Impact of subclinical hypothyroidism on clinical, hormonal, and metabolic parameters in women with polycystic ovary syndrome: the role of levothyroxine therapy

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Abstract

Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder in women of reproductive age, often associated with metabolic abnormalities. Subclinical Hypothyroidism (SCH) frequently coexists in women with PCOS; however, its clinical and metabolic implications remain inadequately defined. This study aimed to determine the prevalence of SCH in women with PCOS and assess its impact on clinical, hormonal, and metabolic parameters, as well as the potential benefits of levothyroxine therapy. A cross-sectional study was conducted at Azadi Teaching Hospital in Duhok, Iraq, involving 139 women diagnosed with PCOS. Participants were categorised into three groups: euthyroid (n = 95), untreated SCH (n = 24), and treated SCH (n = 20). Clinical features and biochemical markers, including Fasting Blood Sugar (FBS), lipid profile, reproductive hormones, and blood pressure, were evaluated. SCH was identified in 31.7% of participants. The untreated SCH group had a lower median FBS (90.5 mg/dL) than the euthyroid group (92 mg/dL), with a further reduction in the treated group (86.5 mg/dL). Subfertility was most prevalent in the euthyroid group (56.7%) compared to the treated (30.0%) and untreated (13.3%) SCH groups ($p = 0.025$). Acne was significantly more common in the euthyroid group (71.1%) than in the untreated (20.6%) and treated (8.2%) groups ($p = 0.004$). Diastolic blood pressure (DBP) was highest in the treated SCH group (80.5 mmHg; $p = 0.002$), and a weak but significant correlation was observed between Thyroid-Stimulating Hormone (TSH) and DBP ($\rho = 0.231$, $p = 0.006$). These findings suggest that SCH is prevalent among women with PCOS, and levothyroxine therapy may contribute to improved clinical and metabolic outcomes.

Introduction

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder affecting women in the reproductive age, with a global prevalence estimated at 15–20%.[1] It is characterised by various hormonal imbalances, most notably a persistent elevation in Luteinizing Hormone (LH) secretion. A hallmark feature of PCOS is hyperandrogenism, resulting from dysregulation of both ovarian and adrenal androgen production. This androgen excess contributes to many of the clinical manifestations of PCOS, including hirsutism, acne, and ovulatory dysfunction. This hormonal disturbance is often worsened by obesity and reduced levels of Sex Hormone-Binding Globulin (SHBG), leading to an increase in the availability of circulating androgens. Clinically, PCOS presents with a spectrum of symptoms, including menstrual irregularities, infertility, hirsutism (excess hair growth in a male pattern), and acanthosis nigricans, a skin condition marked by dark, velvety patches, especially

in body folds.[2] The diagnosis of PCOS is based on the Rotterdam criteria, which require the presence of at least two out of the following three features: clinical and/or biochemical signs of hyperandrogenism, oligo or anovulation, and polycystic ovarian morphology on ultrasound after exclusion secondary causes such as thyroid dysfunction, hyperprolactinemia, Cushing's syndrome and congenital adrenal hyperplasia.[3]

PCOS is closely linked to metabolic syndrome, featuring central obesity, Insulin Resistance (IR), dyslipidemia, hypertension, and an elevated risk of cardiovascular disease and type 2 diabetes. Even in PCOS patients with a normal Body Mass Index (BMI), IR is present due to a post-receptor defect in insulin signalling, affecting the ovaries and peripheral tissues. [4]

Recent research suggests a significant overlap between hypothyroidism and PCOS, as both share common features like IR and dyslipidemia. Subclinical Hypothyroidism (SCH), which is characterised by elevated Thyroid-Stimulating Hormone (TSH) levels and normal Free Thyroxine (FT4), is the most common thyroid dysfunction among PCOS patients, with a prevalence of 11–43.6%.[5,6] Thyroid hormones are critical regulators of metabolic processes, influencing glycemic control and lipid metabolism. Centrally, triiodothyronine (T3) modulates hepatic glucose synthesis through the sympathetic nervous system. Peripherally, thyroid hormones enhance glucose transporter type 4 (GLUT-4) expression in skeletal muscle, increasing insulin-dependent glucose uptake. They also regulate lipid synthesis, metabolism, and degradation by modulating gene expression.[7,8]

SCH in PCOS is associated with weight gain, IR, hyperlipidemia, and exacerbation of hyperandrogenism due to increased testosterone and prolactin levels, along with decreased SHBG levels.[9,10] This complex interplay between thyroid dysfunction and PCOS has significant implications for metabolic and reproductive health, underscoring the importance of understanding their overlap. This study aimed to evaluate the prevalence of SCH in women with PCOS, examine the clinical, hormonal, and metabolic characteristics of PCOS patients concerning SCH, and explore the impact of levothyroxine therapy on improving these parameters.

Materials and Methods

This cross-sectional study was conducted in the Gynecology Department of Azadi Teaching Hospital, Duhok, Kurdistan Region, Iraq, between October 1, 2024, and January 1, 2025. Ethical approval was obtained from the relevant ethics committee (Reference number: 25092024-8-17), and written informed consent was secured from all participants before enrolment. The required sample size was calculated using a standard formula for cross-sectional studies ($n = Z^2pq/d^2$), assuming a 95% confidence level ($Z = 1.96$), a 5% margin of error ($d = 0.05$), and an estimated prevalence (p) of thyroid disorders in women with PCOS of 26.9%, based on previous literature.[11] This yielded a target sample size of approximately 302 participants. However, due to the study's single-centre design and time limitations, a total of 139 women were included in the final analysis. These participants, aged 14 to 40 years, were diagnosed with PCOS based on the 2003 Rotterdam criteria established by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM).[3] The diagnosis required the presence of at least two out of the following three features: i) oligo- or anovulation, indicated by menstrual cycles exceeding 35 days or the absence of menstruation for three months or longer; ii) clinical or biochemical signs of hyperandrogenism; and iii) polycystic ovarian morphology detected by ultrasound. To assess hyperandrogenism, both clinical and biochemical markers were evaluated. Clinical hyperandrogenism was assessed through the evaluation of hirsutism and acne, based on both patient history and clinical examination. Due to variability in the application of the Ferriman-Gallwey scoring system,[12,13] hirsutism was recorded as a binary variable (present or absent). It was identified through self-reported excessive terminal hair growth in androgen-sensitive regions, such as the upper lip, chin, chest, lower abdomen, thighs, and back, and confirmed by clinical observation. Acne was also considered a clinical sign of hyperandrogenism and was evaluated by identifying inflammatory lesions (papules, pustules, and nodules), primarily on the face but also in other androgen-responsive areas, including the neck, chest, shoulders, upper arms, and back. Biochemical hyperandrogenism was determined by measuring total testosterone levels, with a diagnostic cutoff value set at 0.73 ng/mL. Pelvic ultrasound was employed to determine the presence of polycystic ovarian morphology, which constitutes one of the diagnostic criteria for PCOS. In consideration of cultural sensitivities and ethical standards, a transabdominal ultrasonographic approach was used for most participants. However, for married women who gave informed consent, transvaginal ultrasonography was performed to obtain higher-resolution images. All scans were conducted using the Samsung HS30 ultrasound system (Samsung Medison Co., Ltd., Seongnam, South Korea). Ovarian morphology was classified as polycystic if more than 10 subcapsular follicles measuring 2–8 mm were observed, along with increased stromal echogenicity. According to thyroid function and treatment status, the participants were classified into three distinct groups. The largest group consisted of 95 women with PCOS and normal thyroid function (euthyroid), confirmed by TSH and FT4 levels within the reference range of 0.3–3.6 mIU/L, as established by the Central Public Health Laboratory in Duhok, Iraq. A second group included 24 women with PCOS who exhibited SCH, indicated by elevated TSH levels above 3.6 mIU/L with normal FT4 concentrations and no thyroid treatment. The third group comprised 20 women with PCOS and SCH who were receiving levothyroxine therapy and had achieved normalized TSH levels through treatment.

Sociodemographic data were collected through structured interviews and included age, marital status, place of residence, occupation, and family history of PCOS or SCH, as presented in Table 1. Height and weight were measured to calculate BMI (kg/m²), and blood pressure was recorded after a five-minute rest. Women with

Table 1. Sociodemographic characteristics of participants.

Variable	Category	Frequency (%)
Residence	Rural	49 (35.3)
	Urban	90 (64.7)
Occupation	Employed	23 (16.5)
	Student	43 (30.9)
	Unemployed	73 (52.5)
Marital state	Married	42 (30.2)
	Single	97 (69.8)
Family history of PCOS	No	71 (51.1)
	Yes	68 (48.9)
Family history of TD	No	91 (65.5)
	Yes	48 (34.5)
Group classification	Euthyroid PCOS	95 (68.3)
	Treated SCH PCOS	20 (14.4)
	Untreated SCH PCOS	24 (17.3)

PCOS, polycystic ovary syndrome; SCH, subclinical hypothyroidism; TD, thyroid disorder.

diabetes mellitus, other thyroid disorders, Cushing's syndrome, congenital adrenal hyperplasia, autoimmune or chronic inflammatory diseases, or those who had used hormonal therapies, ovulation induction agents, anti-androgens, or lipid-lowering medications within the past three months were excluded from the study. A non-probability consecutive sampling technique was used to recruit eligible participants.

Laboratory analysis

Blood samples were collected during the early follicular phase of the menstrual cycle (on the 2nd or 3rd day) in women with regular cycles; for amenorrheic women, samples were taken on the 2nd or 3rd day of induced withdrawal bleeding, initiated with oral progestin (norethisterone, 5 mg tablets) administered twice daily for 5 days. All participants underwent a 12-hour fasting period before sample collection. A total of 8 mL of blood was drawn aseptically from the cubital vein using phlebotomy. Blood samples were collected in plain gel tubes, allowed to clot at room temperature for 30 minutes, and subsequently centrifuged at 3,000 rpm for 10 minutes at 4°C to separate the serum. Hormonal analyses, including measurements of follicle-stimulating hormone (FSH; reference range 3.5–9.2 mIU/mL in the follicular phase), luteinizing hormone (LH; 2.4–12.6 mIU/mL during the follicular phase), prolactin (6.2–23.4 ng/mL in women of reproductive age), total testosterone (0.05–0.73 ng/mL), thyroid-stimulating hormone (TSH; 0.300–3.600 mIU/L), and free thyroxine (FT4; 10–20.4 pmol/L), were conducted using the fully automated LIAISON® chemiluminescence immunoassay system (DiaSorin S.p.A., Saluggia, Italy). Metabolic markers such as fasting blood sugar (FBS; reference range 74–99 mg/dL), total cholesterol (TC; 120–200 mg/dL), triglycerides (TG; 35–150 mg/dL), high-density lipoprotein cholesterol (HDL-C; 40–60 mg/dL), and low-density lipoprotein cholesterol (LDL-C; 50–100 mg/dL) were quantified with the Roche 6000 analyser's Cobas c 501 module (Roche Diagnostics, Mannheim, Germany).

Statistical analysis

The recorded data were analysed using SPSS (version 30.0) and Microsoft Excel. The Shapiro-Wilk test was employed to assess the normality of continuous variables. Results were expressed as mean ± Standard Deviation (SD) for normally distributed data and median and Interquartile Range (IQR) for non-normally distributed data. Group comparisons were performed using one-way ANOVA for normally distributed variables and the Kruskal-Wallis H test for non-parametric variables. Post-hoc analysis was conducted using the Tukey HSD test for normally distributed variables and the Dunn-Bonferroni test for non-parametric variables. Categorical variables were analysed using Chi-square tests. A p value < 0.05 was considered statistically significant. For correlation analysis, Spearman's rank correlation or Pearson's correlation tests were applied depending on the distribution of the variables.

Results

When examining anthropometric and vital parameters, no significant differences were found in BMI, systolic blood pressure (SBP), or pulse rate between the groups. However, a notable difference emerged in DBP, as the treated SCH PCOS group exhibited the highest median DBP (80.5 mmHg, IQR: 78.25–85.25), compared to the untreated SCH-PCOS (77 mmHg, IQR: 71–81) and euthyroid PCOS (73 mmHg, IQR: 64–78) groups, which was statistically significant (p = 0.002) (Table 2); despite this difference, all values remained within the normal reference range. The untreated SCH-PCOS group exhibited the highest median TSH levels (4.74 mIU/L, IQR: 4.03–6.70), followed by the treated SCH-PCOS group (2.57 mIU/L, IQR: 2.30–3.18) and the euthyroid PCOS group (1.95 mIU/L, IQR: 1.43–2.48) (p < 0.001) (Table 3). FT4 levels, however, were comparable in all groups and did not differ significantly (Figure 1).

The levels of hormonal markers, including LH, FSH, and prolactin, showed no significant differences among the groups (p = 0.544, 0.488, and 0.238, respectively). Similarly, testosterone levels did not differ significantly between the groups (p = 0.133). Regarding metabolic markers, the study found a significant difference in FBS levels across the study groups (p = 0.042). The lowest median FBS levels were observed in the treated SCH-PCOS group (86.5 mg/dL, IQR: 79–92), followed by the untreated SCH-PCOS group (90.5 mg/dL, IQR: 85.25–96.75), while the euthyroid PCOS group exhibited the highest levels (92 mg/dL, IQR: 86–99). As for lipid levels, no significant differences were observed among the groups. TG levels were similar (p = 0.771), as were HDL-C (p = 0.190), LDL-C (p = 0.348), and TC levels (p = 0.535) (Table 3). Furthermore, correlation analysis (Table 4) revealed a significant positive association between TSH and DBP (ρ = 0.231, p = 0.006), whereas no significant correlations were observed between TSH and other clinical, hormonal, or metabolic variables.

When it came to clinical features, significant differences were found in subfertility and acne. Subfertility was notably more common in the euthyroid PCOS group, with 56.7% of women reporting difficulty in conceiving, compared to 30.0% in the treated SCH-PCOS group and only 13.3% in the untreated SCH-PCOS group (p = 0.025). Similarly, acne was significantly more prevalent in the euthyroid PCOS group (71.1%), the untreated SCH-PCOS group had a lower prevalence (20.6%), while the treated SCH-PCOS group exhibited the lowest rate of acne (8.2%), indicating a statistically significant difference (p = 0.004). In contrast, no significant differ-

Table 2. Comparison of anthropometric and vital parameters among study groups.

Variable	Euthyroid PCOS	Treated SCH PCOS	Untreated SCH PCOS	p value
BMI (kg/m²)	27.93±5.24	26.37±4.16	28.74±5.91	0.243
PR (bpm)	87.69±13.36	87.10±10.82	85.83±10.21	0.761
SBP (mmHg)	114 (103-123)	119.50 (113.25-124.75)	112.50 (103-122.75)	0.315
DBP (mmHg)	73 (64-78)	80.5 (78.25-85.25)	77 (71-81)	0.002*

Variables are presented as mean±SD for BMI and PR (analysed by ANOVA) or as median (IQR) for non-normal data (analysed by Kruskal–Wallis). A p value <0.05 indicates statistical significance. *Post hoc significant difference was found between euthyroid PCOS and treated SCH PCOS, but no significant differences were found between the other group pairs (euthyroid PCOS vs. untreated SCH-PCOS, and untreated SCH-PCOS vs. treated SCH-PCOS) after adjusting for multiple tests.
PCOS, polycystic ovary syndrome; SCH, subclinical hypothyroidism; BMI, body mass index; PR, pulse rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; bpm, beats per minute; mmHg, millimetres of mercury.

ences were found in the prevalence of hirsutism, as the majority of women across all groups reported having this condition. Cycle patterns also showed no significant variation, with similar proportions of women experiencing amenorrhea, oligomenorrhea, and regular cycles across the groups (p = 0.353) (Table 5).

Discussion

This study revealed a 31.7% prevalence of SCH among women with PCOS, underscoring a significant co-occurrence of these endocrine disorders. Notably, this prevalence exceeds that reported in other regions; For instance, Sinha *et al.* reported in India a prevalence of 22.5%,[14] Yu and Wang in China observed 27.0%,[15] and Enzevaei *et al.* in Iran documented 25.5%.[16] A notably lower prevalence of 11.3% was reported by Benetti-Pinto *et al.* in Brazil.[5]

Despite their distinct diagnostic criteria, thyroid dysfunction and PCOS share overlapping clinical manifestations, including menstrual irregularities, infertility, obesity, dyslipidemia, and an increased risk of spontaneous abortion.[17,18] Such overlap complicates clinical evaluation and may lead to underdiagnosis of one condition when the other is present. Hypothyroidism, particularly in its subclinical form, may mimic or exacerbate PCOS symptoms by promoting IR and contributing to ovarian dysfunction. Thyroid disorders, especially SCH, are more prevalent in women with PCOS compared to healthy, age-matched controls.[18] This suggests a possible pathophysiological link, potentially involving shared genetic susceptibilities or environmental triggers; however, the exact mechanisms underlying this association remain poorly

Table 3. Analysis of metabolic and hormonal profiles among the study groups.

Variable	Euthyroid PCOS	Treated SCH PCOS	Untreated SCH PCOS	p value
LH (mIU/mL)	5.44 (3.52-9.78)	5.82 (3.34-10)	7.82 (4.63-10.34)	0.544
FSH (mIU/mL)	6.17 (4.75-7.09)	6.72 (5.17-8.14)	5.91 (5.17-7.34)	0.488
Prolactin (ng/mL)	20.00 (14.53-26.75)	22.48 (15.21-32.73)	24.15 (18.02-30.84)	0.238
Testosterone (ng/mL)	0.35 (0.26-0.52)	0.28 (0.07-0.50)	0.34 (0.17-0.54)	0.133
FBS (mg/dL)	92 (86-99)	86.5 (79-92)	90.5 (85.25-96.75)	0.042*
TSH (mIU/L)	1.95 (1.43-2.48)	2.57 (2.30-3.18)	4.74 (4.03-6.70)	<0.001
FT4 (pmol/L)	16.30 (14.5-18.4)	15.15 (14.50-19.25)	15.85 (14.88-18.18)	0.989
TG (mg/dL)	97 (77-136)	95.5 (67-132.25)	98 (83.75-144.00)	0.771
HDL-C (mg/dL)	44 (41-54)	49.5 (45-55)	48.7 (43.15-62)	0.190
LDL-C (mg/dL)	100 (82-117)	93.4 (79-101.25)	103 (87-121)	0.348
TC (mg/dL)	167.31±32.54	160.14±25.09	167.42±30.57	0.535

Variables are presented as median (IQR) for non-normal data (analysed using the Kruskal–Wallis test) or as mean±SD for TC (analysed using ANOVA). A p value <0.05 indicates statistical significance. *Post hoc significant difference was found between treated SCH-PCOS and euthyroid PCOS. No significant differences were observed between treated SCH PCOS and untreated SCH-PCOS, or between untreated SCH-PCOS and euthyroid PCOS after adjusting for multiple comparisons.
PCOS, polycystic ovary syndrome; SCH, subclinical hypothyroidism; FBS, fasting blood sugar; TSH, thyroid-stimulating hormone; FT4, free thyroxine; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

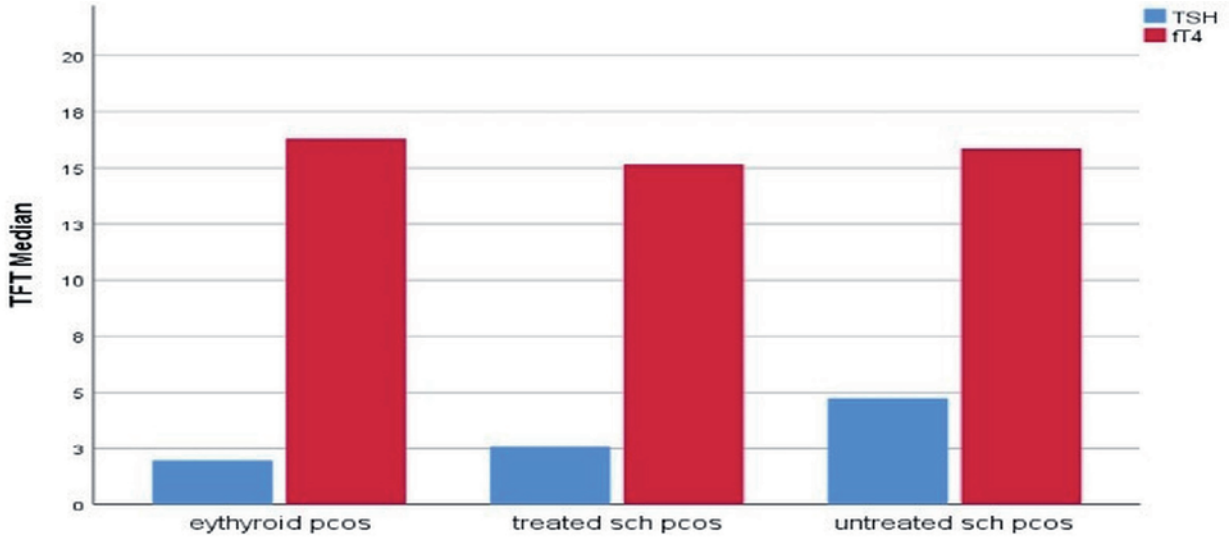

Figure 1. Median Thyroid Function Test (TFT) parameters among PCOS Groups. Comparison of median serum thyroid-stimulating hormone (TSH, blue bars) and free thyroxine (FT4, red bars) levels among women with euthyroid polycystic ovary syndrome (PCOS), treated subclinical hypothyroidism (SCH), and untreated SCH.

understood. This underscores the importance of evaluating thyroid function in this population.[14] In regions like Kurdistan, which is endemic for goiter due to iodine-depleted soil resulting from mountainous terrain and heavy rainfall, iodine deficiency may significantly contribute to the elevated SCH prevalence.[19] Supporting this, Zaman *et al.* found SCH to be the most common thyroid disorder in Duhok, accounting for 94.85% of cases. [20]

Elevated TSH has been shown to stimulate ovarian theca cells to produce excess androgens, thereby aggravating the clinical features of PCOS,[21] a pattern also observed among SCH-PCOS patients in the present study. Consistently elevated TSH levels have been reported in untreated SCH-PCOS individuals across various studies.[22,23] Although levothyroxine therapy is known to reduce TSH concentrations, the degree of reduction appears to vary among different investigations.[22,23] In the current study, treated patients exhibited a decline in TSH levels, but post-treatment values remained higher compared to those reported by Kowalczyk *et al.* and Trummer *et al.*[22,23] These discrepancies may be attributed to variations in levothyroxine dosage, treatment duration, and TSH reference ranges or threshold values used for classification. Furthermore, the ideal TSH cutoff value for defining SCH in PCOS patients remains a subject of ongoing debate.

PCOS is among the most common conditions impacting women in the reproductive age.[24] In this study, the median age of the study population was 24 years, reflecting the typically young age range impacted by this condition. The current study found no significant differences in BMI among women with SCH-PCOS, including those treated with levothyroxine, and those with normal thyroid function, although the treated group exhibited the lowest mean BMI. These findings align with previous studies by Yu and Wang,[15] Benetti-Pinto *et al.*,[5,] and Enzevaei *et al.*,[16,] which reported no substantial BMI differences between SCH-PCOS and euthyroid-PCOS groups. In contrast, Kowalczyk *et al.* found that women with compensated hypothyroidism receiving levothyroxine had significantly higher BMI compared to controls.[22]

SCH has been linked to alterations in blood pressure, as demonstrated by a study reporting increases in both systolic and diastolic values.[14] Similarly, hypertension is more common among women with PCOS, suggesting that SCH may further contribute to elevated blood pressure in PCOS patients.[25] However, research findings remain inconsistent, as other studies have reported no significant differences in blood pressure between PCOS patients with and without SCH.[5,26]

Our study found no significant differences in SBP among the groups. However, DBP was significantly higher in the treated SCH-PCOS group compared to both the euthyroid PCOS and untreated SCH-PCOS groups, though it remained within the normal range. Additionally, PCOS women receiving thyroid replacement therapy had higher TSH levels than euthyroid women, suggesting that levothyroxine dosing may have been insufficient to fully restore thyroid function. While Trummer *et al.*[23] reported an increase in SBP

Table 4. Correlation of clinical, metabolic, and hormonal parameters with TSH

Correlation Variable		TSH
SBP (mmHg)	ρ	0.044
	P	0.610
DBP (mmHg)	ρ	0.231*
	P	0.006
LH (mIU/mL)	ρ	0.069
	P	0.422
FSH (mIU/mL)	ρ	-0.037
	P	0.665
Prolactin (ng/mL)	ρ	0.135
	P	0.113
Testosterone (ng/mL)	ρ	0.002
	P	0.983
FBS (mg/dL)	ρ	-0.068
	P	0.426
TG (mg/dL)	ρ	0.055
	P	0.517
HDL-C (mg/dL)	ρ	0.097
	P	0.255
LDL-C (mg/dL)	ρ	0.036
	P	0.677
TC (mg/dL)	r	0.048
	P	0.578
PR (bpm)	r	0.040
	P	0.641
BMI (kg/m²)	r	0.086
	P	0.578

This table presents the Spearman's correlation coefficients (ρ) and p values (P) for the relationship between TSH, thyroid stimulating hormone, levels and several clinical, hormonal, and metabolic factors, including SBP, systolic blood pressure; DBP, diastolic blood pressure; LH, luteinizing hormone; FSH, follicle-stimulating hormon; PRL, prolactin; T, Testosterone; FBS, fasting blood sugar; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; PR, pulse rate; BMI, body mass index. Statistically significant correlations (p <0.05) are marked with an asterisk (*).

Table 5. Analysis of clinical features and reproductive characteristics among study groups.

Variable	Category	Euthyroid PCOS	Treated SCH PCOS	Untreated SCH PCOS	p value
Subfertility*	No	78 (71.6)	11 (10.1)	20 (18.3)	0.025
	Yes	17 (56.7)	9 (30.0)	4 (13.3)	
Hirsutism	No	11 (100)	0 (0.0)	0 (0.0)	0.066
	Yes	84 (65.6)	20 (15.6)	24 (18.8)	
Acne	No	26 (61.9)	12 (28.6)	4 (9.5)	0.004
	Yes	69 (71.1)	8 (8.2)	20 (20.6)	
Cycle pattern	Amenorrhea	37 (69.8)	5 (9.4)	11 (20.8)	0.353
	Oligomenorrhea	45 (70.3)	9 (14.1)	10 (15.6)	
	Regular	13 (59.1)	6 (27.3)	3 (13.6)	

Categorical variables are presented as frequency (percentage) and analysed using the Chi-Square test. A p value <0.05 indicates statistical significance. *Subfertility was defined as the inability to conceive after one year of regular, unprotected intercourse, despite a normal semen analysis for the husband. PCOS, polycystic ovary syndrome; SCH, subclinical hypothyroidism.

among women on thyroid replacement therapy, our findings suggest a greater effect on DBP, indicating potential differences in blood pressure regulation related to treatment response. Although we observed a weak but statistically significant correlation between TSH and DBP ($\rho = 0.231$, $p = 0.006$), this suggests that thyroid dysfunction has only a minor impact on blood pressure regulation.

Kamrul-Hasan *et al.* reported no significant difference in subfertility rates between SCH-PCOS and euthyroid-PCOS groups.[27] However, the present study found subfertility to be significantly more common in the euthyroid PCOS group, with over half of the participants experiencing difficulty conceiving. In comparison, subfertility was less prevalent among women in the treated SCH-PCOS group, suggesting that levothyroxine therapy may enhance thyroid function and improve reproductive outcomes.

Menstrual cycle patterns in the SCH-PCOS and euthyroid-PCOS groups were comparable and consistent with those by Kamrul-Hasan *et al.*[27] Similarly, hirsutism prevalence showed no significant differences between the groups, which is consistent with the studies by Yu and Wang,[15] Benetti-Pinto *et al.*, [5] and Enzevaei *et al.*[16] also reported no discernible differences in hirsutism prevalence between SCH-PCOS and euthyroid-PCOS groups. Unlike other clinical features, acne prevalence varied notably across the study groups. It was highest in the euthyroid PCOS group, less common in the untreated SCH-PCOS group, and lowest in the SCH-PCOS undergoing levothyroxine treatment. This pattern contrasts with the findings reported by Freitas De-Medeiros *et al.*[12] who found a higher prevalence of acne in women with SCH-PCOS compared to those with PCOS alone. The observed downward trend in acne prevalence with levothyroxine treatment in the current study may indicate a potential therapeutic benefit of correcting thyroid dysfunction in reducing acne among women with SCH. Our study, consistent with Ganie *et al.* findings,[28] did not reveal significant differences in LH, FSH, testosterone, or prolactin levels between SCH-PCOS and euthyroid-PCOS groups. However, Enzevaei *et al.* observed significantly higher free testosterone levels in SCH-PCOS patients compared to euthyroid PCOS patients.[16] Additionally, Benetti-Pinto *et al.* found higher prolactin levels in women with SCH and PCOS.[5] Our study found no significant difference in FBS levels between the untreated SCH-PCOS and euthyroid PCOS groups, which aligns with previous studies by Kamrul-Hasan *et al.*,[27] Freitas De-Medeiros *et al.*,[12] and Fatima *et al.*,[29] where similar FBS levels were reported across study groups. Our study also found that levothyroxine treatment in SCH-PCOS patients led to significantly lower FBS levels compared to euthyroid PCOS, consistent with Kowalska *et al.*,[30] suggesting that thyroid hormone replacement may improve glucose regulation in these patients. However, we did not observe a significant correlation between TSH and FBS, which contrasts with Bedaiwy *et al.*[31] Both PCOS and SCH have been linked to lipid metabolism disturbances, including elevated triglycerides, decreased HDL-C, and increased LDL-C and non-HDL cholesterol, independent of BMI.[32–34] However, our study did not reveal significant differences in lipid profiles between SCH-PCOS patients, whether treated with levothyroxine or untreated, and euthyroid women. Although the treated SCH-PCOS group exhibited the lowest LDL-C levels and the untreated group had the highest, these variations were not statistically significant ($p = 0.348$). This aligns with Brenta *et al.*[35] and Bedaiwy *et al.*,[31] who similarly reported no significant lipid abnormalities in SCH-PCOS. A meta-analysis by Li *et al.* found modest reductions in total cholesterol and LDL-C following levothyroxine treatment, while HDL and triglyceride levels remained largely unchanged.[36] Similarly, Kowalczyk *et al.* observed slightly higher HDL in the treated SCH group.[22]

This study has several important strengths. It is among the very few investigations, only the third to our knowledge, that specifically examine the clinical and metabolic impact of SCH and levothyroxine therapy in women with PCOS. The study focused on a clearly defined population and applied rigorous biochemical and hormonal assessments to provide a comprehensive analysis of reproductive and metabolic parameters. By comparing euthyroid PCOS patients with both treated and untreated SCH-PCOS groups, it offers novel insights into how thyroid dysfunction and its management may influence PCOS manifestations.

While the study provides valuable contributions to a relatively underexplored area, some limitations should be acknowledged. The cross-sectional and single-centre design may limit generalizability and does not permit causal conclusions. A healthy control group was not included due to ethical considerations and resource limitations; however, this was consistent with the study's main objective, to assess variation among PCOS subgroups based on thyroid function. Additionally, data on thyroid autoantibodies and insulin resistance were not collected, which could have enhanced mechanistic understanding. Despite these constraints, the findings underscore the potential clinical relevance of routine thyroid function screening and the careful consideration of levothyroxine therapy in PCOS management. Future longitudinal studies with larger and more diverse populations are needed to validate and expand on these results.

Conclusions

This study demonstrates a high prevalence of SCH among women with PCOS, supporting the need for routine thyroid screening in this group. While SCH had no significant impact on lipid or sex hormone profiles, levothyroxine therapy improved fasting blood glucose and acne, suggesting some clinical benefits. Subfertility was more frequently observed in the euthyroid PCOS group, while levothyroxine was commonly administered to SCH-PCOS patients to support fertility, suggesting a possible therapeutic role in enhancing reproductive outcomes. However, persistent elevation in DBP despite treatment highlights the need for further research into the cardiovascular effects of SCH and its management.

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