

## RESEARCH ARTICLE

### Thyroid function tests in polycystic ovarian syndrome

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#### ABSTRACT


**Background:** Polycystic ovarian syndrome (PCOS) or polycystic ovarian disease (PCOD) is the most common endocrine problem in young females with chronic anovulatory cycles occurring in 5-10% of reproductive women. PCOS is viewed as a heterogeneous disorder of multifactorial etiology also associated with increased metabolic and cardiovascular risk factors. Both PCOD and thyroid dysfunction have multiple common presentations and both have profound effect on fertility and reproductive biology. Hypothyroidism can initiate, maintain or worsen PCOD. **Aims and Objectives:** This study has been contemplated to investigate the prevalence of thyroid disorders in PCOS patients from Central India. **Materials and Methods:** Female patients in the age group between 18 and 30 years meeting Rotterdam criteria for the diagnosis of PCOS were included in the study. The patients were asked to report in fasting state for the following investigations: Fasting blood sugars, fasting insulin levels, serum luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), serum testosterone, dehydroepiandrosterone, and serum prolactin were done. FSH and LH were done on the 2<sup>nd</sup> or 3<sup>rd</sup> day of menstrual cycle. Gynecological ultrasound was done to assess ovarian condition and presence or absence of multiple cysts. **Results:** LH/FSH ratio of more than 2 was found in 60% of the cases, 41 subjects (68%) were insulin resistant. Raised serum testosterone was found in 64% of the cases. The mean TSH level in subjects was  $4.219333 \pm 1.877632$ . Subclinical hypothyroidism was seen in 16 (26.6%) cases and overt hypothyroidism in 12 (20%) cases. Total thyroid dysfunction (clinical and subclinical) was seen in 28 (46.66%) cases. **Conclusion:** The prevalence of thyroid dysfunction in PCOS is very high. All patients with PCOS should be screened for thyroid dysfunction.

**KEY WORDS:** Polycystic Ovarian Syndrome; Thyroid Dysfunction; Ferriman–Gallwey Score; Hirsutism; Rotterdam Classification

#### INTRODUCTION

Polycystic ovarian syndrome (PCOS) or polycystic ovarian disease (PCOD) is the most common endocrine problem in young females with chronic anovulatory cycles associated

with androgen excess; perhaps occurring in 5-10% of reproductive women.<sup>[1]</sup> PCOS is viewed as a heterogeneous disorder of multifactorial etiology. It is also associated with increased metabolic and cardiovascular risk factors.<sup>[2]</sup> These risks are linked to insulin resistance (IR) and compounded by the common occurrence of obesity, (although IR is also present in non-obese woman with PCOS), infertility, irregular uterine bleeding, and increased pregnancy loss.<sup>[3]</sup> Polycystic ovaries are defined as the presence of 12 or more follicles in each ovary measuring 2-9 mm and/or increased ovarian volume greater than 10 mL. The hyperandrogenic state is believed to be a cause of incomplete follicular development.<sup>[4]</sup>

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Thyroid dysfunction is associated with alteration in a number of metabolic processes. Early stages of thyroid dysfunction can lead to subtle change in ovulation and endometrial receptivity, which may have profound effect on fertility. If untreated it may cause a delay in the onset of puberty followed by anovulatory cycles. Even subclinical hypothyroidism can affect fertility adversely.

Hence, it is evident that both of these (PCOD and thyroid dysfunction) conditions have multiple common presentations and both have profound effect on fertility and reproductive biology. More interestingly hypothyroidism can initiate, maintain or worsen PCOD.<sup>[1]</sup> Hence, in the past few years, different studies from various parts of the world regarding thyroid disorders in PCOS patient, have tried to explore the PCOS-thyroid interface. Mostly the results showed a higher incidence of elevated thyroid stimulating hormone (TSH) levels and four times higher prevalence of autoimmune thyroiditis in PCOS subjects.<sup>[7]</sup> With this background, this study has been contemplated to investigate the prevalence of thyroid disorders in PCOS patients attending NKP Salve Institute of Medical Sciences and Research Center outpatient department (OPD).

## MATERIALS AND METHODS

This is a cross-sectional study for which 60 diagnosed patients of PCOS were selected randomly from those attending gynecology OPD for menstrual problems or hirsutism. The Institutional Ethics Committee has approved this project. Female patients in the age group between 18 and 30 years who were ready to give written consent and meeting Rotterdam criteria for the diagnosis of PCOS were included in the study. The patients on oral contraceptives or hormone replacement therapy, liver and kidney diseases, congenital adrenal hyperplasia simple virilizing or severe, adrenal insufficiency, Cushing's syndrome, primary amenorrhea due to any cause, Sheehan syndrome, pregnancy, lactation, treatment for infertility, premature ovarian failure, and hyperprolactinemia were excluded.

Treatment naïve patients meeting inclusion-exclusion criteria were recruited for the study. A thorough clinical examination and history was taken. Menstrual history noted. Diagnosis of PCOS was done by Rotterdam classification (Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met: Oligoovulation and/or anovulation, excess androgen activity [clinical and or biochemical] and polycystic ovaries (by gynecologic ultrasound multiple cysts more than 2 in number of 2-9 mm size)). Hirsutism was graded by Ferriman–Gallwey score. Based on this score pattern and other clinical tests, hirsutism can be evaluated as mild, moderate or severe.

Another relevant history about symptoms of hyper/hypothyroidism was asked. History of primary or secondary

infertility was asked. The patients were asked to report in fasting state for the following investigations: Fasting blood sugars, fasting insulin levels, serum luteinizing hormone (LH), follicle stimulating hormone (FSH), TSH, serum testosterone, dehydroepiandrosterone, and serum prolactin were done. FSH and LH were done on the 2<sup>nd</sup> or 3<sup>rd</sup> day of menstrual cycle. Gynecological ultrasound was done to assess ovarian condition and presence or absence of multiple cysts.

## Statistical Analysis

Descriptive statistics are expressed as mean  $\pm$  standard deviation.

## RESULTS

In all 84 patients were screened for the study of which 60 met the diagnostic criteria of PCOS. The mean age of the patients with PCOS was  $19 \pm 4.84$  years. All the patients had some form of menstrual irregularities either oligomenorrhea, irregular menses or secondary amenorrhea. A total of 73% had body mass index  $\geq 25$  kg/m<sup>2</sup>. Clinical hirsutism was present in significant number 70% of cases (Ferriman–Gallwey score  $>7$ ) Table 1. LH/FSH ratio of more than 2 was found in 60% of the cases. Homeostatic model assessment IR (HOMA-IR) was calculated from fasting blood sugar and fasting insulin levels (Table 1), and 41 subjects (68%) were insulin resistant.

The mean TSH levels in subjects were  $4.219333 \pm 1.877632$ . The distribution of thyroid dysfunction among subjects. Subclinical hypothyroidism was seen in 16 (26.6%) cases and overt hypothyroidism in 12 (20%) cases (Table 3).

**Table 1:** Statistical values of different variables among PCOS cases

Variables	PCOS (n=60)
Age (years)	19 $\pm$ 4.84
BMI (kg/m <sup>2</sup> )	26.42 $\pm$ 4.59
Hirsutism	42 (70%)
Ferriman–Gallwey score	16 $\pm$ 5.008499
Serum testosterone (ng/ml)	21.52467 $\pm$ 54.46328
Serum DHEAS (ug/ml)	3.483333 $\pm$ 1.658785
Fasting sugar (mg/dl)	88.93333 $\pm$ 11.21247
Fasting serum insulin (uIU/ml)	22.238333 $\pm$ 8.646163
HOMA-IR	3.871.578 $\pm$ 2.75
LH (mIU/ml)	12.58 $\pm$ 5.6421
FSH (mIU/ml)	5.692 $\pm$ 2.331
PRL (ng/ml)	6.74 $\pm$ 4.39

PCOS: Polycystic ovarian syndrome, BMI: Body mass index, HOMA-IR: Homeostatic model assessment insulin resistance, DHEAS: Dehydroepiandrosterone-sulfate, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, PRL: Prolactin

**Table 2:** Thyroid function tests in PCOS subjects

Investigations	Number of patients n=60
fT3 (pg/ml)	2.932±1.537608
fT4 (ng/dl)	1.578±1.150606
TSH (mIU/ml)	4.219333±1.877632

Raised serum testosterone was found in 64% of the cases.

PCOS: Polycystic ovarian syndrome

**Table 3:** Various thyroid abnormalities in patients with PCOS

Thyroid abnormalities	PCOS (n=60) (%)
Goiter	4 (6.66)
Subclinical hypothyroidism	16 (26.6)
Overt hypothyroidism	12 (20)
Grave's disease	Nil
Multinodular goiter	Nil

PCOS: Polycystic ovarian syndrome

Total thyroid dysfunction (clinical and subclinical) was seen in 28 (46.66%) cases. Thyrotoxicosis and multinodular goiter was not seen in our study.

## DISCUSSION

Our study reports a high percentage of thyroid dysfunction in subjects with PCOD. We found that 46.6% of the cases have either clinical (20%) or subclinical (26.6%) hypothyroidism. Although hyperthyroidism was not seen in any of the case. The overall percentage of thyroid dysfunction among females in general population has been shown to be around 11.4% in an epidemiological study from India.<sup>[8]</sup> Many other studies have reported a very high percentage of thyroid dysfunction in PCOS cases.<sup>[7,9]</sup> Sinha et al. have reported 22.5% subclinical hypothyroidism and clinical hypothyroidism in 2.5% the findings of which are very close to our study. Janssen et al. observed a high percentage of autoimmune thyroid dysfunction in PCOS though in our study we have not looked at the autoimmune nature of thyroid dysfunction.

Researchers suggest an increased estrogen and estrogen/progesterone ratio to be directly involved in high anti-thyroid peroxidase levels in PCOS patients.<sup>[9]</sup> Both genetic and environmental factors are believed to be contributing to thyroid disorders in PCOS. Hypothyroidism is known to cause PCOS-like ovaries and overall worsening of PCOS and IR.<sup>[10,11]</sup> Estrogen's immune stimulatory activity is normally countered by anti-inflammatory actions of progesterone levels of which are near zero in PCOS because of anovulatory cycles. As a result immune system is over-stimulated resulting in autoimmunity and high incidence of autoimmune thyroid dysfunction.<sup>[12]</sup> Ghosh et al. did comparative analysis and suggested that hypothyroidism

led to lowering of sex hormone-binding globulin levels and increment of testosterone levels.<sup>[13]</sup>

All our patients had some form of menstrual problem ranging from oligomenorrhea, irregular menses to secondary amenorrhea. This matches with other studies in which menstrual irregularities were observed from 60% to 93%.<sup>[9,14,15]</sup>

High incidence of obesity and IR as measured by HOMA-IR in our study is also similar to findings of others.<sup>[9,15]</sup>

We report LH/FSH ratio of more than 2 in 60% of the cases. Sinha et al. and Anwary et al. have found this high LH/FSH ratio in 55% and 56%<sup>[9]</sup> while Anlakash<sup>[16]</sup> has reported this to be 64%.

A hypothesis has been established that hypothyroidism worsens PCOS by decreasing sex hormone binding globulin levels, which increases conversion of androstenedione to testosterone and reduction in metabolic clearance rate of androstenedione and estrone. Since thyroid hormones in gonadotropin-induced estradiol and progesterone secretion by granulose cells, hypothyroidism may interfere with ovarian function and fertility.<sup>[17]</sup>

## CONCLUSION

The prevalence of thyroid dysfunction in PCOS is very high. All patients with PCOS should be screened for thyroid dysfunction.

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