandrogenism in PCOS (30%) seen in our study was similar to that (30.95%) found in another study in Indian adolescent girls [4]. But it was much higher when compared to a prevalence of 8.3% reported in another study in Australian girls [13].

This is one of the very few studies to provide information on the pattern of menstrual disturbances and prevalence of endocrine abnormalities in adolescents with menstrual disorders. Restricting the inclusion age to 10–19 years reflects the prevalence in adolescent girls. The number of controls was lesser than that of cases, as the adolescent girls presenting to the outpatient department without menstrual disturbances were limited within the data collection period. Since the study population was recruited from a tertiary hospital, the distribution of symptoms and causes might not represent those of all adolescent girls with menstrual problems.

Although immaturity of hypothalamic pituitary ovarian axis is considered to be the most common cause of menstrual irregularities in adolescent girls, endocrine abnormalities, namely thyroid dysfunction and hyperandrogenism, may be responsible in some cases, thus warranting further evaluation.

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#### Compliance with ethical standards

**Conflict of interest** All authors declare that they have no conflict of interest.

**Informed consent in studies with human subjects** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

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