

Association of Thyroid Dysfunction and Hyperprolactinemia with Menstrual Irregularities in Subfertile Women

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DOI: <https://doi.org/10.36348/sijog.2025.v08i10.002>

| Received: 08.08.2025 | Accepted: 06.10.2025 | Published: 10.10.2025

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Abstract

Background: Menstrual irregularities are common among subfertile women and often reflect underlying endocrine dysfunctions. Thyroid hormones and prolactin play key roles in the regulation of menstruation, and abnormalities in their levels may disrupt ovulation and fertility. This study aimed to investigate the association between thyroid dysfunction and hyperprolactinemia with menstrual irregularities in subfertile women attending a tertiary care hospital. **Methods:** A case-control study was conducted at BIRDEM General Hospital, Dhaka, from January 2022 to March 2024. A total of 100 women were enrolled in the study: 50 with primary subfertility (cases) and 50 fertile women (controls). Menstrual history and clinical features were also recorded. Serum TSH, FT3, FT4, and prolactin levels were measured using a chemiluminescent magnetic microparticle assay. Anovulation was assessed using mid-cycle ultrasonography. Data were analyzed using SPSS version 27.0. **Results:** Acyclical menstruation (42.0% vs. 28.0%) and oligomenorrhea (26.0% vs. 14.0%) were more frequent in the cases than in the controls. Anovulation was significantly more common in subfertile women than in fertile women (24.0% vs. 8.0%, $p=0.029$). Biochemical analysis revealed higher TSH (4.92 ± 5.35 vs. 3.83 ± 6.04 $\mu\text{IU/mL}$, $p=0.041$) and prolactin levels (38.09 ± 29.3 vs. 22.27 ± 12.6 ng/mL , $p=0.005$), and lower FT4 (5.45 ± 3.44 vs. 16.92 ± 3.28 pmol/L , $p=0.032$) in cases. Galactorrhoea was also more frequent among subfertile women, though not statistically significant. **Conclusion:** Thyroid dysfunction and hyperprolactinemia are strongly associated with menstrual irregularities in subfertile women. Routine hormonal screening may enable early diagnosis and treatment, thereby improving reproductive outcomes of patients.

Keywords: subfertility, menstrual irregularities, thyroid dysfunction, hyperprolactinemia.

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INTRODUCTION

Menstrual irregularities represent one of the most frequent clinical manifestations of endocrine dysfunction in reproductive-aged women and are a significant contributor to subfertility [1]. Among the endocrine factors implicated, thyroid dysfunction and hyperprolactinemia are particularly important due to their regulatory roles within the hypothalamic-pituitary-ovarian axis. The balance of thyroid hormones is crucial

for ovarian steroidogenesis, follicular maturation, and endometrial receptivity, while prolactin exerts direct and indirect effects on ovulation and menstrual cycle regulation [2]. Disruption in these hormonal pathways has been consistently linked to disorders such as oligomenorrhea, amenorrhea, anovulation, and abnormal uterine bleeding [3].

The prevalence of menstrual disturbances among women with thyroid disorders is well-

Citation: Jannatul Ferdous Chowdhury, Effat Aziz, Md. Mahbobul Haque, Rubab Sarmin, Mahzabin Husain, Tasnia Sultana, Salma Akter (2025). Association of Thyroid Dysfunction and Hyperprolactinemia with Menstrual Irregularities in Subfertile Women. *Sch Int J Obstet Gynec*, 8(10): 306-311.

documented. Hypothyroidism, for example, may lead to polymenorrhoea and menorrhagia due to impaired coagulation and estrogen breakthrough bleeding, whereas hyperthyroidism is often associated with oligomenorrhoea or hypomenorrhoea [4,5]. These abnormalities are mediated through changes in sex hormone-binding globulin, luteinizing hormone, and follicle-stimulating hormone regulation, which together influence ovarian cyclicity [6]. Hyperprolactinemia, on the other hand, disrupts the pulsatile secretion of gonadotropin-releasing hormone, reducing luteinizing hormone release and subsequently impairing ovulation. This mechanism often results in oligomenorrhoea, amenorrhoea, or luteal phase defects, all of which negatively impact fertility [7,8].

In clinical practice, women presenting with infertility frequently report menstrual cycle abnormalities. Studies have shown that 40–60% of subfertile women demonstrate irregular menstruation, often associated with subtle or overt thyroid dysfunction and raised prolactin levels [9]. Moreover, the coexistence of hypothyroidism and hyperprolactinemia appears to compound the risk of cycle disruption, as thyrotropin-releasing hormone can simultaneously elevate thyroid-stimulating hormone (TSH) and prolactin secretion [10]. This interplay underscores the clinical necessity of evaluating both thyroid and prolactin levels in women presenting with subfertility, particularly when accompanied by menstrual disturbances.

The context of Bangladesh is particularly relevant. Subfertility and menstrual disorders are prevalent, but their association with thyroid dysfunction and hyperprolactinemia remains understudied in this setting [11]. Given the socio-cultural impact of infertility in South Asian societies, where childlessness carries stigma and a significant psychological burden, understanding the hormonal determinants of menstrual irregularities in subfertile women is crucial [12]. Such evidence would not only clarify pathophysiological mechanisms but also strengthen recommendations for early hormonal screening in women with abnormal cycles before the onset of invasive investigations.

This study aimed to investigate the association of thyroid dysfunction and hyperprolactinemia with menstrual irregularities in subfertile women at a tertiary care hospital in Bangladesh. By analyzing clinical, biochemical, and cycle-related parameters, it sought to delineate the hormonal contributions to menstrual disturbance within this population.

METHODOLOGY & MATERIALS

This case–control study was conducted at the Centre for Assisted Reproduction (CARE) and the outpatient department of Obstetrics and Gynecology, BIRDEM General Hospital, Dhaka. The study was carried out over a period of two years and three months,

from January 2022 to March 2024. A total of 100 women were recruited: 50 with primary subfertility (cases) and 50 fertile women (controls).

Sample selection

Inclusion criteria

- Women aged 18–40 years with primary subfertility.
- Fertile controls matched for age and parity, with no history of infertility.
- Male partners with normal semen parameters.

Exclusion criteria

- Women with systemic diseases such as diabetes mellitus, hypertension, renal or liver disease, or autoimmune disorders.
- Women previously treated for thyroid disorders.
- Women with pelvic pathologies, including endometriosis, pelvic infection, tubal block, genital tuberculosis, or polycystic ovarian syndrome.

Data collection and study procedure

Participants were purposively recruited after screening for inclusion and exclusion criteria. A structured questionnaire was used to capture demographic and clinical variables. Clinical evaluation included menstrual history (cyclical/acyclical, menorrhagia, oligomenorrhea) and physical signs such as galactorrhea and cold intolerance. Ovulatory status was assessed using mid-cycle transvaginal ultrasonography (day 16–18). Venous blood samples were collected in a fasting state to measure serum TSH, FT3, FT4, and prolactin levels using a chemiluminescent magnetic microparticle assay (CMIA). Data integrity was ensured by double-checking the entries and routine supervision.

Ethical considerations

Ethical approval was obtained from the BIRDEM Institutional Review Board. Written informed consent was secured from all participants. Confidentiality was maintained by assigning coded identifiers, and participants were informed of their right to withdraw at any stage without consequence.

Statistical analysis

Data were analyzed using SPSS version 27. Descriptive statistics were used to summarize baseline characteristics. Group comparisons were performed using the chi-square test for categorical variables and the unpaired t-test or Mann–Whitney U test for continuous variables, depending on distribution. Correlations between serum TSH and prolactin were assessed with Pearson's correlation test. A p-value <0.05 was considered statistically significant.

RESULTS

Table I: Demographic characteristics of the study subjects in two groups (n=100)

Demographic Characteristics		Case (n=50)	Control (n=50)	p-value
Age group	<20	3 (6.0)	1 (2.0)	0.083
	21–30	35 (70.0)	27 (54.0)	
	31–40	12 (24.0)	22 (44.0)	
	Mean \pm SD	27.94 \pm 4.28	29.66 \pm 4.27	0.097
Residence	Urban	33 (66.0)	38 (76.0)	0.27
	Rural	17 (34.0)	12 (24.0)	
Occupational Status	Housewife	29 (58.0)	24 (48.0)	0.654
	Service	13 (26.0)	12 (24.0)	
	Business	6 (12.0)	11 (22.0)	
	Labourer	2 (4.0)	3 (6.0)	
Educational Status	Primary	6 (12.0)	4 (8.0)	0.753
	Secondary	13 (26.0)	17 (34.0)	
	Higher Secondary	24 (48.0)	21 (42.0)	
	Graduate	7 (14.0)	8 (16.0)	

The age distribution showed more individuals aged 21-30 in the case group versus controls (70.0% vs. 54.0%), while those aged 31-40 were more prevalent in controls (44.0% vs. 24.0%). The mean age was 27.94 ± 4.28 years for cases and 29.66 ± 4.27 years for controls; the difference was not statistically significant ($p=0.097$).

Regarding residence, no significant association existed between groups ($p>0.05$). Most female participants had completed HSC examination (Case=48% vs Control=42%). The maximum females were housewife (Case=58% vs Control=48%).

Table II: Comparison of BMI between two groups (n=100)

BMI (kg/m ²)	Case (n=50)	Control (n=50)	p-value
18.5–24.9	16 (32.0)	26 (52.0)	0.132
25.0–29.9	19 (38.0)	13 (26.0)	
≥ 30.0	15 (30.0)	11 (22.0)	
Mean \pm SD	27.8 \pm 4.14	26.5 \pm 4.48	

BMI comparison showed most women in the case groups were overweight (25-29.9 kg/m²), while controls fell within a healthy range (18.5-24.9). Mean

BMI was higher in cases than controls, though not statistically significant ($p=0.132$).

Table III: Comparison of menstrual history between two groups (n=100)

Menstrual history		Case (n=50)	Control (n=50)	p-value
Menstrual cycle	Cyclical	29(58.0)	36(72.0)	0.142
	Acyclical	21(42.0)	14(28.0)	
Menorrhagia	No	42(84.0)	39(78.0)	0.444
	Yes	8(16.0)	11(22.0)	
Oligomenorrhoea	No	37(74.0)	43(86.0)	0.134
	Yes	13(26.0)	7(14.0)	

Table III shows the comparison of menstrual history between the two study groups. For menstrual history, more women in the control group had cyclical cycles (72.0%) compared to the cases (58.0%), with no significant difference ($p = 0.142$). Regarding

menorrhagia, no significant difference existed between groups ($p=0.444$). For oligomenorrhoea, more women in the case group (26.0%) experienced it compared to controls (14.0%), though not statistically significant ($p=0.134$).

Table IV: Comparison of clinical examination between two groups (n=100)

Clinical examination		Case (n=50)	Control (n=50)	p-value
Appearance	Normal	48(96.0)	49(98.0)	0.558
	Hypothyroid	2(4.0)	1(2.0)	
Galactorrhoea		6(12.0)	2(4.0)	0.14
Cold intolerance		2(4.0)	1(2.0)	0.557
Anovulation		12(24.0)	4(8.0)	0.029

Table IV shows the clinical examination findings between groups. Most women in both groups had a normal appearance (96.0% case group, 98.0% control group), with no significant difference ($p=0.558$). Galactorrhea was reported by 12.0% in the case group and 4.0% in the control group, showing no significant

difference ($p=0.140$). Cold intolerance occurred in 4.0% of the case group and 2% of the control group, with no significant difference ($p=0.557$). Anovulation was more prevalent in the case group (24.0%) versus the control group (8.0%), showing statistical significance ($p=0.029$).

Table V: Comparison of clinical examination between two groups (n=100)

Parameter	Case (Median; Mean \pm SD)	Control (Median; Mean \pm SD)	p-value
TSH (μ IU/mL)	3.50; 4.92 \pm 5.35	2.95; 3.83 \pm 6.04	0.041
FT3 (pmol/L)	2.65; 2.77 \pm 0.98	2.84; 3.10 \pm 1.25	0.147
FT4 (pmol/L)	14.8; 5.45 \pm 3.44	16.85; 16.92 \pm 3.28	0.032
Prolactin (ng/mL)	22.2; 38.09 \pm 29.3	20.15; 22.27 \pm 12.59	0.005

Table V compares clinical examination results between groups. TSH levels were significantly higher in the case group, with a median of 3.50 versus 2.95 in controls ($p=0.041$). FT3 levels showed no significant difference between groups, with medians of 2.65 in the case group and 2.84 in controls ($p=0.147$). FT4 levels were significantly lower in the case group, median 14.8 versus 16.85 in controls ($p=0.032$). Prolactin levels were significantly higher in the case group, median 22.2 versus 20.15 in controls ($p=0.005$).

DISCUSSION

This study examined the association between thyroid dysfunction, hyperprolactinemia, and menstrual irregularities in subfertile women. The findings revealed that women with subfertility had higher rates of oligomenorrhea, galactorrhea, and anovulation than fertile controls. These clinical manifestations were supported by biochemical abnormalities, including elevated serum TSH and prolactin levels and reduced FT4 concentrations. Together, these results emphasize the importance of thyroid and prolactin assessment in women with subfertility, particularly when menstrual disturbances are present.

In this study, the mean age in the case group was 27.94 ± 4.28 and the mean age in the control group was 29.66 ± 4.27 , which was lower than control. This was in accordance with other studies like Nargis *et al.*, who reported a mean age of in the primary subfertile group 26.52 ± 3.12 and the mean age at control was 27.13 ± 2.31 [13]. Another study by Lal *et al.*, with an age of 27.5 ± 3 in primary subfertile group and age of the control group was 23.52 ± 2.48 [14]. In contrast, another study conducted in Pakistan by Rahman *et al.*, found a mean age of the case group of 27 ± 3.86 and the mean age of the control group was 30 ± 4.83 among their participants [15].

It was observed that weight gain was more pronounced in the case group, particularly in those with a BMI > 25 , in about 34 (68%) in the case group, than control who reported a more normal weight of 26(52%), which is consistent with findings from previous research conducted by Deeba *et al.*, [16]. Socio-demographic

variables such as occupation, residence, align with the findings of a study conducted by Chowdhury *et al.*, which was based on the Bangladeshi population [11]. This similarity in results underscores the relevance and consistency of our findings within the context of the local population.

Oligomenorrhoea was observed more frequently among subfertile women (26.0%) than in controls (14.0%). This aligns with reports that hypothyroidism and hyperprolactinemia interfere with gonadotropin secretion, impair ovulatory function, and prolong menstrual cycles [17]. Goswami *et al.*, also reported that oligomenorrhoea and amenorrhoea were significantly more common among women with thyroid dysfunction and hyperprolactinemia [18]. Although menorrhagia was not significantly different between groups in the present study, prior research has shown that hypothyroidism may contribute to menorrhagia due to altered estrogen metabolism and coagulation factor disturbances [3].

Anovulation was another significant finding in this study, occurring in 24.0% of subfertile women compared to 8.0% of controls ($p=0.029$). This supports the notion that thyroid dysfunction and hyperprolactinemia directly impair ovulatory mechanisms. Hyperprolactinemia, in particular, disrupts gonadotropin-releasing hormone pulsatility, which reduces luteinizing hormone secretion and may cause luteal phase defects [4]. In agreement, Kumkum *et al.*, reported that nearly half of infertile women with endocrine dysfunction experienced anovulatory cycles [19].

The biochemical results further reinforced these clinical patterns. Subfertile women showed significantly higher serum TSH levels and lower FT4 values, pointing to a higher prevalence of both overt and subclinical hypothyroidism in this group. Similar findings were reported by Sharma *et al.*, who noted that thyroid dysfunction—particularly subclinical hypothyroidism—was more common among infertile women [20]. In addition, prolactin levels were significantly elevated in the case group (mean 38.09 ng/mL vs. 22.27 ng/mL in controls, $p=0.005$). Hyperprolactinemia was detected in

32% of cases compared with 10% of controls, reinforcing its role in disrupting ovarian steroidogenesis and menstrual cycle regularity [9]. Nath *et al.*, likewise identified elevated prolactin levels in infertile women and demonstrated a positive correlation between prolactin and TSH [10].

The present study also noted a trend toward increased galactorrhoea in the subfertile group (12.0% vs. 4.0%), although the difference was not statistically significant. Galactorrhoea is a classical manifestation of hyperprolactinemia and its occurrence here further supports the pathogenic role of prolactin excess in menstrual dysfunction. Comparable frequencies of galactorrhoea have been reported in South Asian populations, highlighting a consistent clinical association [11].

Taken together, these findings underline the intertwined effects of thyroid dysfunction and hyperprolactinemia on menstrual irregularities in subfertile women. Thyroid hormone abnormalities can alter estrogen and androgen metabolism, lower sex hormone-binding globulin levels, and provoke hyperprolactinemia through thyrotropin-releasing hormone pathways [5]. Elevated prolactin levels further suppress ovarian cyclicity, contributing to oligomenorrhea, amenorrhea, and anovulation. This bidirectional relationship creates a high-risk hormonal profile for menstrual disorders and infertility.

From a clinical perspective, these results have important implications for patient care. In low-resource settings, where access to advanced fertility treatments is limited, the identification and correction of reversible hormonal abnormalities is essential. Screening for thyroid dysfunction and hyperprolactinemia in subfertile women with irregular cycles may enable timely interventions, such as thyroid hormone replacement or dopamine agonist therapy, which can restore fertility without invasive procedures.

Limitations of the study

This study was limited by its single-center design and relatively modest sample size, which may restrict the generalizability of findings. The cross-sectional nature also precludes establishing causality. Additionally, the study excluded women with polycystic ovarian syndrome, a common cause of menstrual irregularity, which may have narrowed the spectrum of findings.

CONCLUSION

Thyroid dysfunction and hyperprolactinemia were significantly associated with menstrual irregularities in subfertile women. Elevated TSH and prolactin levels, along with reduced FT4 levels, were associated with acyclicity, oligomenorrhea, and anovulation. These findings emphasize the need for routine thyroid and prolactin screening in subfertile

women presenting with abnormal cycles, as the correction of these endocrine disorders may restore reproductive function and reduce the burden of infertility.

Acknowledgment

I would like to express my sincere gratitude for the invaluable support and cooperation provided by the staff, participants, and my co-authors/colleagues who contributed to this study.

Conflicts of interest: There are no conflicts of interest.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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