Research article

Evaluation of thyroid autoimmunity markers in polycystic ovarian syndrome in women

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ABSTRACT

Introduction and Aim: Polycystic ovarian syndrome (PCOS) is characterized by chronic anovulation and hyperandrogenism. PCOS also affects thyroid hormones, with multiple studies showing a link between autoimmune thyroid disease (AITD) and polycystic ovarian syndrome, although the exact pathophysiology of this interaction remains unknown. In this study the autoimmune thyroid indicators in women with PCOS were examined in order to demonstrate a link between polycystic ovarian syndrome and autoimmune thyroid disease.

Materials and Methods: The study included 85 polycystic ovarian syndrome (PCOS) patients and 50 controls with similar ages. Thyroid autoantibodies (anti-thyroglobulin (Anti-Tg) and anti-peroxidase (anti-TPO), thyroid hormones (free thyroxine (T4), triiodothyronine (T3), and thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH), and luteinizing hormone (LH) were determined in both study groups of women.

Results: In women with polycystic ovarian syndrome (PCOS) the blood levels of anti-thyroid peroxidase antibody (anti-TPO), antithyroglobulin antibody (anti-TG)) and thyroid stimulating hormone (TSH) were higher than women without PCOS. However, no difference was observed for free thyroxine (FT4) levels among PCOS and no PCOS women.

Conclusion: Thyroid dysfunction and thyroid autoimmunity was found to be linked in women with PCOS.

Keywords: Polycystic ovarian syndrome; Autoimmune thyroid disease; Antithyroglobulin antibody.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is an endocrine disorder affecting women in their reproductive age (1,2). The global prevalence of PCOS in women is approximately 9.2%. The diagnosis of PCOS is made based on the Rotterdam criteria, which includes the presence of two out of the three symptoms: Hyperandrogenism, oligo or/and anovulation, and polycystic ovaries (3,4). External indications of PCOS include weight gain, acne, dark skin spots, alopecia, hirsutism, and infertility (5). Metabolic syndrome, obesity, dyslipidemia, insulin resistance, type 2 diabetes, hypertension, and cardiovascular disease have been associated to PCOS (6,7). A study by Hefler-Frischmuth *et al*., showed autoimmunity immunity disorders to be more frequent in women and linked to PCOS (8). Autoimmune thyroid and thyroid hormone abnormalities can induce menstrual issues and sex hormone disruption, which might result in infertility. Anti-thyroid peroxidase antibodies (Anti-TPO Ab) and Anti-thyroglobulin antibodies (Anti-TG Ab) are predominant in thyroid autoimmune diseases. Since thyroid hormones are the primary cause of infertility in women with PCOS, the rise in thyroid autoimmune antibodies in women with PCOS should be periodically checked as a measure of infertility (9). To ascertain if autoimmune thyroid diseases and PCOS are related, this study examined the levels of thyroid hormones, luteinizing hormones, follicle-stimulating hormones, and autoimmune thyroid autoantibodies in women with PCOS.

MATERIALS AND METHODS

Study group

The study involved 85 women participants suffering from PCOS. The Rotterdam criteria were used to define the symptoms of PCOS (3). Clinical history of each participant which included, family history of PCOS, monthly irregularities, alopecia, acne, hirsutism, and prior abortions was collected. Each participant was measured for their waist circumference (in cm) and Body Mass Index (BMI) calculated using the formula weight (in kilograms)/ height (in meters).

The study also included 50 women between the ages of 15 and 40 who had regular menstrual cycles, normal levels of androgen hormones, no symptoms of PCOS and hirsutism.

Analysis of hormonal and autoimmune thyroid antibodies

Blood drawn from each woman in the PCOS and control group was coagulated for 5 mins., to separate out the serum. Serum collected was centrifuged at 3000 rpm for 15 minutes, then frozen until analysis. A mononuclear enzyme-linked immunosorbent assay (ELISA) kit was used to assess the thyroid hormones: Free thyroxine (T4), triiodothyronine (T3), and thyroid stimulating hormone (TSH)), follicle stimulating

hormone (FSH), luteinizing hormone (LH), and antibodies (Anti-thyroid peroxidase antibody (anti-TPO) and Antithyroglobulin antibody (anti-TG).

Statistical analysis

Data was statistically analyzed using the Statistical Package of the Social Sciences (SPSS) version 23 software. Descriptive statistics have been displayed as mean ± standard deviation. To compare more than two means, a one-way ANOVA analysis was used. The significance threshold (p-value) was set at 0.05 in all statistical analyses, and the results have been reported as tables.

RESULTS

Table 1 demonstrates that the BMI of the PCOS group was significantly higher than the BMI in the healthy control group (P<0.001). Age of the case group was greater than that of the control group, but there was no statistically significant difference (P > 0.05). In comparison to the control group, the PCOS group had a greater percentage of female acne (71.1%).

Our study showed the TSH levels in women with PCOS to be considerably higher (3.28± 1.13) compared to participants without PCOS (2.88±1.09), p-value: (<0.001). LH levels in PCOS participants were also found to be substantially higher than in controls ($p <$ 0.001), and slightly increased in FT4 and FSH levels (Table 2).

Table 3 demonstrates that anti-TPO antibody levels were higher in the PCOS group (58.72 ± 18.60) than in the control group (22.25±15.9), and the difference to be statistically significant (p <0.001). Levels of anti-TG were higher in the PCOS group (88.66 ± 25.34) than in the control group (43.35 ± 27.02), and the difference was statistically significant (p <0.001).

DISCUSSION

Thyroid hormones have a variety of effects on the female reproductive system. Ovulatory dysfunction and reduced female fertility can be caused by changes in thyroid function, particularly hypothyroidism. Increased serum free testosterone, luteinizing hormone (LH), and elevated cholesterol are common symptoms of hypothyroidism and PCOS (10). Ovarian cysts retreat and ovarian volume reduces when thyroid hormone replacement therapy is started, in addition to stabilization of thyroid hormone levels (11). According to several studies, autoimmunity contributes to the etiology of PCOS, and women who have the condition are three to five times more likely to develop Hashimoto's thyroiditis (12,13). Both PCOS and Hashimoto's thyroiditis are linked to infertility and miscarriage in women of reproductive age, as well as comorbidities such as gestational hypertension, preeclampsia, premature delivery, postpartum haemorrhage, and low birth weight (14). Some autoimmune serologic indicators were raised in PCOS patients, and numerous systemic and organ-specific autoantibodies were discovered in PCOS patients (15).

Table 1: Participant demographics, both those with and without PCOS

Variables	PCOS group	Control group	P value
Age	27.200 ± 6.4433	26.700 ± 4.4272	0.76
BMI	27.4575 ± 1.70508	23.0571 ± 1.99720	<0.001
Acne	61(71.7%)	12(14%)	<0.001

Data presented as mean ± SD (standard deviation) or frequency and percentage;
BMI: Body mass index, PCOS: Polycystic ovary syndrome.

Table 2: Hormone profile of women with and without PCOS

Test	PCOS group	Control group	P value
FSH	8.68±5.93	6.621± 1.77	0.012
LH	10.88 ± 4.39	3.87 ± 1.58	<0.001
FT4	1.23 ± 0.57	1.24± 0.36	0.006
TSH	3.28± 1.13	2.88±1.09	<0.001

Data presented as mean ± SD

Table 3: Level and comparison of different auto-antibodies of participants with and without PCOS

Antibodies	PCOS group	Control group	P-value
Anti-TG	88.66 ± 25.34	43.35 ± 27.02	<0.001
Anti-TPO	58.72 ± 18.60	22.25 ±15.9	<0.001

Data presented as mean ± SD

The mean BMI of women in this study was greater in the PCOS group than in the control group, which is consistent with the findings of most prior investigations (16,17). PCOS is characterized by an increase in BMI. According to the proposed pathophysiological link between obesity and thyroid function, increased adipose tissue stimulates insulin resistance and the release of pro-inflammatory markers at the pituitary level via decreased deiodinase-2 activity, resulting in a relative T3 deficiency and an increase in TSH levels. Leptin is increased by adiposity, resulting in the hypothalamus releasing more TRH. Additionally,

leptin increases the amount of effector T cells while it lowers the number of regulatory T cells, which results in autoimmunity (17).

Our study also found that the prevalence of acne was more prevalent in women with PCOS than in controls, which is consistent with a study by Begum *et al*., (18) that found a higher frequency and proportion of acne in women with PCOS compared to normal women.

Thyroid measurements showed that PCOS patients had greater TSH but not a significant rise in T4 when compared to the control group. FSH and LH levels were found to be considerably higher after further hormonal testing. Pushpagiri *et al*. observed similar findings, with considerable high TSH and low FT3 and FT4 values in hypothyroid individuals (19). LH and FSH levels were found to be higher in PCOS individuals in the current investigation. Numerous *in vitro* experiments on both people and animals, suggest a substantial relationship between thyroid and ovary. Immunohistochemistry can identify thyroglobulin (TBG) and TSH receptors in bovine luteal cells, for example. The ability of reproductive axis to function is impacted by thyroid activity because human chorionic gonadotropin (HCG) has a thyroid stimulating hormone (TSH)-like action, and TSH has been observed to be greatly raised in ovarian hyperstimulation syndrome (OHSS) and PCOS patients (20).

In this study, anti-TPO antibody levels were slightly higher in PCOS than controls. Other researchers Sinha *et al*. suggested anti-TPO levels of 28±9.1 in PCOS and 26±8.2 in controls, while Ganie and Kalra documented anti-TPO antibody levels of 321±190 IU/mL in PCOS and 22±7.2 IU/mL in healthy controls (21).

In this study, although the mean anti-TG serum levels were greater in the PCOS group than in the control group, there was no statistically significant difference between the two groups, which is consistent with earlier studies (22,23). Studies with a population of Iranian women showed anti-thyroglobulin antibody (anti-Tg ab) prevalence to be significantly higher in PCOS patients than in healthy controls (23). A similar prospective multicenter study carried out in Germany had also shown a high prevalence of autoimmune thyroiditis in patients with PCOS (12).

A greater estrogen to progesterone ratio is typically seen in PCOS patients due to decreased progesterone secretion. In the absence of progesterone inhibitory effect, estrogen can increase the expression of interleukin-6 in T cells, over stimulating the immune system and increasing the risk of autoimmune diseases (24). Thyrocyte lysis and autoimmune hypothyroidism (Hashimoto's thyroiditis) are caused by TH1-mediated autoimmunity, whereas hyperthyroidism (Grave's disease) is caused by stimulatory TH2 reactions against the TSH receptor (25). An excess of testosterone has been associated with the suppression of most immune system elements, the activation of T suppressor cells, the promotion of the TH1 response, and the activation of CD8C in PCOS (26). Levels of progesterone may also restrict the development of macrophages, the synthesis of IL6, and the production of peripheral antibodies (27). Low levels of luteal phase progesterone and higher estrogen-to-progesterone ratios are common in the ovulatory cycles of women with PCOS, which may make them more susceptible to autoimmune illnesses. This heightened susceptibility could be related, at least in part, to estrogen immune system stimulatory effect (12). In contrast, while studies have suggested that androgens may protect against autoimmune illness, the influence of androgens on the immune system at levels seen in PCOS is likely insufficient to prevent autoimmunity (28).

CONCLUSION

The present findings show that PCOS was associated with increased positive results for thyroid autoantibodies in our population; in addition, the patients with PCOS had an increased risk of thyroid disorders. Serum autoantibodies against thyroid should be screened in women with PCOS

CONFLICT OF INTEREST

There are no conflicts of interest.

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