



## Original Research Article

## Estimating thyroid profile in women with polycystic ovarian syndrome and comparing it with healthy individuals

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## ABSTRACT

**Background:** The Polycystic Ovarian Syndrome (PCOS) is considered as one of the most common endocrinopathies in women of reproductive age having the issues related to the hyperandrogenism and oligo-anovulation. The rate of prevalence in premenopausal women is between 6-10% worldwide and in India it is around 5-10%. Interaction of small number of key genes responsible for most of the endocrine and metabolic symptom with environmental risk factors have impact on high prevalence of PCOS.

**Aim:** To analyse thyroid profile in women with polycystic ovarian syndrome and compare it with healthy individuals

**Materials and Methods:** The samples were collected from PCOS patients diagnosed according to Rotterdam criteria, ascertained by ultrasonography, attending the OPD in the department of Obstetrics and Gynecology, Rajarajeshwari Medical college and Hospital, Bangalore from December 2014 to May 2016. Seventy-five cases of PCOS patients in the age group of 20-40 years, and seventy-five age-matched healthy women (control) with regular menstrual cycle were selected.

**Results:** The mean age of cases was 30.13 (SD=5.32) years and mean age of control group was 28.54 (SD=6.78) years. Further, in case group, 73.33% patients were Euthyroid, 6.66% were sub-clinical hyperthyroid, 14.66% were subclinical hypothyroid and 5.33% were clinical hypothyroid. The mean value of T3 for case group was 127.13 (SD = 51.23) and control group was 137.57 (SD = 59.49). Moreover, the mean value of T4 for case group was 8.17 (SD = 2.50) and control group was 9.45 (SD = 2.24). In case group, 12.7% Euthyroid patients, 54.5% subclinical hypothyroid and 75% clinical hypothyroid had anti-thyroid peroxidase+ (TPO+). On the other hand, in control group 7.7% Euthyroid and 66.9% subclinical hypothyroid were anti-TPO+.

**Conclusion:** Euthyroid PCOS cases with anti TPO positive are at risk of developing hypothyroidism. Thus T3, T4 and TSH should be periodically evaluated in these subjects.

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### 1. Background

The health and wellbeing of people is essential for maintaining the healthy lifestyle and achieving the goals.

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In recent times, there has been increasing emphasis on association between autoimmune thyroid disease and polycystic ovary syndrome (PCOS). However, the causality of the association is uncertain, but these two conditions share a bidirectional relationship.<sup>1</sup> Although, both the syndromes share similar traits, yet no study has been able

to determine the exact nature between these two.<sup>2</sup> As per the studies, PCOS is very common endocrinopathy in reproductive women and those with oligo-anovulation and hyperandrogenism. The rate of prevalence in premenopausal women is between 6-10% worldwide and in India it is around 5-10%.<sup>3</sup> Globally, PCOS is directly associated with high economic burden. Infertility, use of fertility hormone treatment and hospitalization are the major contributing factors. In 2020, the estimated economic burden of PCOS in USA was \$3.7 billion annually.

It is characterized by oligo or anovulation, hyperandrogenism and polycystic ovaries. According to analysis, the family history is also playing a significant role in pathogenesis of PCOS. Interaction of small number of key genes responsible for most of the endocrine and metabolic symptom with environmental risk factors have impact on high prevalence of PCOS.<sup>4</sup> According to analysis of previous studies, PCOS is clinically manifest syndrome. The etiopathophysiology of PCOS is unclear and it can be occurred from the abnormal functions of the hypothalamic-pituitary-ovarian (HPO) axis. There is also an association between PCOS and peripheral insulin resistance and hyper-insulinemia, which are directly associated with obesity.<sup>5</sup> PCOS is considered as an endocrine metabolic disorder that occurs due to multiple imbalances of the thyroid gland. The imbalance in the thyroid is having impact on the reproductive biology.<sup>6</sup> According to clinical study, this kind of condition is having a significant impact on Sex Hormone Binding Globulin (SHBG), Prolactin and GnRH secretion.<sup>7,8</sup>

Thyroid dysfunction and PCOS is considered to have a profound effect on fertility and reproduction.<sup>9</sup> Thyroid dysfunction interferes with ovarian functions and infertility that have direct impact on the menstrual pattern. As per the outcome of the clinical studies, the low SHBG in hypothyroid increases the serum testosterone that contribute to the symptoms of PCOS.<sup>10</sup> Dysfunctional uterine bleeding and infertility are the consequences of anovulatory menstrual cycles. The menstrual irregularities in PCOS usually present around the time of menarche.<sup>11</sup> Thus, this paper intends to evaluate the thyroid function and autoimmune status in subjects with PCOS and determine if routine evaluation of these parameters should be considered to improve the menstrual rhythm, fertility and pregnancy related outcome in these subjects.

## 2. Aim of the Study

The study aims to estimate thyroid profile in women with polycystic ovarian syndrome and comparing it with healthy cases. It also focuses to estimate anti TPO in cases and control.

## 3. Method and Material

The samples were collected from PCOS patients attending the OPD in the department of Obstetrics and Gynecology, Rajarajeshwari Medical college and Hospital, Bangalore from December 2014 to May 2016. Seventy-five cases of PCOS patients in the age group of 20-40 years, diagnosed according to Rotterdam criteria, ascertained by ultrasonography, and seventy-five age matched healthy women (control) with regular menstrual cycle in the age group of 20-40 years were selected.

### 3.1. Inclusion criteria

1. 75 women diagnosed with PCOS ascertained by USG – as per Rotterdam Criteria in the age group of 20 – 40 years attending OPD of Department of OBG at RRMCH are included in the study.
2. 75 aged matched, healthy women attending the OBG OPD as control groups (with menstrual regularities)

### 3.2. Exclusion criteria

1. Other etiologies of hyperandrogenism (Clinically diagnosed)
2. Congenital adrenal hyperplasia
3. Androgen secreting tumors
4. Cushings syndrome
5. Subjects with known thyroid diseases
6. Women with regular mensuration in cases

### 3.3. Method of collection of data

Patients satisfying the inclusion criteria were enrolled in the study after obtaining written informed consent. A thorough medical history and detailed physical examination was performed for everyone. A pre-structured and pre-tested proforma was used to collect the data.

### 3.4. Method of collection of sample

Under full aseptic precautions, 5ml of venous whole blood sample was collected from the cubital vein from both study and control group, in clot activator containing vacuum evacuated tubes and were properly labelled. Precautions were taken to prevent hemolysis. Samples were brought to Clinical Biochemistry laboratory and centrifuged after clotting and retraction at room temperature. Clear serum was collected and subsequently analyzed.

The following investigations were performed by fully automated analyzer

1. Anti TPO Ab by — Chemiluminescence immune assay.
2. T3, T4, TSH by – Chemiluminescence immune assay.
3. Fasting blood glucose – Glucose oxidase-peroxidase (GOD-POD) method.

### 3.5. Statistical analysis

The data was entered in Microsoft Excel and analyzed in SPSS V28. Mean and standard deviation for quantitative variables were calculated for the study population. Difference in the group means of quantitative variables was compared by two tailed student t test at 95% significance level.

## 4. Results

Table 1 has provided the information related to the age distribution for both case and control group. Both groupshad 75 patients and mean age of case group was 30.13 (SD = 5.32) years and mean age of control group was 28.54 (SD = 6.78) years.

Table 2 has provided the comparative analysis of T3 for both groups. As per the analysis, the mean value of T3 for case group was 127.13 (SD = 51.23) and control group was 137.57 (SD = 59.49). There was no significant difference in T3 between the two groups ( $p > 0.05$ ).

Table 3 has compared T4 between both groups. According to analysis, the mean value of T4 for case group was 8.17 (SD = 2.50) and control group was 9.45 (SD = 2.24), showing significant difference in T4 between the groups ( $p < 0.05$ ). T4 was significantly lower in case group.

Table 4 has analysed the mean value of TSH for both groups. As per the analysis, the mean value for case group was 4.05 (SD = 4.09) and for control group was 2.92 (SD = 2.64). Analysis shows a significant difference in TSH between the groups ( $p < 0.05$ ). TSH was significantly higher for case group.

Table 5 has provided the information related to the prevalence of thyroid disorder in case group considering the TSH with respect to age. According to analysis, the 73.33% patients were euthyroid, 6.66% were sub clinical hyperthyroid, 14.66% were subclinical hypothyroid and 5.33% were clinical hypothyroid.

According to Table 6, 65 subjects had the normal TSH value, and most numbers of subjects were between the ages of 20-25 year. There were 2 subclinical Hyperthyroid subjects, 6 Subclinical Hypothyroid subjects, and 2 subjects had Clinical Hypothyroid.

Table 7 has analysed the anti-TPO for case and control. According to analysis, the mean value for case group was 55.40 (SD = 143.17) and control group was 21.97 (SD = 26.99). There was a significant difference in Anti TPO between the groups ( $p < 0.05$ ). Anti TPO was significantly higher for case group.

According to Table 8, out of 16 positive cases 43.75% were euthyroid, 37.5% were subclinical hypothyroid and 18.75% were clinical hypothyroid. On the other hand, out of 9 anti-TPO positive control 55.55% were euthyroid and 44.44% were subclinical hypothyroid.

Table 9 has provided the information related to prevalence of anti-TPO positivity in euthyroid and hypothyroid PCOS for both case and control group. According to analysis, in case group, out of 55 euthyroid patients, 12.7% were Anti TPO+, out of 11 subclinical hypothyroid patients, 54.5% were Anti TPO+, and out of 4 clinical hypothyroid patients, 75% were Anti TPO+. On the other hand, in control group, out of 65 euthyroid patients, 7.7% were Anti TPO+, and out of 6 subclinical hypothyroid patients, 66.9% were Anti TPO+.

## 5. Discussion

PCOS is associated with elevated androgen level and is most common form of chronic anovulation with a prevalence of 5-10%.<sup>12</sup> It has been considered as heterogeneous disorder of multi-factorial etiology. Apart from this, it is involving the obesity and insulin resistance and compounded by the non-obese women with PCOS. According to analysis, PCOS is associated with reproductive morbidity that include infertility, irregular uterine bleeding and increased pregnancy loss.

As per current study, both groups had 75 patients and mean age of case group was 30.13 (SD = 5.32) years and mean age of control group was 28.54 (SD = 6.78) years. According to analysis, the 73.33% patients were euthyroid, 6.66% were sub clinical hyperthyroid, 14.66% were subclinical hypothyroid and 5.33% were clinical hypothyroid. As per the findings of current study, the mean value of T3 for case group was 127.13 (SD = 51.23) and control group was 137.57 (SD = 59.49). There was no significant difference in T3 between the two groups ( $p > 0.05$ ). Moreover, the mean value of T4 for case group was 8.17 (SD = 2.50) and control group was 9.45 (SD = 2.24), showing significant difference in T4 between the groups ( $p < 0.05$ ). T4 was significantly lower in case group. As per the study of Uma Sinha et al (2013)<sup>13</sup> with a mean value of  $2.97 \pm 1.56$  vs  $2.12 \pm 1.05$   $p < 0.001$  for T3 and  $1.37 \pm 3.04$  vs  $1.05 \pm 3.14$   $p < 0.001$  for T4 respectively.

According to analysis, out of 16 anti-TPO positive cases, 43.75% were euthyroid, 37.5% were subclinical hypothyroid and 18.75% were clinical hypothyroid. On the other hand, out of 9 anti-TPO positive control, 55.55% were euthyroid and 44.44% were subclinical hypothyroid. Moreover, in case group, 12.7% euthyroid patients, 54.5% subclinical hypothyroid patients and 75% clinical hypothyroid patients were anti-TPO+. In control group, 7.7% euthyroid and 66.9% subclinical hypothyroid were anti-TPO positivity. Additionally, the mean value of anti-TPO for case was 55.40 (SD = 143.17) and control group was 21.97 (SD = 26.99). There was a significant difference in Anti TPO between the groups ( $p < 0.05$ ). Anti TPO was significantly higher for case group. A study done by Janssen et al (2004)<sup>14</sup> also revealed the same with anti TPO. They got the mean values as  $(10 \pm 18$  for controls vs

**Table 1:** Distribution of cases and control according to their age

| Age Group       | Cases (n=75)        | Control (n=75)      | Total              |
|-----------------|---------------------|---------------------|--------------------|
| 20 – 25         | 15(20%)             | 31(41.33%)          | 47(31.33%)         |
| 26 - 30         | 29(38.66%)          | 21(28%)             | 50(33.33%)         |
| 31 - 35         | 13(17.33%)          | 9(12%)              | 22(14.66%)         |
| 36 - 40         | 18(24%)             | 14(18.66%)          | 32(21.33%)         |
| <b>Total</b>    | <b>75(100%)</b>     | <b>75(100%)</b>     | <b>150(100%)</b>   |
| <b>Mean± SD</b> | <b>30.13 ± 5.32</b> | <b>28.54 ± 6.78</b> | <b>29.33 ±6.05</b> |

**Table 2:** Comparison of T3 for case and control group

| T3 | Group    | Mean   | Std Dev | SE of Mean | Mean Difference | T      | P-Value |
|----|----------|--------|---------|------------|-----------------|--------|---------|
|    | Cases    | 127.13 | 51.23   | 5.92       | -10.446         | -1.152 | 0.251   |
|    | Controls | 137.57 | 59.49   | 6.87       |                 |        |         |

**Table 3:** Comparison of T4 for case and control group

| T4 | Group    | Mean | Std Dev | SE of Mean | Mean Difference | T      | P-Value |
|----|----------|------|---------|------------|-----------------|--------|---------|
|    | Cases    | 8.17 | 2.50    | 0.29       | -1.282          | -3.306 | 0.001*  |
|    | Controls | 9.45 | 2.24    | 0.26       |                 |        |         |

**Table 4:** Comparison of TSH for case and control group

| TSH | Group    | Mean | Std Dev | SE of Mean | Mean Difference | T     | P-Value |
|-----|----------|------|---------|------------|-----------------|-------|---------|
|     | Cases    | 4.05 | 4.09    | 0.47       | 1.129           | 2.008 | 0.0425  |
|     | Controls | 2.92 | 2.64    | 0.31       |                 |       |         |

**Table 5:** Prevalence of thyroid disorders in cases according to TSH with respect to age.

| Age Group    | Euthyroid (n) TSH (0.4-4.5µIU/dl) | Sub clinical Hyperthyroid (n) TSH (0.1-0.39µIU/dl) | Subclinical Hypothyroid (n) TSH (4.5-10µIU/dl) | Clinical Hypothyroid TSH (>10µIU/dl) | Total     |
|--------------|-----------------------------------|--|--|--------------------------------------|-----------|
| 20 – 25      | 13                                | 1  | 0  | 1                                    | 15        |
| 26 – 30      | 24                                | 1  | 3  | 1                                    | 29        |
| 31 – 35      | 6                                 | 2  | 4  | 1                                    | 13        |
| 36 – 40      | 12                                | 1  | 4  | 1                                    | 18        |
| <b>Total</b> | <b>55(73.33)</b>                  | <b>5(6.66%)</b>                                    | <b>11(14.66%)</b>                              | <b>4(5.33%)</b>                      | <b>75</b> |

**Table 6:** Distribution of controls as per TSH focusing on age

| Age Group    | Euthyroid (n) TSH (0.4-4.5µIU/dl) | Sub clinical Hyperthyroid (n) TSH (0.1-0.39µIU/dl) | Subclinical Hypothyroid (n) TSH (4.5-10µIU/dl) | Clinical Hypothyroid TSH (>10µIU/dl) | Total           |
|--------------|-----------------------------------|--|--|--------------------------------------|-----------------|
| 20 - 25      | 30                                | 0  | 1  | 0                                    | 31              |
| 26 - 30      | 17                                | 1  | 2  | 1                                    | 21              |
| 31 - 35      | 6                                 | 0  | 2  | 1                                    | 9               |
| 36 - 40      | 12                                | 1  | 1  | 0                                    | 14              |
| <b>Total</b> | <b>65(86.7%)</b>                  | <b>2(2.7%)</b>                                     | <b>6(8%)</b>                                   | <b>2(2.7%)</b>                       | <b>75(100%)</b> |

**Table 7:** Comparison of anti-TPO for case and control group

| Anti TPO | Group    | Mean  | Std Dev | SE of Mean | Mean Difference | T     | P-Value |
|----------|----------|-------|---------|------------|-----------------|-------|---------|
|          | Cases    | 55.40 | 143.17  | 16.53      | 33.426          | 1.987 | 0.0452  |
|          | Controls | 21.97 | 26.99   | 3.12       |                 |       |         |

**Table 8:** Anti-TPO+ classification based on TSH value

| Group    | Age Group | EU Thyroid | Subclinical Hypothyroid | Clinical Hypothyroid | Grand Total |
|----------|-----------|------------|-------------------------|----------------------|-------------|
| Cases    | 20 – 25   | 2          | 0                       | 0                    | 2           |
|          | 26 – 30   | 4          | 2                       | 1                    | 7           |
|          | 31 – 35   | 1          | 2                       | 1                    | 4           |
|          | 36 – 40   | 0          | 2                       | 1                    | 3           |
|          | (Total)   | 7(43.75%)  | 6(37.5%)                | 3(18.75%)            | 16(64.0%)   |
| Controls | 20 – 25   | 3          | 1                       | 0                    | 4           |
|          | 26 – 30   | 1          | 2                       | 0                    | 3           |
|          | 31 – 35   | 1          | 0                       | 0                    | 1           |
|          | 36 – 40   | 0          | 1                       | 0                    | 1           |
|          | (Total)   | 5(55.55%)  | 4(44.44%)               | 0(0.0%)              | 9(36.0%)    |

**Table 9:** Prevalence of anti TPO positivity in Euthyroid and Hypothyroid PCOS in cases and control group

| Thyroid Status          | Cases (n) | Anti TPO + cases | Control(n) | Anti TPO+ controls |
|-------------------------|-----------|------------------|------------|--------------------|
| Euthyroid               | 55        | 7 (12.7%)        | 65         | 5 (7.7%)           |
| Subclinical Hypothyroid | 11        | 6 (54.5%)        | 6          | 4 (66.9%)          |
| Clinical Hypothyroid    | 4         | 3 (75%)          | 2          | 0                  |

123 ± 328 for cases, p<0.001) respectively. Another study done by Johannes Ott et al (2010)<sup>15</sup> got the similar findings with anti TPO, being significantly higher in PCOS subjects than in controls (2.5 ± 2.3 vs 1.8 ± 1.0 μU/ml, p<0.001; 40.0 ± 81.7 vs 12.0 ± 36.7 IU/ml, p<0.001 respectively).

## 6. Conclusion

From the analysis, it has been found that PCOS is key issue among the women during the reproductive years. PCOS subjects are prone for thyroid disorders, particularly Hypothyroidism. Autoimmunity as Autoimmune thyroiditis is more prevalent in PCOS subjects. Positivity for Anti TPO antibodies is more common in PCOS subjects. Euthyroid PCOS cases with anti TPO positive are at risk of developing hypothyroidism. Thus T3, T4 and TSH should be periodically evaluated in these subjects.

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

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