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PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN REPRODUCTIVE-AGED WOMEN AND ITS ASSOCIATION WITH MENSTRUAL IRREGULARITIES: A CROSS-SECTIONAL STUDY

Original Research

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ABSTRACT

Background: Subclinical hypothyroidism (SCH), characterized by elevated TSH with normal thyroid hormone levels, often remains undiagnosed despite its potential effects on reproductive health. In women of reproductive age, even mild thyroid dysfunction can disrupt the hypothalamic-pituitary-ovarian axis, contributing to menstrual irregularities that impact fertility and overall quality of life.

Objective: To determine the prevalence of subclinical hypothyroidism and evaluate its association with menstrual irregularities among women aged 18–40 years.

Methods: A cross-sectional study was conducted over eight months in tertiary care hospitals in Lahore, Pakistan, enrolling 422 women aged 18–40 years. Participants were assessed using a structured questionnaire and underwent serum TSH, FT4, and FT3 testing. Subclinical hypothyroidism was defined as TSH >4.0 mIU/L with normal FT4 and FT3. Menstrual patterns were categorized as regular or irregular. Data were analyzed using SPSS v26 with Chi-square and logistic regression tests; significance was set at $p<0.05$.

Results: The prevalence of subclinical hypothyroidism was 19.9% (n=84). Among these, 57.1% reported menstrual irregularities, compared to 17.8% in the euthyroid group. Women with SCH had 6.2 times higher odds of experiencing menstrual disturbances (95% CI: 3.7–10.5, $p<0.001$), independent of age and BMI.

Conclusion: Subclinical hypothyroidism is significantly associated with menstrual irregularities in reproductive-aged women. Routine thyroid screening should be considered in women presenting with menstrual disturbances to enable early diagnosis and appropriate management.

Keywords: Endocrine system, Female reproductive health, Menstrual irregularities, Pakistan, Prevalence, Subclinical hypothyroidism, Thyroid function tests.

INTRODUCTION

Subclinical hypothyroidism (SCH) is a condition defined by elevated thyroid-stimulating hormone (TSH) levels in the presence of normal circulating thyroid hormone concentrations. Though often asymptomatic, it represents a subtle form of thyroid dysfunction that may have significant clinical implications, particularly for women in their reproductive years (1). Thyroid hormones play a vital role in maintaining normal reproductive physiology, influencing everything from follicular development to ovulation and endometrial receptivity. Even mild deviations in thyroid function, as seen in SCH, can disrupt these processes, potentially leading to menstrual irregularities, infertility, and adverse pregnancy outcomes (2,3). Yet despite its potential impact, SCH remains underdiagnosed and underappreciated in clinical practice, especially in young women who may attribute menstrual disturbances to stress or other common life factors (4). Menstrual irregularities, ranging from oligomenorrhea and polymenorrhea to amenorrhea, are among the most frequent gynecological complaints reported by women of reproductive age. While these disturbances may be caused by a variety of factors—such as polycystic ovary syndrome (PCOS), lifestyle changes, or emotional stress—the role of underlying endocrine dysfunction, particularly related to thyroid health, is increasingly being recognized (5,6). Thyroid hormones exert their effects on the hypothalamic-pituitary-ovarian (HPO) axis and modulate the secretion of gonadotropin-releasing hormone, luteinizing hormone, and follicle-stimulating hormone, all of which are critical to the menstrual cycle. Even subclinical disruptions in thyroid homeostasis can disturb this delicate hormonal balance, potentially manifesting as irregular cycles, anovulation, or even infertility (7).

Several studies have explored the relationship between thyroid dysfunction and menstrual disturbances, with overt hypothyroidism well established as a contributing factor (7,8). However, the data on subclinical hypothyroidism remain inconclusive and sometimes contradictory. Some research has suggested a significant association between SCH and various menstrual abnormalities, including menorrhagia and oligomenorrhea, while others have failed to demonstrate a consistent pattern (9). This lack of consensus may be due to variations in study populations, diagnostic criteria, and the definition of menstrual irregularities. Furthermore, cultural and environmental factors, such as iodine intake and access to healthcare, can influence both the prevalence of SCH and its clinical manifestations (10). Consequently, a clearer understanding of how subclinical hypothyroidism affects menstrual health in specific populations is urgently needed. The reproductive years, defined broadly as ages 18 to 40, represent a critical window in a woman's life, encompassing key milestones such as family planning, conception, and pregnancy. Ensuring optimal endocrine health during this period is essential not only for reproductive success but also for long-term well-being. Early identification of subtle thyroid dysfunctions such as SCH could allow for timely interventions, potentially alleviating menstrual issues and improving fertility outcomes (11,12).

Yet, despite the increasing awareness of thyroid disorders in general, routine screening for SCH among women with menstrual irregularities is not universally practiced. This gap between potential clinical impact and actual diagnostic effort underscores the need for targeted epidemiological studies that examine the prevalence of SCH and its correlation with menstrual patterns in reproductive-aged women. Against this backdrop, the present study seeks to address two interrelated concerns: first, to determine the prevalence of subclinical hypothyroidism among women aged 18 to 40 years; and second, to evaluate its association with menstrual irregularities within this population. By focusing on a cross-sectional sample of reproductive-aged women, this research aims to provide updated evidence that may inform clinical guidelines and enhance early detection strategies. The objective is not only to quantify the burden of SCH but also to clarify its reproductive significance—thereby offering insights that may ultimately improve women's health outcomes through more nuanced and proactive endocrine care.

METHODS

This cross-sectional study was conducted over a period of eight months in gynecology and endocrinology outpatient departments of tertiary care hospitals located in the urban region of Lahore, Pakistan. The study aimed to determine the prevalence of subclinical hypothyroidism and explore its association with menstrual irregularities among women in the reproductive age group of 18 to 40 years. These hospitals cater to a diverse population across varying socioeconomic backgrounds, making them well-suited for a study that seeks to generalize findings across a broad demographic segment. A sample size of 384 participants was calculated using the Cochran formula, based on an expected prevalence rate of subclinical hypothyroidism of approximately 15% in the target population, a confidence level

of 95%, and a margin of error set at 5%. To account for possible non-responses and incomplete data, an additional 10% was added, bringing the final target sample size to 422 women. Participants were selected through non-probability consecutive sampling, ensuring that every eligible individual attending the clinics during the study period had the opportunity to be included (2,3).

Inclusion criteria for the study were women aged between 18 and 40 years who had experienced menstruation for at least the past one year and were willing to provide informed consent. Women who were pregnant, breastfeeding, diagnosed with polycystic ovary syndrome (PCOS), taking hormonal contraception, or known to have any previously diagnosed thyroid disorder or chronic systemic illness (such as diabetes mellitus or renal disease) were excluded to minimize confounding variables that could independently affect menstrual regularity or thyroid function. After obtaining informed written consent, each participant was interviewed using a pretested structured questionnaire administered by trained female medical staff. The questionnaire collected demographic data (age, marital status, education, occupation), menstrual history (cycle regularity, frequency, flow, duration, and associated symptoms), and general medical history. Menstrual irregularities were classified based on standard clinical definitions: oligomenorrhea (cycles >35 days), polymenorrhea (<21 days), menorrhagia (excessive bleeding), and amenorrhea (absence of menstruation for ≥3 months). Blood samples were collected from all participants during the early follicular phase of their menstrual cycle (days 2 to 5) to control for physiological hormonal fluctuations. Samples were drawn after an overnight fast and analyzed for serum thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3) levels using electrochemiluminescence immunoassay (ECLIA) techniques. Subclinical hypothyroidism was defined as a serum TSH level above 4.0 mIU/L with normal FT4 and FT3 levels, in line with the American Thyroid Association guidelines (13). All laboratory tests were conducted at the hospital's central diagnostic laboratory, adhering to standard operating procedures and quality control protocols. Participants identified as having overt hypothyroidism or hyperthyroidism were excluded post hoc from the analysis to ensure that only subclinical cases were considered.

Data were entered and analyzed using IBM SPSS version 26. Descriptive statistics were used to summarize participant characteristics and prevalence rates. Continuous variables such as age and TSH levels were expressed as mean ± standard deviation. Categorical variables such as the presence or absence of menstrual irregularities were presented as frequencies and percentages. The association between subclinical hypothyroidism and menstrual irregularities was examined using the Chi-square test for independence. A p-value of less than 0.05 was considered statistically significant. For variables with potential confounding effects, binary logistic regression analysis was performed to adjust for age, body mass index, and marital status, yielding adjusted odds ratios and 95% confidence intervals. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the respective hospitals. All procedures were conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its subsequent amendments. Participants were assured of the confidentiality of their data, the voluntary nature of their participation, and the freedom to withdraw from the study at any point without consequences. This methodological framework was carefully designed to ensure rigorous data collection, minimize bias, and allow for meaningful analysis of the relationship between subclinical hypothyroidism and menstrual disturbances in a representative sample of reproductive-aged women.

RESULTS

The study enrolled a total of 422 women aged between 18 and 40 years. The mean age of participants was 28.4 ± 5.6 years, and the mean BMI was 24.7 ± 3.8 kg/m². The majority of participants were married (73.9%), and nearly half had tertiary-level education (47.9%). Full demographic characteristics are presented in Table 1. Among the participants, 84 women (19.9%) were found to have subclinical hypothyroidism based on elevated TSH levels with normal FT4 and FT3 levels, while the remaining 338 women (80.1%) had normal thyroid function. The distribution of thyroid function status is illustrated in Table 2 and Figure 1. Regarding menstrual patterns, 314 participants (74.4%) reported regular menstrual cycles, whereas 108 (25.6%) reported irregularities. When stratified by thyroid function, it was found that among women with subclinical hypothyroidism, 48 (57.1%) experienced menstrual irregularities compared to 60 (17.8%) among those with normal thyroid function. These findings are detailed in Table 3 and visually represented in Figure 2. A statistically significant association was observed between subclinical hypothyroidism and menstrual irregularities ($p < 0.001$). Logistic regression analysis demonstrated that women with subclinical hypothyroidism were 6.2 times more likely to report menstrual irregularities compared to those with normal thyroid function, with a 95% confidence interval of 3.7–10.5. This association remained significant even after adjusting for confounding variables such as age and BMI. The results of this analysis are summarized in Table 4. These findings underscore a meaningful correlation between subclinical thyroid dysfunction and altered menstrual patterns in reproductive-aged women, supporting the clinical relevance of thyroid screening in cases of unexplained menstrual disturbances.

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Table 1. Demographic Characteristics of Study Participants

Variable		Mean ± SD / n (%)
Age (years)		28.4 ± 5.6
BMI (kg/m²)		24.7 ± 3.8
Marital Status	Married	312 (73.9%)
	Unmarried	110 (26.1%)
Education Level	Primary	80 (18.9%)
	Secondary	140 (33.2%)
	Tertiary	202 (47.9%)

Table 2. Thyroid Function Status Among Participants

Thyroid Status	n (%)
Normal	338 (80.1%)
Subclinical Hypothyroidism	84 (19.9%)

Table 3. Comparison of Menstrual Irregularities by Thyroid Status

Menstrual Pattern	Normal Thyroid n (%)	Subclinical Hypothyroidism n (%)
Regular	278 (82.2%)	36 (42.9%)
Irregular	60 (17.8%)	48 (57.1%)

Table 4. Association Between Subclinical Hypothyroidism and Menstrual Irregularities

Variable	Odds Ratio	95% Confidence Interval	p-value
Subclinical Hypothyroidism	6.2	3.7 – 10.5	<0.001

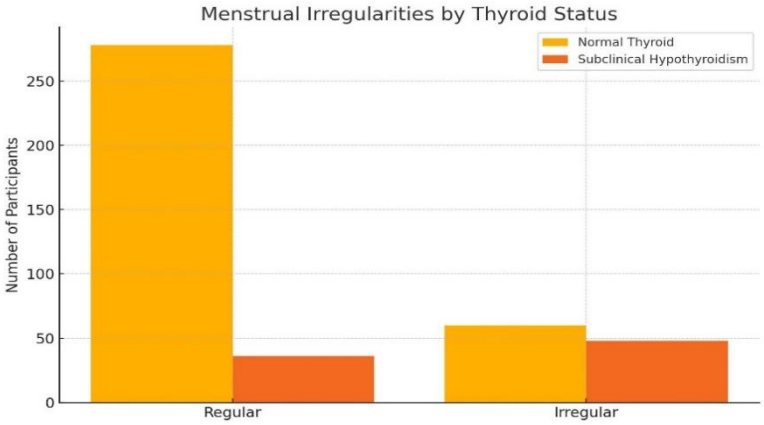

Figure 1 Menstrual Irregularities by Thyroid Status

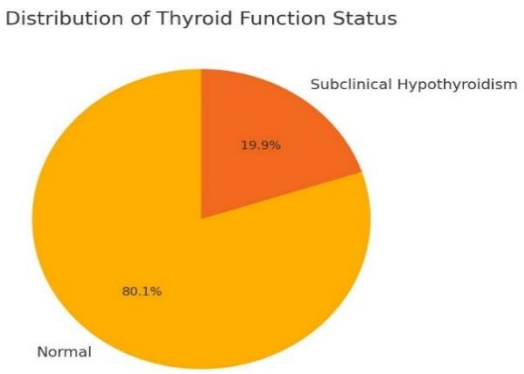

Figure 2 Distribution of Thyroid Function Status

DISCUSSION

The findings of this study confirm a significant association between subclinical hypothyroidism and menstrual irregularities among women of reproductive age. With a prevalence of 19.9% for subclinical hypothyroidism and menstrual disturbances reported by 57.1% of affected women, the data aligns with mounting evidence that even subtle thyroid dysfunction can disrupt menstrual physiology. These results lend weight to previous investigations that identified subclinical hypothyroidism as a frequent, though often under-recognized, contributor to menstrual abnormalities. Comparable studies reinforce the current findings. For instance, a study observed a 25% prevalence of subclinical hypothyroidism in reproductive-aged women presenting with menstrual irregularities and reported significant correlations with oligomenorrhea and menorrhagia (14,15). Similarly, a study reported that 23.5% of their participants had subclinical

hypothyroidism, with menorrhagia being the most common presentation (16). These findings underscore that, subclinical thyroid abnormalities may present primarily through menstrual symptoms long before other systemic signs become apparent. A striking feature of the current study is the magnitude of the association, with women affected by subclinical hypothyroidism having 6.2 times higher odds of reporting menstrual irregularities. This is higher than reported in several comparable analyses, potentially reflecting regional variations in iodine intake, health literacy, and access to screening. A study similarly highlighted a 22% prevalence of thyroid dysfunction among women with abnormal menstrual cycles, particularly menorrhagia and oligomenorrhea, in a Pakistani cohort (17), which supports the current study's setting and methodology.

The present findings have critical clinical implications. The consistent presence of menstrual irregularities as an early indicator of subclinical hypothyroidism presents an opportunity for early diagnosis through routine TSH screening in gynecology clinics. Given the substantial reproductive burden of undiagnosed thyroid dysfunction, timely intervention could prevent infertility, miscarriage, and progression to overt hypothyroidism. Studies emphasized the cost-effectiveness of routine thyroid evaluation in women with abnormal uterine bleeding (18,19). This study's strengths lie in its robust sample size, well-defined inclusion criteria, and standardized hormone assays during the follicular phase, ensuring hormonal consistency. Moreover, controlling for potential confounders like BMI and age enhances the reliability of the observed associations. However, several limitations merit consideration. As a cross-sectional design, the study cannot establish causality. Longitudinal studies would be essential to evaluate whether normalization of TSH through levothyroxine therapy restores menstrual regularity. Additionally, while this study excluded women with overt PCOS or chronic systemic diseases, subtle contributors such as subclinical insulin resistance or emotional stress were not quantitatively measured.

Another limitation is the reliance on self-reported menstrual data, which may be subject to recall bias. Future research may benefit from utilizing menstrual tracking applications or hormonal markers such as progesterone to confirm ovulatory patterns. Moreover, autoimmune markers like thyroid peroxidase antibodies were not assessed in the current cohort. As recent evidence suggested, autoimmune thyroiditis is a significant underlying factor in many SCH cases and may have additional reproductive implications (20,21). In light of these findings, integrating routine thyroid screening into the diagnostic workup of women presenting with unexplained menstrual irregularities is justified. This is particularly relevant in South Asian populations, where higher baseline prevalence of thyroid dysfunction has been observed. Future research should prioritize interventional studies assessing the reproductive outcomes of treating subclinical hypothyroidism in asymptomatic women. In conclusion, this study substantiates a strong and clinically meaningful association between subclinical hypothyroidism and menstrual irregularities in reproductive-aged women. The data aligns with recent literature and reinforces the role of thyroid health in reproductive endocrinology. Recognizing and addressing even subtle thyroid dysfunction early may not only improve menstrual health but also safeguard fertility and overall well-being.

CONCLUSION

This study highlights a significant association between subclinical hypothyroidism and menstrual irregularities among reproductive-aged women, emphasizing the need for routine thyroid screening in women presenting with unexplained menstrual disturbances. Early detection and management of subclinical hypothyroidism can potentially restore menstrual regularity and improve reproductive outcomes, supporting its clinical relevance in gynecological care.

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AUTHOR CONTRIBUTION

Author	Contribution
Samabia Abdul Subhan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Daniyal Abbasi	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Eesha Imran	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Isha Maqsood	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Maira Muzammal	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Fiza Abbas	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Shaista Hamid	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Farhan Muhammad Qureshi	Writing - Review & Editing, Assistance with Data Curation

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