Original Article

Assessment of Thyroid Auto-antibodies in Euthyroid Infertile Women with Polycystic Ovarian Syndrome - A Cross-sectional Analytical Study

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Abstract

Background: Thyroid auto-antibodies could be one of the many causes of infertility in women, especially with polycystic ovarian syndrome (PCOS) with a prevalence of 5%–15%. Patients with anti-thyroid antibodies have shown significantly lower fertilisation rates, implantation rates, lower pregnancy rates and increased risk of first-trimester abortions when compared with those without anti-thyroid antibodies. **Aim:** The aim of the study was to assess the prevalence of thyroid auto-antibodies in euthyroid infertile women with PCOS and to compare the prevalence of thyroid autoantibodies in euthyroid infertile women with PCOS and without PCOS. **Settings and Design:** This is a cross sectional analytical study involving 132 Infertile women with and without PCOS visiting the department of OBG in a tertiary care center. The study was conducted for period of 2 years. **Materials and Methods:** A total of one hundred two women were enrolled in to the study. Sixty six women (66) had features of PCOS based on Rotterdam's criteria and 66 women were controls without PCOS features. Detailed history and examination were done for all women after taking informed and written consent. Previous hospital records were collected along with all biochemical investigations. The blood sample was collected for hormonal levels and thyroid auto-antibodies (anti-thyroid peroxidase [TPO] and anti-thyroglobulin [TG]) were assessed by enzyme-linked immunosorbent assay. The antibody levels were compared between the two groups along with the other parameters. **Statistical Analysis Used:** Statistical tests were done using SPSS version 26. The Chi-square test or Fisher's exact test would be used to study the association of categorical data like the presence of hirsutism, acne, etc. The association of independent variables with outcome variables was assessed using Chi-square. The $P < 0.05$ was considered significant with a confidence interval of 95%. **Results:** Anti-TPO antibody levels were found to be elevated in 25.4% of the PCOS group in comparison to only 3% of the non-PCOS group. Anti-TG antibodies of >100 U/mL were seen in 23 patients (34.3%) in PCOS group in comparison to two patients (3%) in non-PCOS group ($P = 0.001$). Both the antibodies (anti-TPO and anti-TG) were present in 21.2% of the PCOS group and 1.5% of the non-PCOS group. **Conclusion:** Women with PCOS were found to be 11 times more likely to have anti-TPO antibodies and 20 times more likely to have anti-TG antibodies compared to non-PCOS women. This heightened prevalence of anti-thyroid antibodies suggests that testing for these antibodies may be warranted in women with PCOS, even if they have normal thyroid function. However, further studies with larger sample sizes are needed to validate these findings.

Keywords: *Anti-thyroid antibodies, infertility, polycystic ovarian syndrome, thyroid autoimmunity*

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Introduction

Polycystic ovarian syndrome (PCOS) is a significant health issue among women of reproductive age. It affects a large percentage of this population (2.2%–26%)[1] and is known for being the leading cause of anovulatory infertility, meaning it prevents women from ovulating properly. In fact, PCOS is responsible for about 90%–95% of cases where women are infertile due to ovulation problems. In addition, women with PCOS face a higher risk of pregnancy loss, which further complicates their reproductive health.

On the other hand, autoimmune thyroid disorders are common in women of childbearing age and involve the immune system mistakenly attacking the thyroid gland. This attack often leads to the production of antibodies against the thyroid, such as anti-thyroid peroxidase (TPO) and anti-thyroglobulin (TG) antibodies. These disorders can occur even when the thyroid appears to be functioning normally, meaning many women may have these antibodies without showing any symptoms of thyroid problems.[2] This condition is called 'euthyroid', where thyroid function remains normal despite the presence of these antibodies.

Studies suggest that autoimmune thyroid disorders are more common in women with PCOS, with a prevalence of 5%–15% in this group.[3] Unfortunately, since these women often do not show immediate signs of thyroid dysfunction, the condition can remain undiagnosed until it progresses to hypothyroidism (underactive thyroid) later in life.[4] This lack of early detection may lead to serious consequences, especially for women trying to conceive.

This study hypothesises that infertile women with PCOS have a higher prevalence of autoimmune thyroid antibodies compared to infertile women without PCOS. The research involves comparing two groups of women – those with PCOS and those without – who are struggling with infertility. The aim is to determine how frequently autoimmune thyroid antibodies (such as TPO and TG antibodies) appear in both groups and then compare the results.

Higher prevalence of thyroid antibodies in women with PCOS could carry significant implications. For instance, healthcare providers might be able to identify autoimmune thyroid disorders earlier in women with PCOS, even in the absence of clear thyroid symptoms. Early detection could enable more effective management of both PCOS and thyroid conditions, potentially reducing risks like miscarriage.[1-3] In addition, these insights could inform more tailored infertility treatments for women with PCOS, potentially enhancing their chances of successful pregnancy outcomes.

Materials and Methods

This study was an analytical study (cross-sectional study) conducted at our tertiary care hospital for 2 years. The study was approved from the institute ethics committee and funded by institute intramural grant for research. Research was performed according to the 'World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects'. Written informed consent was obtained from all participants during the enrolment into the study.

The primary objectives of the study were to assess the prevalence of thyroid autoantibodies (anti-TPO and anti-TG) in euthyroid infertile women with PCOS and to compare the prevalence of thyroid autoantibodies in euthyroid infertile women with PCOS and without PCOS.

The sample size was estimated using the statistical formula for comparing two means with equal variance. The expected mean difference in anti-TPO antibody levels between the PCOS and controls was 20.4 ng/mL. The sample size was estimated using this as the minimum expected difference at 5% level of significance and 80% power. The sample size was calculated using OpenEpi.

Women between the age group of 21 and 40 years and with euthyroid status: (Thyroid-stimulating hormone [TSH]: 0.35–4.94 IU/mL, free T4 [FT4]: 0.7–1.48 ng/dL), infertile PCOS women according to Rotterdam 2003 criteria were included in the study. Infertile women with hypo/hyperthyroidism (deranged TSH and FT4 levels) or other endocrine abnormalities such as congenital adrenal hyperplasia, adrenal tumours, Cushing syndrome, women on oral contraceptive pills and corticosteroids were excluded. Based on the above criteria, a total of 132 women were enrolled for the study [Figure 1].

All participants meeting the inclusion and exclusion criteria were recruited into the study and an appropriate consent form approved by the ethics committee was used before data collection [Figure 1]. A detailed history was taken including current age, age at menarche, history of menstrual irregularity, acne, hirsutism, infertility, obstetric history, thyroid disorders, history of similar disorders in the family, contraceptive methods and the current medications. Clinical and anthropometric data including body mass index (BMI) and waist/hip ratio were ascertained for each participant. Biochemical parameters of all individuals were studied after 12 h of fasting on the 2nd–5th days of the follicular phase. TSH and FT4 levels were quantified. Enzyme-linked immunosorbent assay was used for the measurement of anti-TG antibody (anti-TG Ab) and anti-TPO Ab levels.

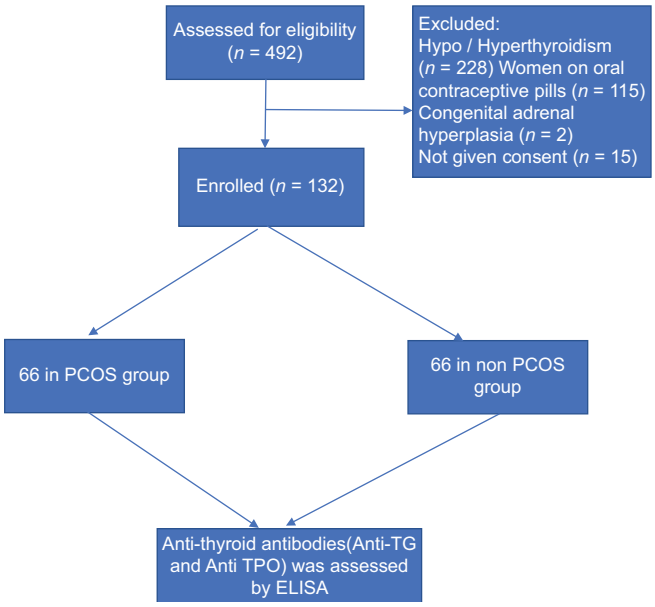

Figure 1: Flow chart showing subject inflow into the study. ELISA = Enzyme-linked immunosorbent assay, TG = Thyroglobulin, TPO = Thyroid peroxidase

Reference range is as follows for each: TSH levels: 0.35–4.94 μIU/mL, FT4: 0.7–1.48 ng/dL and anti-TPO levels: 0–0.9 U/mL – negative and >0.9 U/mL – positive. Anti-TG levels: 0–100 U/mL – negative, 100–150 U/mL – weakly positive and levels >150 U/mL – strongly positive. Levels above the upper limits of anti-TPO Ab and anti-TG Ab were considered positive. Data collection was done in researcher-designed pro forma and Epicollect prospectively after obtaining informed consent from the patient till December 2021.

Participants were divided into two groups: study group (Group A): euthyroid infertile women with PCOS attending the outpatient department/infertility clinic. Control group (Group B): euthyroid infertile women without PCOS attending outpatient department/infertility clinic. Various physical and biochemical parameters were compared between the two groups to compile the results.

Study variables and statistical tests

Continuous variables such as age, duration of infertility and various hormonal levels were analysed in two ways depending on their distribution. If they followed a normal distribution, they were expressed as means and assessed using a *t*-test. If they were not normally distributed, they were presented as medians and evaluated using the Kruskal–Wallis or Mann–Whitney test. For categorical variables, such as the presence of hirsutism, acne, biochemical hyperandrogenism (HA), irregular menstrual cycles, ultrasound features of PCOS and types of infertility (primary or secondary), either the Chi-square test or Fisher's exact test was used to study their associations.

The levels of anti-thyroid antibodies were compared between women with PCOS and those without. In addition, variations in these antibody levels among PCOS women were analysed according to different morphological classifications of PCOS. The Chi-square test was used to explore the relationships between independent variables and outcome variables. A $P < 0.05$ was considered statistically significant, with a 95% confidence interval (CI). All statistical analyses were performed using SPSS version 26.0 (Armonk, NY, USA: IBM Corp.).

Results

The demography profile and baseline characteristics of the participants are depicted in Table 1. Lean PCOS was observed in 34.3% of patients with a BMI (kg/m^2) of ≤24.9 and 14% of patients in the PCOS group were obese. Most of the patients in the non-PCOS group had a BMI of <24.9 (61%). The difference in BMI between both groups was statistically significant with $P < 0.01$.

A comparison of biochemical investigations between PCOS and non-PCOS groups is shown in Table 2. There was a statistically significant difference in testosterone and anti-Mullerian hormone (AMH) levels between both groups. Nearly 90% women with PCOS had HA in comparison to 10.6% in PCOS group. The mean TSH and FT4 were almost similar in both the groups as normal thyroid levels were mandatory for inclusion in the study.

Women in the PCOS group were classified based on the features of PCOS into four phenotypes. Phenotype A constituted around 58.2% of cases, Phenotype B accounted for 16.4%, Phenotype C constituted 14.9% and Phenotype D around 6% of the PCOS group. Serum testosterone was found to be highest in Phenotype A with the mean value of 88.8 ± 25.6 ng/dL compared to Phenotype B (78.1 ± 19.9 standard deviation) and Phenotype C (82.7 ± 23.8) and this difference was statistically significant ($P = 0.01$).

The levels of anti-thyroid antibodies in both groups are summarised in Table 3. Anti-TG antibody levels were elevated in 34.3% versus 3% and anti-TPO antibody levels were elevated in 25.4% versus 3% in the PCOS group in comparison to non-PCOS group, respectively, and this difference was statistically significant. Both the antibodies (anti-TPO and anti-TG) were present in 21.2% of the PCOS group and 1.5% of the non-PCOS group and this difference between both groups was statistically significant.

Among women with anti-TPO antibodies, 65% had phenotype A (HA + ovulatory dysfunction + polycystic ovarian) and similarly, 62.5% of those with anti-TG antibodies also fell into phenotype A. In contrast, 17.6%

of women with anti-TPO antibodies were classified under phenotype B and 18.7% of those with anti-TG antibodies belonged to phenotype C. Notably, none of the women with phenotype D had detectable anti-thyroid antibodies [Table 4].

Anti-TPO antibodies and anti-TG antibodies were found in women with PCOS than in the non-PCOS group with an odds ratio of 11.12 for anti-TPO and 20.8 for anti-TG antibodies with a CI of 95%. In other words, the risk of having anti-TPO antibodies in PCOS women was 11 times in comparison to non-PCOS women. Similarly, PCOS women had a 20 times higher risk of having anti-TG compared to those of non-PCOS women [Table 5]. No significant distribution pattern of anti-thyroid antibodies was observed when they were compared among various age groups, BMI groups and type of infertility both in PCOS and non-PCOS groups.

Discussion

The mean age of our study population was 28.7 ± 3.2 years, consistent with findings by Pratt *et al.*[4] The PCOS group typically had a higher mean age than the non-PCOS group across studies, as changes in ovarian morphology, androgen levels and ovulatory function with age can make diagnosing PCOS more challenging in younger women. Most of the women with PCOS features were obese consistent with other studies[5,6] and this may be often driven by androgen-related lipolysis, insulin resistance, hyperinsulinaemia and increased steroidogenesis, which are further associated with heightened luteinising hormone (LH) release and anovulatory cycles.[7] This prolonged infertility period observed in PCOS women is similar to Ganesh *et al.*'s study[8] and is commonly linked to anovulatory cycles in PCOS, driven by neuroendocrine or hypothalamic–pituitary–ovarian (HPO) axis dysfunction, as well as ovarian factors causing hyperandrogenaemia.

The mean hormonal levels (LH, follicle-stimulating hormone [FSH], TSH and prolactin) were comparable between both the groups, which was similar to the various studies.[6,9-11] High levels of TSH adversely affect the metabolic and hormonal profile in PCOS leading to anovulation[7] hyperprolactinaemia in PCOS could be explained by a decrease in the dopaminergic tone in PCOS women leading to high levels of LH and prolactin. Another hypothesis suggests that PCOS causes hyperprolactinaemia because of relative hyperestrogenemia.[12] This increased prolactin suppresses FSH and LH leading to anovulation. Elevated levels of LH levels in our study were comparable to the study done by Garelli *et al.*,[13] which may be due to the dysregulation of the neuroendocrine system leading to the imbalance in HPO axis which causes overproduction of gonadotrophins. This gonadotrophins further favours increased LH production causing hyperplasia of theca cells, increased number of follicles and HA leading to polycystic ovaries, anovulation, hirsutism, alopecia and insulin resistance.[14] Various studies showed increase in testosterone levels in women with PCOS[15-17] similar to our study and this can be attributed to HA and hyperinsulinaemia commonly seen in PCOS women where hyperinsulinaemia secondary to insulin resistance causes reduced sex hormone binding globulin (SHBG) and hence increased levels of androgens.

Table 1: Baseline characteristics of the study population

Variables	PCOS	Non PCOS
Age in years		
Mean (SD)	28.73 (3.28)	29.27 (3.97)
BMI		
Mean (SD)	26.52 (4.6)	24.31 (3.1)
Type of infertility - Number (%)	57(86.3)	42(63.3)
Primary	9(13.6)	24(36.3)
secondary		
Number of years of infertility		
Mean (SD)	5.3 (2.21)	4.2 (4.2)
Ovulatory dysfunction - Number (%)		
Irregular	56(83.6)	10(14.6)
Regular	10(14.6)	56(83.6)
FSH mIU/mL-Mean (SD)	7.41(6.7)	10.35(6.3)
LH mIU/mL -Mean (SD)	8.9(5.4)	2.1 – 92
Prolactin ng/mL -Mean (SD)	14.4(7.7)	12.4 (5.6)
Testosterone ng/mL -Mean (SD)	82.0(26.3)	46.07 (20.9)
AMH ng/mL -Mean (SD)	6.3(5.1)	2.77 (1.8)
TSH mcgIU/mL -Mean (SD)	2.69(1.05)	2.2 (0.81)

Table 2: Hormone levels in different phenotypes

	FSH Mean (SD)	LH Mean (SD)	Prolactin Mean (SD)	Testosterone Mean (SD)	AMH Mean (SD)
*P**	0.911	0.108	0.499	<0.001	0.980
Phenotype A	7.71(8.5)	9.37(4.9)	14.34(8.8)	88.81(25.6)	7.14(3.6)
Phenotype B	6.61(2.04)	6.18(4.2)	14.5(5.5)	78.1(19.9)	6.4(3.3)
Phenotype C	6.4(2.1)	8.2(3.9)	12.4(5.7)	82.7(23.8	6.1(5.12)
Phenotype D	8.4(3.4)	12.6(10.1)	18.6(5.7)	44.2(10.4)	6.22(5.8)

*ANOVA test is used for comparing multiple means

Table 3: Distribution of anti-thyroid antibodies in cases and controls

Anti-thyroid antibodies	PCOS (%)	Non-PCOS (%)	*P**
Anti-Thyroid peroxidase antibody	17(25.4)	2 (3)	<0.01
Anti-Thyroglobulin antibody	16(23.9)	1 (1.5)	<0.01
Both of the Antibodies	14(21.2)	1 (1.5)	<0.01

*Chi-square test was used to calculate the *P* value

Table 4: Anti-thyroid antibodies compared in PCOS phenotypes

Phenotype	Anti-thyroid antibodies	
	Anti-TPO (*n*=17) *P=0.51	Anti-TG (*n*=16) *P=0.53
Phenotype A/Full blown PCOS	11 (64.7)	10 (62.5)
Phenotype B/NonPCO PCOS	3 (17.6)	3 (18.7)
Phenotype C/Ovulatory PCOS	3 (17.6)	3 (18.7)
Phenotype D/Nonhyperandrogenic PCOS	0	0

*Chi-square test was used to calculate the *P* value

Table 5: Risk of having anti-thyroid antibodies in PCOS and Non PCOS groups

	Anti-TPO	Odds ratio 95% CI	Anti-TG	Odds ratio 95% CI
PCOS	17	11.12	16	20.8
NON-PCOS	2		1	

In our study, the prevalence of anti-thyroid antibodies in euthyroid PCOS women was higher (anti-TPO: 25.4%, anti-TG: 23.9%) in comparison to euthyroid non-PCOS women which was similar to the studies done by Abbara *et al*.[9] and Hepsen *et al*.[6] In a systematic review and meta-analysis done by Romitti *et al*.[18] on the association between PCOS and anti-thyroid antibodies, they found an increased prevalence of anti-thyroid antibodies in PCOS women with odds ratio of 3.27 and CI of 2.32–4.63. Studies have shown the association between inflammation and autoimmunity in women with PCOS and also chronic low-grade inflammation has been linked to obesity and metabolic manifestations in PCOS.[18]

It has been hypothesised that the prevalence of anti-thyroid antibodies in PCOS women could be due to the low levels of progesterone in PCOS leading to hyper-stimulation of the immune system, which further led to the production of various auto-antibodies in PCOS.[18] Although, a study done by Van Gelderen and Gomes dos Santos[19] suggested the role of anti-ovarian antibodies in explaining the pathophysiology of PCOS, similar to other studies done by Petríková *et al*.[20] proposed the role of non-organ specific antibodies in PCOS leading to systemic immune activation. This was further supported by the study conducted by Quintero *et al*.[21] who showed the association of androgen excess leading to the reduction of immune system elements, increased suppressor T-cell activity and promotion of TH1 response altogether contributing to autoimmunity.

Further, our study is also comparable with studies conducted by Karaköse *et al*.[5] Menon and Ramachandran,[16] Arora *et al*.[15] Janssen *et al*.,[22] but these studies were done in patients with underlying thyroid disorders. Therefore, it can be concluded that the prevalence of thyroid autoantibodies in euthyroid status is comparable to the prevalence of thyroid auto-antibodies in patients with underlying thyroid disorders, thus warranting the need to investigate for anti-thyroid antibodies in euthyroid status.

The mean levels of AMH in PCOS women in our study who had tested positive for thyroid autoantibodies were higher in comparison to those who tested negative for thyroid auto-antibodies. This was comparable to the study done by Garelli *et al*.[13] However, a study done by Adamska *et al*.[23] showed low levels of AMH in women who tested positive for antibodies. This variation in AMH levels in PCOS could be explained by the study done by Hasegawa *et al*.[24] who suggested that thyroid autoimmunity can be implicated in the depletion of follicles in adults following extensive activation of primordial follicles in adolescents. However, further studies are required to study the association between thyroid autoimmunity and AMH levels in PCOS.

Several factors could have been further addressed in this study to strengthen its findings. A family history of thyroid autoimmunity, which may act as a confounding factor, was not accounted for. In addition, follow-up of patients for pregnancy outcomes among those who tested positive for anti-thyroid antibodies was not conducted. The relationship between anti-thyroid antibodies and clomiphene citrate resistance or failure was also not assessed, which could provide insight into treatment outcomes. Finally, a larger sample size could have improved the study's statistical power and the generalisability of the results.

Conclusion

In this study, 25.4% of euthyroid, infertile women with PCOS tested positive for anti-TPO antibodies and 23.9% for anti-TG antibodies. In contrast, only 3% and 1.5% of women without PCOS had anti-TPO and anti-TG antibodies, respectively. This indicates that women with PCOS are at an 11-fold higher risk of having anti-TPO antibodies and a 20-fold higher

risk for anti-TG antibodies compared to non-PCOS women. These findings suggest that screening for anti-thyroid antibodies may be beneficial in women with PCOS, even when they show normal thyroid function. Larger studies are needed to confirm these results and support broader screening recommendations.

Author contribution

All the authors were involved in concept, design, literature search, data collection and analysis, statistical analysis and manuscript preparation.

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Conflicts of interest

There are no conflicts of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to restrictions (their containing information that could compromise the privacy of research participants).

References

1. Poppe K, Glinoer D, Van Steirteghem A, Tournaye H, Devroey P, Schiettecatte J, *et al.* Thyroid dysfunction and autoimmunity in infertile women. Thyroid 2002;12:997-1001.
2. Artini PG, Uccelli A, Papini F, Simi G, Di Berardino OM, Ruggiero M, *et al.* Infertility and pregnancy loss in euthyroid women with thyroid autoimmunity. Gynecol Endocrinol 2013;29:36-41.
3. Geva E, Amit A, Lerner-Geva L, Azem F, Yovel I, Lessing JB. Autoimmune disorders: Another possible cause for *in-vitro* fertilization and embryo transfer failure. Hum Reprod 1995;10:2560-3.
4. Pratt D, Novotny M, Kaberlein G, Dudkiewicz A, Gleicher N. Antithyroid antibodies and the association with non-organ-specific antibodies in recurrent pregnancy loss. Am J Obstet Gynecol 1993;168:837-41.
5. Karaköse M, Hepsen S, Çakal E, Saykı Arslan M, Tutal E, Akın Ş, *et al.* Frequency of nodular goiter and autoimmune thyroid disease and association of these disorders with insulin resistance in polycystic ovary syndrome. J Turk Ger Gynecol Assoc 2017;18:85-9.
6. Hepşen S, Karaköse M, Çakal E, Öztekin S, Ünsal İ, Akhanlı P, *et al.* The assessment of thyroid autoantibody levels in euthyroid patients with polycystic ovary syndrome. J Turk Ger Gynecol Assoc 2018;19:215-9.
7. Sam S, Scoccia B, Yalamanchi S, Mazzone T. Metabolic dysfunction in obese Hispanic women with polycystic ovary syndrome. Hum Reprod 2015;30:1358-64.
8. Ganesh A, Goswami SK, Chattopadhyay R, Chaudhury K, Chakravarty B. Comparison of letrozole with continuous gonadotropins and clomiphene-gonadotropin combination for ovulation induction in 1387 PCOS women after clomiphene citrate failure: A randomized prospective clinical trial. J Assist Reprod Genet 2009;26:19-24.
9. Abbara A, Eng PC, Phylactou M, Clarke SA, Hunjan T, Roberts R, *et al.* Anti-müllerian hormone (AMH) in the diagnosis of menstrual disturbance due to polycystic ovarian syndrome. Front Endocrinol (Lausanne) 2019;10:656.
10. Latha P, Ravi BV, Sadaria R. Study of TSH and prolactin in PCOS subjects: A case control study. Int J Clin Biochem Res 2021;8:62-5.
11. Mustari M, Hasanat M, Hasan Q, Tuqan S, Emran MS, Aktar N, *et al.* Association of altered thyroid function and prolactin level in polycystic ovarian syndrome. Bangladesh Med J 2016;45:1-5.
12. Delcour C, Robin G, Young J, Dewailly D. PCOS and hyperprolactinemia: What do we know in 2019? Clin Med Insights Reprod Health 2019;13:1-7.
13. Garelli S, Masiero S, Plebani M, Chen S, Furmaniak J, Armanini D, *et al.* High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2013;169:248-51.
14. Fauser BC, Pache TD, Lamberts SW, Hop WC, de Jong FH, Dahl KD. Serum bioactive and immunoreactive luteinizing hormone and follicle-stimulating hormone levels in women with cycle abnormalities, with or without polycystic ovarian disease. J Clin Endocrinol Metab 1991;73:811-7.
15. Arora S, Sinha K, Kolte S, Mandal A. Endocrinal and autoimmune linkage: Evidences from a controlled study of subjects with polycystic ovarian syndrome. J Hum Reprod Sci 2016;9:18-22.
16. Menon M, Ramachandran V. Antithyroid peroxidase antibodies in women with polycystic ovary syndrome. J Obstet Gynaecol India 2017;67:61-5.
17. Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN, Pal SK. Thyroid disorders in polycystic ovarian syndrome subjects: A tertiary hospital based cross-sectional study from Eastern India. Indian J Endocrinol Metab 2013;17:304-9.
18. Romitti M, Fabris VC, Ziegelmann PK, Maia AL, Spritzer PM. Association between PCOS and autoimmune thyroid disease: A systematic review and meta-analysis. Endocr Connect 2018;7:1158-67.
19. van Gelderen CJ, Gomes dos Santos ML. Polycystic ovarian syndrome. Evidence for an autoimmune mechanism in some cases. J Reprod Med 1993;38:381-6.
20. Petríková J, Lazúrová I, Yehuda S. Polycystic ovary syndrome and autoimmunity. Eur J Intern Med 2010;21:369-71.
21. Quintero OL, Amador-Patarroyo MJ, Montoya-Ortiz G, Rojas-Villarraga A, Anaya JM. Autoimmune disease and gender: Plausible mechanisms for the female predominance of autoimmunity. J Autoimmun 2012;38:J109-19.
22. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol 2004;150:363-9.
23. Adamska A, Łebkowska A, Krentowska A, Hryniewicka J, Adamski M, Leśniewska M, *et al.* Ovarian reserve and serum concentration of thyroid peroxidase antibodies in euthyroid women with different polycystic ovary syndrome phenotypes. Front Endocrinol (Lausanne) 2020;11:440.
24. Hasegawa Y, Kitahara Y, Osuka S, Tsukui Y, Kobayashi M, Iwase A. Effect of hypothyroidism and thyroid autoimmunity on the ovarian reserve: A systematic review and meta-analysis. Reprod Med Biol 2022;21:e12427.