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A Cross-Sectional Study to Evaluate the Presence of Anti-Thyroid Peroxidase Antibodies in Women With Polycystic Ovary Syndrome

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Abstract

Objective: To find the prevalence of thyroid autoimmunity in PCOS women of reproductive age group.

Methods: Observational study done in the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur. Forty cases of women with PCOS based on Rotterdam's criteria and an equal number of age-matched controls (women without PCOS) were included in the study. Thyroid profile, antithyroid peroxidase titre, serum progesterone, testosterone and fasting blood sugar were estimated using standardised techniques.

Results: Menstrual irregularity (oligomenorrhoea and amenorrhoea) was the most common abnormality found in patients with PCOS compared with non-PCOS (p\0.0001). Hyperandrogenism was the second most common manifestation present in PCOS of our study group. Hirsutism was the striking hyperandrogenic feature that was present in study group. PCOS patients had higher BMI compared to controls (p\0.001). The prevalence of thyroid dysfunction was not significantly different in both the groups (p\0.80). Anti-TPO titre was higher in PCOS patients (145.13 ± 297.65 IU/ml) compared to the controls (29.20 ± 15.13 IU/ml) (p\0.001).

Conclusion: The present study shows that PCOS was associated with increased anti-TPO titres, thus emphasising the importance of screening all PCOS patients for anti-TPO along with routine thyroid profile.

Keywords: Anti-TPO antibodies, Polycystic ovary syndrome, Auto immunity

Introduction

PCOS is a common metabolic disorder in women of reproductive age group and is associated with a multitude of endocrine abnormalities. The present prevalence of PCOS is around 5–20 % and is on the rise in parallel with the rise in obesity and sedentary life style.[1] Inflammatory and autoimmune causes are also reported to have contribution to the pathogenesis of PCOS.[2]

The clinical manifestation of PCOS includes oligomenorrhea, infertility, acne, hirsutism, and acanthosis nigricans and so on. In addition, these patients may develop many other related endocrine and metabolic diseases and have increased risk of suffering endometrial cancer, impaired glucose tolerance, diabetes, and cardiovascular disease. Autoimmune thyroid disease (AITD) is common autoimmune disorder that affects 5-20% of women in childbearing age. AITD is most frequent cause of hypothyroidism in young women and it may present without thyroid dysfunction for many years hence it is often ignored resulting in hypothyroidism later in life.[3]

Association between thyroid autoimmunity and adverse pregnancy outcome has been reported, most patients with PCOS are in childbearing age therefore it is important to maintain normal thyroid function, before and during pregnancy to ensure the best possible outcome of the mother and progeny.[3]

Moreover recent studies have reported an association between thyroid autoimmunity and PCOS.[2]

Anti thyroid peroxidase antibodies (Anti TPO Ab) and Anti Thyroglobulin antibodies (Anti-Tg Ab) are fundamental markers of thyroid autoimmunity. Thyroid autoantibodies are significantly higher in infertile patient reported by Poppe et al[4]. Close follow-up of thyroid hormone are considered important in patients with PCOS because of it being the most common reason of medically treatable infertility.[5]

The latest studies revealed that autoimmune thyroid disease have an increased prevalence in PCOS patients. From this point of view, not only thyroid hormone is substantial for PCOS follow-up but also thyroid antibodies can be guiding for probable thyroid disease.[6]

PCOS is defined according to revised 2003 Rotterdam criteria,[7] which requires the presence of at least two of the following three findings: -

1. Ovulatory disturbances mainly oligomenorrhoea or amenorrhea.
2. Hyperandrogenism as defined either clinically by hirsutism, severe acne, seborrhoea; or biologically by elevated levels of total or free testosterone.
3. Polycystic ovaries at ultrasonography[8]

PCOS is hyperestrogenic state, where estrogen has an immune stimulatory activity due to anovulation and absence of inhibitory action of progesterone this would lead to over stimulated immune system, which may propagate autoimmune disease. Low level of progesterone would appear to be the likely etiology for ATPO positive value in PCOS.[3] This unique hormonal equilibrium in women with PCOS could be a suitable model for studying the hormonal influence on autoimmune disease.

High serum antibodies are found in active phase chronic autoimmune thyroiditis. Thus, an antibody titer can be used to assess disease activity in patients that have developed such antibodies. The majority of anti-TPO antibodies are produced by thyroid infiltrating lymphocytes, with minor contributions from lymph nodes and the bone marrow. They cause thyroid cell damage by complement activation and antibody dependent cell cytotoxicity. However, anti-TPO antibodies are not believed to contribute to the destruction of the thyroid.

This study aimed to determine association of anti-TPO antibodies in women with PCOS and to find whether they were at greater risk of developing thyroid autoimmune disease.

Aims & Objectives

To study the association of Anti-TPO antibodies in women with PCOS.

Material & Methods

A cross-sectional observational study was conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from June 2018 to August 2019. 80, Women attending Gynae OPD were enrolled for the study. Thyroid function test and ani-TPO antibody level was done in all. PCOS was further classified in 4 different phenotypes and results were analysed. They were divided into two groups, Cases and Controls comprising 40 women in each group. Cases - women with PCOS who were diagnosed by Rotterdam's Criteria were cases. Controls - Women of the same age group visiting OPD with problems unrelated to Rotterdam's Criteria of PCOS were controls.

A detailed clinical history, elaborate clinical examination and laboratory investigations were sent. Complete blood count, urine complete and microscopy, fasting blood sugar, thyroid function test, S. TSH, free thyroxin levels, (free T3 and free T4), anti TPO antibodies and free testosterone were done in both case and control group. Normal serum levels of different hormones and peptide defined as: - free T3- 2.4 to 4.2 pg/ml, free T4 -0.7 to 1.24 ng/dl. Serum TSH, Anti TPO antibodies and Free testosterone normal values were 0.34 to 4.25 mUI/ml, <60 IU/ml and 0.52 to 2.43 ηmol/L respectively. Transabdominal USG was performed to detect the size and volume of cystic ovaries in PCOS group number of follicles 12 or more each measuring 2-9 mm in diameter. Statistical outcome was calculated and analyzed. A statistical power >80% and an error <5% was used. Variable between the two groups (PCOS and Control group) that were normally distributed were analysed using student's "t" test. p-value <0.05 was considered statistically significant.

Case: Women with PCOS who were diagnosed by Rotterdam's Criteria were cases.

Inclusion Criteria

- Age group - 13-45 years.
- Giving written informed consent

Exclusion Criteria

- Women on OCPs & steroids, Hyperprolactinemia, Congenital Adrenal Hyperplasia, Cushing's Syndrome, Virilizing tumor of ovary, Vitiligo and Endometriosis

Control: Women of the same age group visiting OPD with problems unrelated to Rotterdam's Criteria of PCOS were controls.

Observation

Table 1: Comparison of variables between PCOS and Control group

Variables	PCOS	Control Group
Oligomenorrhoea / Amenorrhoea (N%)	35 (87.50%)	5 (12.50%)
Hirsutism (N%)	20 (50.00%)	2 (5.00%)
Ultrasound for polycystic ovaries (N%)	35 (84.50%)	5 (12.50%)

Table 2: Comparison of variables between PCOS and Control group

Variables	PCOS	Control Group	p-value
Age (yrs)	24.30 ± 3.59	24.1 ± 3.05	0.07
BMI (kg/m^2)	25.53 ± 2.54	23.2 ± 1.67	0.001
Personal History of	35.00%	12.50%	0.80

Thyroid Disorder			
Waist to Hip Ratio	0.85 ± 0.035	0.88 ± 0.05	0.182

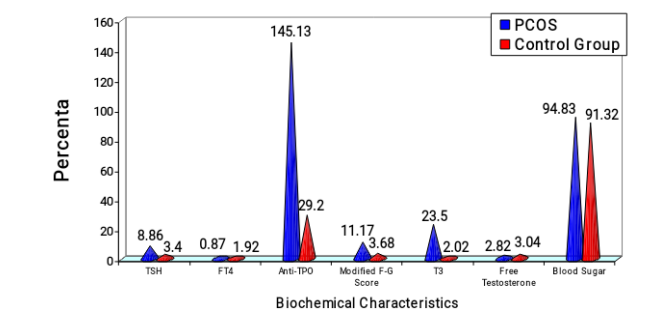
Table-1 & 2 shows the mean age and BMI between the control and PCOS patients which was statistically significant. Menstrual irregularity (oligomenorrhoea and amennorhoea) was the most common abnormality found in patients with PCOS. Hyperandrogenism was the second most common characteristic manifestation present in PCOS. The clinical features, biochemical hyperandrogenism and USG ovary with number of follicles 12 or more, each measuring 2–9 mm were significantly higher in the PCOS group.

Table 3: Comparison of biochemical characteristics between PCOS and Control group

Biochemical Characteristics	PCOS	Control Group	p-value
TSH (µIU/ml)	8.67 ± 7.57	3.40 ± 1.21	0.002
FT_4 (ηg/dl)	0.87 ± 0.75	1.92 ± 0.84	0.001
FT_3 (ρg/ml)	2.50 ± 1.22	2.02 ± 1.24	0.085
Anti TPO (IU/ml)	145.13 ± 297.65	29.20 ± 15.13	0.001
Modified F-G Score	11.17 ± 6.74	3.68 ± 0.98	0.001
Free Testosterone (ρg/ml)	2.82 ± 1.61	3.04 ± 1.98	0.0001
Blood Sugar	94.83 ± 5.94	91.32 ± 4.97	0.001

Table-3 shows the comparison of biochemical characteristics between patients and control which shows higher FBS in PCOS. Comparison of anti-TPO antibody titre between the cases and controls was done using the independent sample *t* test which showed a significant higher value in PCOS. The prevalence of autoimmune thyroiditis between PCOS and controls as defined by an elevated anti-TPO titre >60 IU/ml as positive ATPO and <60 IU/ml as negative ATPO. Our results show that Anti-TPO antibody were more prevalent in women with PCOS. Serum levels of Anti-TPO were significantly higher in these women in contrast to controls.

The mean value of Anti-TPO antibody in PCOS was 145.13 ± 297.65 IU/ml v/s 29.20 ± 15.13 IU/ml in control group. Significant difference was found in both groups (p-value = 0.001). Clinical hirsutism as per modified F-G score (>7) was present in 20 (50%) patients. Mean F-G score was 11.17 ± 6.74 in PCOS while in control group it was 3.68 ± 0.98. Raised serum free testosterone level was detected in 45% cases and highly significant in PCOS group. The mean value of S.TSH of the patient with PCOS and control was 14.24 ± 11.51 v/s 6.55 ± 3.25 µIU/ml respectively. Maximum patient in PCOS women had hypothyroidism and positive correlation was found between Anti-TPO and S.TSH levels (p-value = 0.002) which was highly significant.



Discussion

Patients with PCOS often have defective progesterone secretion which leads to an increased estrogen to progesterone ratio. Oestrogen can increase the expression of IL-6 in T cell and inhibitory action of

progesterone may leads to over stimulated immune system and makes these patients more prone to autoimmune disorder.[3] Majority of PCOS women and controls belong to age group of 21-25 yrs. Mean age in PCOS group was 24.30 ± 3.99 yrs and in control group 24.1 ± 3.05 yrs and p-value = 0.07. Our study is in accordance with a study done by Menon M et al (2017)[3] in which maximum number of PCOS women were in age group of 21-30 yrs and mean age was 31.02 ± 8.51 yrs. Increase in BMI is an integral parts of PCOS. There is a link present between thyroid dysfunction and obesity. Mean BMI was significantly higher in PCOS women as compared to controls (25.53 ± 2.54 kg/m^2 v/s 23.2 ± 1.67 kg/m^2). p-value = 0.001 (highly significant). The study done by Moran L et al (2013)[9] reported a mean BMI significantly higher in PCOS women as compared to non-PCOS (29.3 ± 7.5 kg/m^2 v/s 25.6 ± 5.8 kg/m^2, p < 0.001). These results were consistent with the fact that higher prevalence of overweight and obesity is found in PCOS women.

In our study clinical hirsutism was present in 50% (20) of PCOS women. Mean modified Ferriman-Gallway score (F-G) score 11.17 ± 6.74 as compared to mean F-G score 3.68 ± 0.98 among control, p-value = 0.001. Similar to our study, Sinha U et al (2013)[10] reported clinical hirsutism in 58% of PCOS women and mean F-G score of 18.65 ± 8.91 in PCOS v/s 9.57 ± 4.41 (p-value = 0.041).

We found that higher incidence of thyroid abnormalities in PCOS group specially hypothyroidism and autoimmune thyroiditis. Risk of thyroid disorder in PCOS was found to be 3 times higher than control group. Subclinical hypothyroidism and autoimmune thyroiditis was found to be higher in PCOS group as compared to control group in studies conducted by Arduc A et al (2015)[11], Novais J et al (2015)[12], Sinha U et al (2013)[10] and Ozdemir D et al (2011)[13]. In a study conducted by Kachuei M et al (2012)[6] prevalence of goitre in PCOS patients was found to be higher than control group (62.3% v/s 35.7%) (p = 0.0001).

However free T_4 level was significantly lower in PCOS group with mean free T_4 level 0.87 ± 0.75 ng/ml in PCOS group v/s 1.92 ± 0.84 ng/ml in control group (p-value = 0.001). Similar results were reported by Sinha U et al (2013)[10]. In our study mean serum TSH level was found to be significantly higher in PCOS group (8.86 ± 7.57 IU/ml) and in control group (3.40 ± 1.21 IU/ml) and p-value = 0.001. Significant difference was found between two groups. Similar correlation between TSH and Anti-TPO antibody level was reported by Janssen OE et al (2004)[2]. The mean serum Anti-TPO antibody level was significantly higher in patients with PCOS in comparison with women in control group (p-value = 0.001). Patients with PCOS had higher prevalence of thyroid autoimmunity. Similar results were also reported in the studies done by Sinha U et al (2013)[10], Janseen OE et al (2004)[2].

We found that Anti-TPO antibody level was very significantly higher in PCOS women (29%) with mean Anti-TPO antibody level (145.13 ± 297.65 IU/ml) v/s in control group (7.50%) (29.20 ± 15.13 IU/ml) (p-value = 0.001). In study conducted by Menon M et al (2017)[3] Anti-TPO antibody positive titre among PCOS patients was 25% as compared to the control 5% that was statistically significant (p-value <0.001). Anti-TPO antibody level was significantly higher in PCOS women with mean level 2.8 IU/ml v/s 1.5 IU/ml (p-value = 0.017) in the study conducted by Arduc A et al (2015)[11]. They also found positive correlation between estradiol/progesterone ratio and Anti-TPO antibody level suggesting that imbalance between estradiol and progesterone plays an important role in autoimmunity

among PCOS women. Janssen OE et al (2004)[2] reported that Anti-TPO antibody level was significantly higher in PCOS women as compared to the control group (123 ± 328 IU/ml) in PCOS and (10 ± 18 IU/ml) in control group (p-value < 0.001).

In our study raised serum free testosterone was found to be significantly higher in PCOS group in 45% cases as compared to control (p-value = 0.0001). While free testosterone was elevated in 61% of patients over 130 PCOS cases in study conducted by Sinha U et al (2013)[10].

PCOS is a kind of autoimmune disease and has a close association with autoimmune thyroiditis that cannot be ignored and refuted anymore.

Conclusion

PCOS and thyroid disorder are two of the most common endocrine disorder in the general population. In the present study this disorder was found to be associated with each other. TSH and anti-TPO antibodies were significantly higher in PCOS women. The occurrence of subclinical hypothyroidism and autoimmune thyroiditis was found to be more in PCOS women. Autoimmune thyroditis was more common in adolescent PCOS.

This study found that thyroid profile was deranged in all phenotype of PCOS. So we recommend that all PCOS women should be screened for thyroid dysfunction and anti-TPO antibodies. Accurate identification of phenotype should be done and treatment should be given as required, as they were at greater risk of developing thyroid autoimmune disease.

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