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FREQUENCY AND CLINICAL CORRELATES OF THYROID DYSFUNCTION AND HYPERPROLACTINEMIA AMONG WOMEN EVALUATED FOR POLYCYSTIC OVARY SYNDROME: A RETROSPECTIVE STUDY

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ABSTRACT

Background: Polycystic ovary syndrome is a common endocrine disorder in women of reproductive age, but thyroid dysfunction and hyperprolactinemia may mimic or coexist with its clinical features and complicate diagnosis.
Objective: To determine the frequency and clinical correlates of thyroid dysfunction and hyperprolactinemia among women evaluated for polycystic ovary syndrome.
Methods: This cross-sectional analytical study was conducted at Fatima Memorial Hospital Lahore from March 2023 to March 2026, included 249 women undergoing evaluation for suspected PCOS. Demographic, anthropometric, reproductive, and clinical data were recorded. Thyroid function and serum prolactin levels were assessed, and participants were classified according to thyroid and prolactin status.
Results: The mean age of participants was 27.8 ± 5.9 years and mean BMI was 27.6 ± 4.8 kg/m². Thyroid dysfunction was present in 58 (23.3%) women, including subclinical hypothyroidism in 37 (14.9%), overt hypothyroidism in 14 (5.6%), and hyperthyroidism in 7 (2.8%). Hyperprolactinemia was detected in 37 (14.9%), while 14 (5.6%) had both abnormalities. Thyroid dysfunction was independently associated with age ≥30 years (aOR 1.81, 95% CI: 1.01–3.24), overweight/obesity (aOR 2.03, 95% CI: 1.08–3.82), infertility (aOR 1.92, 95% CI: 1.05–3.50), and weight gain (aOR 1.87, 95% CI: 1.01–3.45). Hyperprolactinemia was independently associated with amenorrhea (aOR 2.71, 95% CI: 1.27–5.78), infertility (aOR 2.26, 95% CI: 1.10–4.65), and menstrual irregularity (aOR 2.84, 95% CI: 1.02–7.89).
Conclusion: Thyroid dysfunction and hyperprolactinemia were relatively common among women evaluated for PCOS. Subclinical hypothyroidism was the predominant thyroid abnormality, while hyperprolactinemia was mainly associated with menstrual disturbance and infertility.

KEYWORDS: Polycystic ovary syndrome, Thyroid dysfunction, Subclinical hypothyroidism, Hyperprolactinemia

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous condition of women of reproductive age, associated with hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, and is one of the most common endocrine conditions [1]. With the current international definitions of PCOS, the prevalence of the condition is estimated at 10–13% of all women in the reproductive age group. Because of its clinical features, which can involve menstrual irregularity, infertility, hirsutism, acne, obesity, insulin resistance, and other metabolic dysregulations, it must be correctly identified for both reproductive and long-term health implications [2]. The diagnosis of PCOS is basically a diagnosis of exclusion since several other endocrinopathy conditions can present similar clinical symptoms. Thyroid dysfunction and hyperprolactinemia are significant because both can manifest as menstrual disturbances, anovulation, and alterations in reproductive hormone profiles, which can lead to infertility [3]. For this reason, the 2023 International Evidence-based Guideline suggests that thyroid-stimulating hormone and serum prolactin should be measured to rule out other causes of the diagnosis of PCOS. When these disorders are not recognised, patients might be misdiagnosed as having PCOS and treatment of underlying endocrine disorders may be delayed [4].
Thyroid dysfunction may contribute to changes in gonadotropin secretion, sex hormone-binding globulin levels, ovarian steroidogenesis and prolactin metabolism, which in turn may impact reproductive function [5]. Hence, hypothyroidism and especially subclinical hypothyroidism have been a subject of interest in women who have been assessed for PCOS. But there's conflicting published research on its link with PCOS. A recent study of women with PCOS versus controls found the overall rates of hypothyroidism, hyperthyroidism, thyrotrophin (TSI) antibody positivity, and hyperprolactinemia were similar for women with PCOS and controls, but subclinical hypothyroidism was more common in one type of PCOS [6]. In this study, the findings indicate that the thyroid abnormalities do not occur in all women with PCOS, but in clinically relevant subgroups. Another important differential diagnosis to

consider is hyperprolactinemia [7]. Oligomenorrhea or amenorrhea is another way elevated prolactin can manifest and influences the secretion of gonadotropin-releasing hormone from the hypothalamus, making the reproductive effects of elevated prolactin very similar to the effects of PCOS [8]. Hyperprolactinemia remains clinically important but is relatively uncommon and has recently been ignored as a possible cause for exclusion before a diagnosis of PCOS was made in these women, who were evaluated in population-based studies. Longstanding elevated prolactin levels can also be a response to drugs, hypothyroidism, pituitary disease, or other disorders that must be treated. Another significant differential diagnosis is hyperprolactinemia [9]. Hyperprolactinemia can hurt the production of gonadotropin-releasing hormone (GnRH) by the hypothalamus, resulting in ovarian irregularities (such as oligomenorrhea or amenorrhea) and resembling the reproductive symptoms of PCOS [10]. However, if prolactin remains elevated, this could also be a side effect of the drug, due to primary hypothyroidism, pituitary disease or other disorder that needs management. A transient elevation may occur with mild elevations, which are associated with stress, venipuncture, sleep, or physiological variation, or persistent elevations, which occur with clinically significant hyperprolactinemia, which should be further investigated [11]. Thus, proper evaluation of prolactin level is essential in women who are suspected of PCOS, to avoid mislabeling and inappropriate treatment otherwise. It can be complicated by thyroid disorders or hyperprolactinemia. In females with multiple endocrine disorders, the clinical picture may be more severe and include menstrual disorders, infertility, obesity, metabolic abnormalities, and other symptoms [12]. These associations may provide clues to the clinician that certain patients may warrant further endocrine evaluation. Other clinical features, including age, BMI, menstrual history, infertility, hirsutism, obesity, and other metabolic features, might also help suggest the likelihood of other endocrine disorders [13].

Objective

Therefore, the present study was conducted to determine the frequency and clinical correlates of thyroid dysfunction and hyperprolactinemia among women evaluated for polycystic ovary syndrome.

METHODOLOGY

This cross-sectional analytical study was conducted at Fatima Memorial Hospital Lahore from March 2023 to March 2026, included 249 women undergoing evaluation for suspected PCOS. Data collected were by non-probability consecutive sampling technique. Women between the ages of 18 to 45 years who had been evaluated for suspected PCOS based on irregular menses, clinical and biochemical markers of hyperandrogenism or PCOS morphology by ovarian ultrasound were included. All women who gave informed consent and who had thyroid function and serum prolactin determinations at the time of their evaluation were eligible for inclusion. Women were excluded if they had been treated for thyroid disease in the past or if they had a known pituitary tumor, pregnancy, lactation, menopause, known congenital adrenal hyperplasia, Cushing syndrome, or tumors secreting androgens, or if they were taking medications known for significant effects on serum prolactin or thyroid function. Patients who did not have all the clinical or laboratory information were also excluded.

Data Collection

After approval from the institutional ethical review committee, eligible women were enrolled after obtaining written informed consent. Structured proforma was used to collect demographic and clinical data. Variables which were included were age, BMI, marital status, menstrual pattern, duration of irregular periods, infertility, hirsutism, acne, weight gain, and medical history. Anthropometric assessment was performed by taking weight and height measurements and calculating BMI as weight (kg/m2). Hirsutism and acne, indicative of hyperandrogenism, were noted. Menstrual abnormalities were classified as oligomenorrhea, amenorrhea or irregular cycles based on the clinical history. Laboratory exams consisted of serum thyroid-stimulating hormone, free thyroxine (if available), and serum prolactin. Thyroid dysfunction was defined by laboratory reference values as hypothyroidism, subclinical hypothyroidism, hyperthyroidism, or euthyroid. Hyperprolactinemia was considered as serum prolactin level greater than the upper limit of the reference range of the laboratory. Repeat prolactin testing was done clinically as a means of confirming persistent, elevated levels. Women with PCOS were assessed using the accepted criteria for diagnosis of PCOS, excluding other endocrine conditions if applicable. The prevalence of thyroid dysfunction and hyperprolactinemia was calculated, and a correlation with demographic and clinical parameters (BMI, age, menstrual irregularity, infertility, hirsutism, obesity) was evaluated.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 26.0 and entered the software. Data for quantitative variables (age, BMI, TSH, prolactin levels) were presented as mean ± standard deviation or median with interquartile range, depending on the distribution of the data. Categorical variables like menstrual irregularity, infertility, hirsutism, thyroid dysfunction, and hyperprolactinemia were presented as frequencies and percentages. Multivariable logistic regression was carried out to determine independent clinical correlates of thyroid dysfunction and hyperprolactinemia. The odds ratios were adjusted for 95% confidence intervals. A p-value < 0.05 was deemed statistically significant.

RESULTS

A total of 249 women were included, with a mean age of 27.8 ± 5.9 years and mean BMI of 27.6 ± 4.8 kg/m². Most participants were married (177, 71.1%), while 157 (63.1%) were overweight or obese. Menstrual irregularity was present in 203 (81.5%) women, including oligomenorrhea in 158 (63.5%) and amenorrhea in 45 (18.1%). Infertility was reported in 101 (40.6%), hirsutism in 139 (55.8%), acne in 98 (39.4%), weight gain in 132 (53.0%), and a family history of PCOS in 61 (24.5%). Regarding endocrine status, 191 (76.7%) women were euthyroid, while 58 (23.3%)

had thyroid dysfunction. Subclinical hypothyroidism was the most frequent thyroid abnormality, occurring in 37 (14.9%), followed by overt hypothyroidism in 14 (5.6%) and hyperthyroidism in 7 (2.8%).

Table 1: Baseline Demographic, Clinical, and Endocrine Characteristics of the Study Population (n = 249)

Category	Variable	Value
Demographic and clinical characteristics	Age, years	27.8 ± 5.9
	BMI, kg/m²	27.6 ± 4.8
	Married	177 (71.1%)
	Overweight/obese	157 (63.1%)
	Menstrual irregularity	203 (81.5%)
	Oligomenorrhea	158 (63.5%)
	Amenorrhea	45 (18.1%)
	Infertility	101 (40.6%)
	Hirsutism	139 (55.8%)
	Acne	98 (39.4%)
	Weight gain	132 (53.0%)
	Family history of PCOS	61 (24.5%)
Thyroid and prolactin status	Euthyroid	191 (76.7%)
	Any thyroid dysfunction	58 (23.3%)
	Subclinical hypothyroidism	37 (14.9%)
	Overt hypothyroidism	14 (5.6%)
	Hyperthyroidism	7 (2.8%)
	Hyperprolactinemia	37 (14.9%)
	Both thyroid dysfunction and hyperprolactinemia	14 (5.6%)
Laboratory parameters	TSH, mIU/L	2.9 (1.8–4.4)
	Free T4, ng/dL	1.12 ± 0.24
	Serum prolactin, ng/mL	17.8 (12.1–25.6)
	TSH in thyroid dysfunction group, mIU/L	6.8 (5.1–9.7)
	Prolactin in hyperprolactinemia group, ng/mL	38.6 (31.4–52.8)

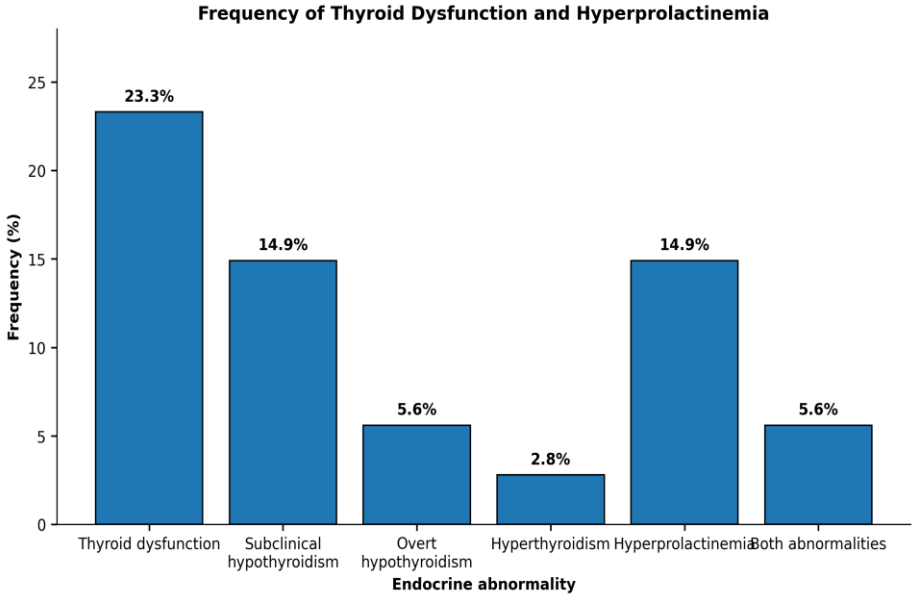


Figure 1. Frequency of Thyroid Dysfunction and Hyperprolactinemia

Women with thyroid dysfunction were significantly older than euthyroid women (29.4 ± 6.1 vs. 27.3 ± 5.7 years; p=0.016) and had a higher mean BMI (29.1 ± 5.0 vs. 27.1 ± 4.6 kg/m²; p=0.005). Overweight or obesity was more frequent among women with thyroid dysfunction (75.9% vs. 59.2%; p=0.021), as were infertility (55.2% vs. 36.1%; p=0.010) and weight gain (67.2% vs. 48.7%; p=0.013). Menstrual irregularity was more common in the thyroid dysfunction group (89.7% vs. 79.1%), although the difference was not statistically significant (p=0.071).

Table 2: Clinical Characteristics According to Thyroid Dysfunction and Hyperprolactinemia

Variable	Thyroid Dysfunction (n = 58)	Euthyroid (n = 191)	p-value	Hyperprolactinemia (n = 37)	Normal Prolactin (n = 212)	p-value
Age, years	29.4 ± 6.1	27.3 ± 5.7	0.016	28.3 ± 5.7	27.7 ± 5.9	0.565
BMI, kg/m²	29.1 ± 5.0	27.1 ± 4.6	0.005	27.9 ± 4.7	27.5 ± 4.8	0.639
Overweight/obese	44 (75.9%)	113 (59.2%)	0.021	—	—	—
Menstrual irregularity	52 (89.7%)	151 (79.1%)	0.071	35 (94.6%)	168 (79.2%)	0.024
Amenorrhea	—	—	—	13 (35.1%)	32 (15.1%)	0.003
Infertility	32 (55.2%)	69 (36.1%)	0.010	22 (59.5%)	79 (37.3%)	0.011
Hirsutism	35 (60.3%)	104 (54.5%)	0.431	19 (51.4%)	120 (56.6%)	0.557
Acne	20 (34.5%)	78 (40.8%)	0.389	13 (35.1%)	85 (40.1%)	0.567
Weight gain	39 (67.2%)	93 (48.7%)	0.013	22 (59.5%)	110 (51.9%)	0.392

On multivariable logistic regression, age ≥30 years was independently associated with thyroid dysfunction (aOR 1.81, 95% CI: 1.01–3.24; p=0.046). Overweight or obesity was associated with approximately two-fold higher odds of thyroid dysfunction (aOR 2.03, 95% CI: 1.08–3.82; p=0.028), while infertility (aOR 1.92, 95% CI: 1.05–3.50; p=0.034) and weight gain (aOR 1.87, 95% CI: 1.01–3.45; p=0.047) were also significant independent correlates. Menstrual irregularity (aOR 1.64, 95% CI: 0.68–3.94; p=0.270) and hirsutism (aOR 1.20, 95% CI: 0.65–2.20; p=0.559) were not independently associated with thyroid dysfunction.

Table 3: Multivariable Logistic Regression for Clinical Correlates of Thyroid Dysfunction and Hyperprolactinemia

Outcome	Predictor	Adjusted OR	95% CI	p-value
Thyroid dysfunction	Age ≥30 years	1.81	1.01–3.24	0.046
	Overweight/obesity	2.03	1.08–3.82	0.028
	Infertility	1.92	1.05–3.50	0.034
	Weight gain	1.87	1.01–3.45	0.047
	Menstrual irregularity	1.64	0.68–3.94	0.270
	Hirsutism	1.20	0.65–2.20	0.559
Hyperprolactinemia	Amenorrhea	2.71	1.27–5.78	0.010
	Infertility	2.26	1.10–4.65	0.027
	Menstrual irregularity	2.84	1.02–7.89	0.046
	Overweight/obesity	1.18	0.56–2.48	0.660
	Hirsutism	0.91	0.44–1.88	0.797
	Acne	0.84	0.39–1.82	0.659

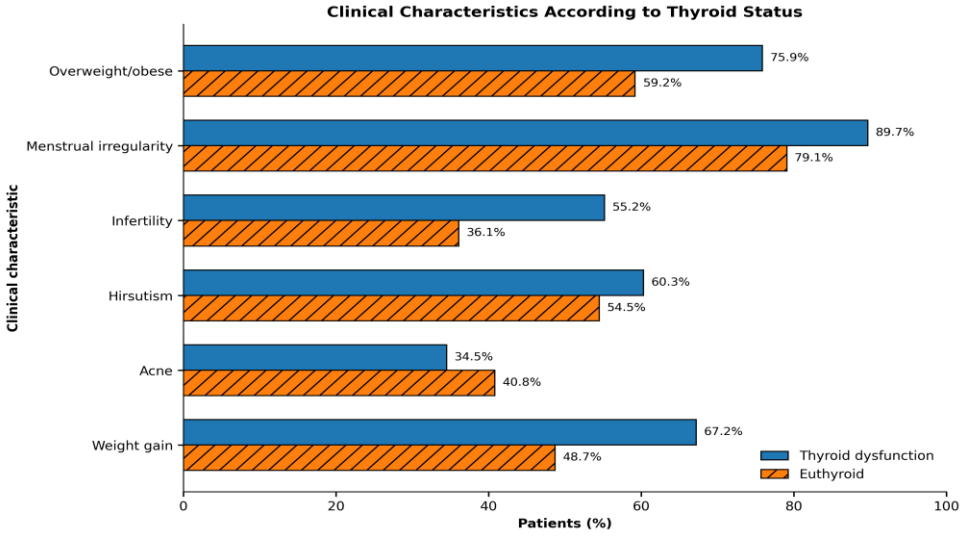


Figure 2: Clinical Characteristics According to Thyroid Status

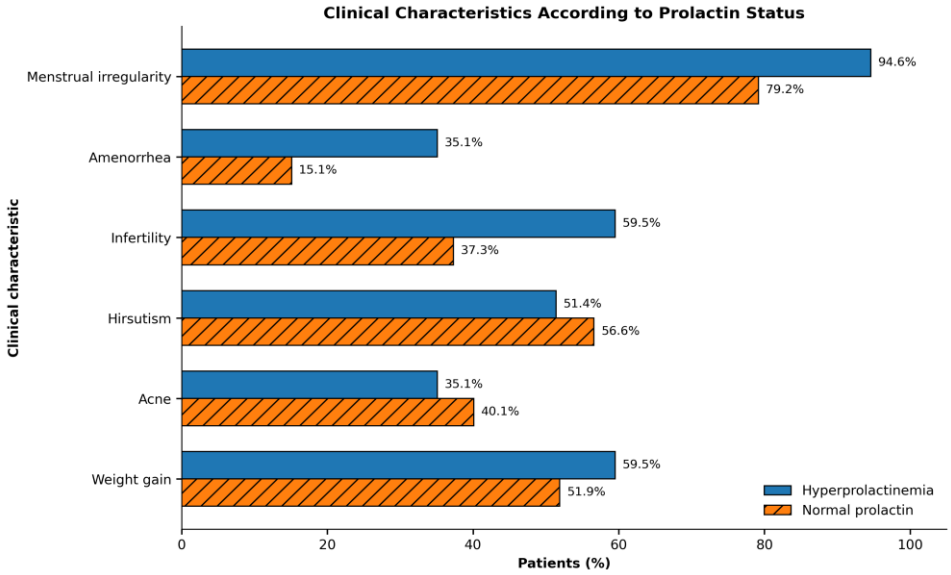


Figure 3: Clinical Characteristics According to Prolactin Status

DISCUSSION

In the present study, we examined thyroid function and hyperprolactinemia in 249 women with suspected PCOS and found a significant prevalence of thyroid and hyperprolactinemia. Thyroid dysfunction was detected in 23.3% of participants, subclinical hypothyroidism the most common abnormality (14.9%), overt hypothyroidism (5.6%) and hyperthyroidism (2.8%). Hyperprolactinemia was noted in 14.9% women and 5.6% women had a combination of thyroid dysfunction and high prolactin. The results indicate the need for assessing alternative or concurrent endocrine disorders in women with symptoms suggestive of PCOS. In the present study, the most common thyroid abnormality was subclinical hypothyroidism. The finding is similar to a recent cross-sectional study of 368 women with PCOS in South India where subclinical hypothyroidism was observed in 14.13% of the women. In the study, women with subclinical hypothyroidism also had higher BMI and less favorable metabolic profiles than euthyroid women. A recent study has found that women with PCOS had 14.9% with subclinical hypothyroidism, while controls had 5.3%, and the PCOS group had higher levels of TSH and greater metabolic abnormalities. These estimates are similar to the current study results, indicating that subclinical thyroid dysfunction could be a significant comorbidity to consider when evaluating women for PCOS, especially in populations where overweight and metabolic abnormalities are prevalent [13,14].

However, a large study of 1429 women with PCOS and 299 controls did not show an increased prevalence of overt thyroid disease in women with PCOS compared to those without PCOS but did indicate an increased prevalence in one specific phenotype of PCOS for subclinical hypothyroidism. These differences could be attributed to differences in the population studied, diagnostic criteria, iodine levels, prevalence of obesity, age distribution, and recruitment of women from general or specialist endocrine/ reproductive clinics [15]. Importantly, the present study was made up of women who were assessed for suspected PCOS, and not a population-based sample; thus, this may be a reason for the relatively high prevalence of thyroid abnormalities. In the present study, women with thyroid dysfunction were older, and their BMI levels were significantly higher than those in women with euthyroidism. The prevalence of overweight or obesity was higher in those with thyroid dysfunction (75.9%) than in those who were euthyroid (59.2%). In multivariate analysis, overweight or obesity maintained its association with thyroid dysfunction, even after controlling for other factors. Recent studies confirm this, as women with PCOS and subclinical hypothyroidism may be more likely to be obese and to exhibit higher metabolic abnormalities than women with PCOS and normal thyroid function [16]. A recent study from Lahore, Pakistan, has also investigated the association of subclinical hypothyroidism and metabolic and reproductive abnormalities in PCOS women, which further highlights the clinical significance of thyroid assessment in local women.

Another important clinical correlate of thyroid dysfunction in the present analysis was infertility, which occurred in 55.2% of women with thyroid dysfunction, and 36.1% of euthyroid women. This association with thyroid dysfunction was independent after adjustment. Thyroid hormones are important in the functioning of the ovary, gonadotropins, endometrial receptivity, and metabolism of reproductive hormones [17]. Therefore, any thyroid dysfunction may lead to ovulatory dysfunction and loss of fertility even if it is subtle. Thus, the association of thyroid dysfunction with infertility in women referred for evaluation for PCOS is of clinical relevance, as the untreated thyroid dysfunction can also complicate the diagnosis and management of the patient for PCOS [18]. Weight gain was also significantly more prevalent among women with thyroid dysfunction and was an independent correlate. This correlation is biologically possible, as thyroid disorders can affect basal metabolic rate, fluid balance, energy expenditure and body weight. The cross-sectional design is not designed, however, to determine whether weight gain preceded thyroid dysfunction or came as a consequence of it. In addition, thyroid dysfunction cannot be assumed clinically in the presence of obesity related symptoms as there is overlap between the symptoms of PCOS and thyroid dysfunction. Females with

hyperprolactinemia also had a significantly higher prevalence of infertility and this was an independent correlate. Excessive prolactin levels can interfere with ovulation and luteal function and thus may play a role in infertility [19]. Hyperprolactinemia that is associated with possible PCOS is therefore significant, as both hyperprolactinemia and PCOS can cause reproductive dysfunction on their own. In the context of this, hyperprolactinemia may affect the subsequent investigations and treatment. In contrast, hirsutism and acne were not significantly associated with thyroid dysfunction or hyperprolactinemia. This indicates that clinical characteristics of the androgen type may be more specific to the PCOS phenotype than to these endocrine abnormalities. Recent studies have also demonstrated the possibility of subclinical hypothyroidism affecting metabolic and thyroid-prolactin axis parameters, although it does not necessarily affect the core reproductive hormone parameters or ovarian morphology [20]. There were several limitations in this study. The first problem is the cross-sectional design which prevented establishing temporal or causal relationships between thyroid dysfunction, hyperprolactinemia, and the clinical features observed in the women assessed for PCOS. Secondly, the study was undertaken in one healthcare facility, and the results might not be applicable to other parts of Pakistan or to community populations. Third, non-probability consecutive sampling may have led to selection bias, due to an increased number of women presenting to a specialist clinic with more pronounced symptoms or burden of endocrine abnormalities than the general population. In addition, important metabolic and hormonal factors such as insulin resistance, lipid profile, androgen level and detailed phenotypes of PCOS were not investigated thoroughly. Lastly, several clinical factors were adjusted for in the multivariable regression but there was a potential of residual confounding by other unmeasured factors.

CONCLUSION

Relatively common among women assessed for PCOS were thyroid dysfunction and hyperprolactinemia. The common thyroid dysfunction was subclinical hypothyroidism and hyperprolactinemia was especially related to menstrual irregularity, amenorrhea and infertile cases. Older age, overweight or obesity, infertility and weight gain were more strongly associated with thyroid dysfunction. The results of this study emphasize the significance of evaluating thyroid function and serum prolactin as part of the diagnostic workup of women with signs and symptoms suggestive of PCOS. Early diagnosis of these other or concurrent hormone issues can increase the precision of diagnosis, direct treatment and prevent erroneous diagnosis of PCOS as the sole diagnosis.

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