Evaluation of Antithyroid Antibodies in Polycystic Ovarian Syndrome of Reproductive Women

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Abstract

Background: Polycystic Ovarian Syndrome (PCOS) is common but a treatable cause of infertility in reproductive women. Thyroid hormone abnormality is commonly seen in Polycystic Ovarian Syndrome of reproductive women. Antithyroid antibodies have been detected in women with PCOS. The aim of the present study is to evaluate the antithyroid antibodies in Polycystic Ovarian Syndrome (PCOS) of reproductive women.

Materials and methods: A hospital based cross-sectional comparative study was conducted in the outpatient Department of Obstetrics and Gynaecology in CMCH, Institute of Nuclear Medicine and Allied Subject and the Department of Biochemistry in CMC. Eighty (80) PCOS women diagnosed by ultrasonography were taken by non-probability convenient sampling, considered as group A and another twenty (20) healthy women were taken, considered as group B. Important variables in this study were serum anti-TPO antibody, anti-Tg antibody, TSH, age, menstrual history, hirsutism, waist circumference and BMI.

Results: This study revealed a statistically significant higher prevalence of autoimmune thyroiditis in PCOS cases in comparison to healthy group (32.5 % and 37.5% patients had increased anti-TPO and anti-Tg antibodies respectively). Mean serum anti-TPO and anti-Tg antibodies were increased significantly in PCOS cases than that of healthy women group. Mean serum TSH was not increased significantly in PCOS cases than that of healthy group.52.5%, 47.5% patients had oligomenorrhea and amenorrhea respectively, 21.2% had hirsutism, 68.8% cases were overweight & obese and 77.5% were central obese.

Conclusion: High prevalence of thyroid autoimmunity in euthyroid PCOS patients refers to the importance of screening not only thyroid hormone levels but also thyroid antibody level during the investigation of PCOS of reproductive women and thereby early diagnosis and management of infertility associated with PCOS.

Key words: Anti thyroid antibodies; Autoimmune thyroiditis; Polycystic Ovarian Syndrome (PCOS).

Introduction

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrinopathies among women of child bearing age and cause of infertility.[1] Menstrual irregularity, hyperandrogenism, and infertility are the main key symptoms of PCOS.[2] The prevalence of PCOS is continuously growing and increasing in parallel with type 2 diabetes mellitus (T2DM)in all over the world.[3] The number of women affected worldwide by PCOS were approximately 116 million.[4] The prevalence of PCOS is generally considered to be between 6-20% depending on population characteristics and diagnostic criteria.[5-6] In Bangladesh, considering infertility, 28.8% women were diagnosed as PCOS patients in a teaching hospital.[7]

According to revised Rotterdam criteria in 2003 developed by the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine Rotterdam consensus (ESHRE/ASRM)) which require the presence of at least two of the three following indications.[8]

- Ovulatory disturbances mainly oligomenorrhoea or amennorhoea.
- Hyperandrogenism as defined either clinically by hirsutism, severe acne, seborrhoea or biologically by the elevated levels of total or free testosterone.
- Polycystic ovaries at ultrasonography.[6]

In PCOS, the level of progesterone is reduced that cannot suppress GnRH/LH pulse frequency. As a result, increased estrogen secretion may produce autoantibodies including anti-nuclear, anti-thyroid and anti-islet cell antibodies.[9]

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Autoimmune Thyroid Diseases (AITD) is considered as most common cause of hypothyroidism in young women as well as most frequent autoimmune disorder which affects 5–20 % of women during childbearing age.[10] In addition, thyroid autoimmunity and adverse pregnancy outcomes have been reported in most PCOS patients' during their childbearing age. Therefore, to ensure the best possible outcome for the mother and progeny, it is crucial to maintain normal thyroid function before and during pregnancy.[11]

In Bangladesh there is insufficient data regarding the prevalence of thyroid dysfunction and thyroid autoimmunity in PCOS patients. The aim of this study is trying to perform a cross-sectional comparative study comparing the measurement of thyroid autoantibodies (Anti-TPO antibody, anti-Tg antibody) in PCOS patientsand to find out the antithyroid antibodies in PCOS of the reproductive women group as well as to find out the association between PCOS and autoimmune diseases.

Materials and methods

A hospital based cross-sectional comparative study was conducted in the outpatient Department of Obstetrics and Gynaecology in Chittagong Medical College Hospital (CMCH) Institute of Nuclear Medicine and Allied Subject and the Department of Biochemistry in Chittagong Medical College from July 2020 to June 2021. Permission for this study was taken from the concerned departments and ethical review committee.

Women with the sign of hyperandrogenism/ oligomenorrhoea, amenorrhea who visited Out-patient Department (OPD) of obstetrics and gynecology in CMCH was included in the study. In this study, PCOS patients were diagnosed by ultrasonography. Women who have medical conditions that cause irregular menstrual cycles and androgen excess such as hyperprolactinemia, hypothyroidism and hyperthyroidism, chronic liver and renal disease cushing's syndrome are excluded from the study.

To include only euthyroid subject, women with abnormal Thyroid Stimulating Hormone (TSH) levels excluded from the study. Women in group (Group-B) were healthy reproductive women with regular menstrual cycle, fertile as well as no signs and symptoms of PCOS and other medical disorders.

After taking a brief history and the preliminary selection was completed and the aim of the study was clarified in-depth to each subject and their detailed written consent was taken. A detailed history was taken. All findings were recorded, in a predesigned data collection form. Anthropometric measurements of each subject were taken. And required blood samples were collected from the subject.

All the data were processed and analyzed using Microsoft Excel and IBM-SPSS (Statistical Package for Social Science) V 22.0 for Windows. Statistical inference was based on 95% Confidence Interval (CI) and p value ≤0.05 was considered statistically significant. Variables (Age, BMI, waist circumference, anti-TPO Ab, anti-Tg Ab, serum TSH) were expressed as mean ± Standard Error of Means (SEM). Comparison between two groups were done using Student t-test. Chi-square test were used to measure the significance of association between categorical variables. The summarized data was presented in the form of tables and figures.

Results

In this cross-sectional comparative study, a total number of 100 subjects with the age range of 15 to 40 years were enrolled according to inclusion criteria and designed into PCOS cases and healthy reproductive women. Group A considered of 80 PCOS patients and group B contained 20 healthy reproductive females (Figure 1).
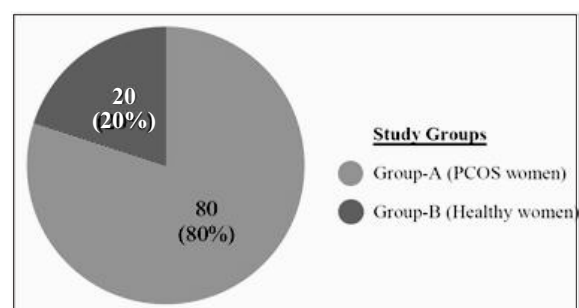

Fig 1 Pie chart shows distribution of the study groups (n = 100)

Table I Distribution of baseline socio-demographic characteristics among the study groups. (n=100)

Socio-demographic Variables		Study Groups				Total (n = 100)	
		Group A (n = 80)		Group B (n = 20)			
		n	%	n	%	n	%
Age in Groups	< 20 Years	22	27.5	0	0	22	22
	20 – 30 Years	49	61.2	10	50	59	59
	> 30 Years	9	11.2	10	50	19	19
Socio-Economic Status	Upper class	20	25	5	25	25	25
	Middle class	35	43.8	8	40	43	43
	Lower class	25	31.2	7	35	32	32

Table I shows the distribution of baseline socio-demographic characteristics among study groups. Most of the participants (49%) were in the age group of 20-30 years. Groups A and group B participants equally resided in the upper, middle and lower classes.

Table II Distribution of clinical variables among the study groups (With Chi-square (χ^2) test significance) (n = 100)

Risk Factors		Study Groups		Total (n = 100)	p Value
		Group A (n = 80)	Group B (n = 20)		
Menstrual History	Regular	0 (0.0)	20 (100.0)	20 (20.0)	p < 0.001 Highly
	Oligomenorrhea	42 (52.5)	0 (0.0)	42 (42.0)	Significant
	Amenorrhea	38 (47.5)	0 (0.0)	38 (38.0)	
Hirsutism	Present	17 (21.2)	0 (0.0)	17 (17.0)	p < 0.05 Significant
	Absent	63 (78.8)	20 (100.0)	83 (83.0)	
Family History of PCOS	Yes	14 (17.5)	0 (0.0)	14 (14.0)	p < 0.05 Significant
	No	66 (82.5)	20 (100.0)	86 (86.0)	

Figures within parentheses indicate percentages.

Table II shows distribution of menstrual history, hirsutism, and family history of PCOS between group A & B are statistically significant (p<0.05).

Table III Distribution of anthropometric status among the study groups (With Chi-square (χ^2) test significance) (n = 100)

Anthropometric Status		Study Groups		Total (n = 100)	p Value
		Group A (n = 80)	Group B (n = 20)		
BMI Status	Overweight & Obese	55 (68.8)	8 (40.0)	63 (63.0)	p < 0.05
	Normal	25 (31.2)	12 (60.0)	37 (37.0)	Significant
WC Status	Central Obese	62 (77.5)	8 (40.0)	70 (70.0)	p < 0.01
	Normal	18 (22.5)	12 (60.0)	30 (30.0)	Highly Significant

Figures within parentheses indicate percentages.

Table III describes BMI is statistically significant in two study groups.

● 68.8% of patients in group A and 40% of patients in group B are overweight & obese (p<0.05).

● Regarding waist circumference, two groups are statistically significant. 77.5% of patients in group A and 40% of patients in group B are central obese (p<0.01).

Table IV Association between serum anti-thyroid antibody status and the study groups (With Chi-square (χ^2) test significance) (n = 100)

Serum anti-thyroid antibody Status		Study Groups		Total (n = 100)	χ^2 Value	p Value
		Group A (n = 80)	Group B (n = 20)			
Serum Anti-TPO Ab Status	Increased	26 (32.5) χ^2 (10.0)	2 (10.0)	28 (28.0)	χ^2 =4.018	p < 0.05
	Normal	54 (67.5)	18 (90.0)	72 (72.0)		Significant
Serum Anti-Tg Ab Status	Increased	30 (37.5)	2 (10.0)	32 (32.0)	χ^2 =5.561	p < 0.05
	Normal	50 (62.5)	18 (90.0)	68 (68.0)		Significant

Figures within parentheses indicate percentages.

Table IV shows increased anti-TPO Ab and anti-Tg Ab that are significantly associated in group A than that of group B. In group A, 32.5% of patients have increased anti-TPO Ab and 37.5% of patients have increased anti-Tg Ab.

Table V Distribution of Serum Anti-Thyroid Antibody and serum hormoneamong the study groups (With independent samples t - test significance) (n = 100)

	Study Groups	N	Mean	± SEM	Range	p Value
Serum Anti-TPO Ab (IU/ml)	Group A	80	95.33	13.62	28.00 – 550.00	p < 0.05
	Group B	20	32.73	4.87	24.00 – 120.00	Significant
	TOTAL	100	82.81	11.21	24.00 – 550.00	
Serum Anti-Tg Ab (IU/ml)	Group A	80	91.75	9.24	21.26 – 340.00	p < 0.01
	Group B	20	38.58	3.73	19.68 – 97.22	Highly
	TOTAL	100	81.11	7.72	19.68 – 340.00	Significant
Serum TSH (IU/ml)	Group A	80	2.21	0.11	0.75 – 4.10	p > 0.05
	Group B	20	2.87	0.19	1.29 – 4.20	Not
	TOTAL	100	2.34	0.1	0.75 – 4.20	Significant

Table V shows mean serum anti-TPO Ab is statistically significant in group A than that of group B (95.33 ± 13.62 vs 32.73 ± 4.87). Also mean serum anti-Tg Ab is statistically highly significant in group A than that of group B (91.75 ± 9.24 vs 38.58 ± 3.73).And mean Serum TSH was not statistically significant in group A than that of group B. (2.21 ± 0.11 mIU/ml vs 2.87 ± 0.19 mIU/ml, p>0.05).

Discussion

In the present study, thyroid autoimmunity was significantly associated with Polycystic Ovarian Syndrome (PCOS). PCOS had a significantly

higher level of antithyroid antibodies compared to healthy normal reproductive females. This study was conducted in euthyroid subjects with PCOS, and this observation gives importance to the investigation of thyroid autoimmunity in such group of patients. Patients with anti-TPO and anti-Tg antibodies may develop thyroid dysfunction later in life.[12]

About thirty-two-point five percent (32.5%) of PCOS patients had increased anti-TPO Ab and about thirty-seven-point five percent (37.5%) of PCOS patients had increased anti-Tg Ab in comparison to healthy group (Table IV). The antithyroid antibodies were significantly associated in subject with PCOS. These findings are very close to the findings of Al-Saab et al, Ozdemir et al, Calvar et al, Maya Menon et al.[11-14]

Mean level of anti-TPO and anti-Tg antibodies were statistically increased in group A than that of group B (Table V). The mean ± SD of serum anti-TPO was (95.33± 13.62) and (32.73 ± 4.87 IU/ml) in group A and in group B respectively (p<0.05). The mean of anti-Tg antibody level was (91.75 ± 9.24 IU/ml) and (38.54 ± 3.73 IU/ml) in group A and group B respectively (p<0.01). These findings are very close to the findings of Janseen et al, Ozdemir et al.[15,13]

In this study, there was no significant differences in the serum TSH level in group A (2.21 ± 0.11 mIU/ml) and group B (2.87 ± 0.19 mIU/ml) (Table V). Al-Saab at el, Sema Hepsen et al also found the same findings. But Janseen et al, Maya Menon et al, Poppe et al found TSH levels were higher in patients with PCOS.[11,12,15-17] This difference may be attributed to the course of the autoimmune thyroiditis. This may be explained by considering that only euthyroid subjects were included in this study.

Menstrual history and hirsutism were significantly associated in two groups (Table II). Patients having symptoms of menstrual disturbance in the form of oligomenorrhoea was (52.5%) or amenorrhea was (47.5%) in PCOS group (Table II). This was also reflected in other studies.[18,19] In this study, hirsutism was detected only in twenty one point two percent (21.2%) of PCOS patients (Table II). Najem, et al, and Marco c Amato, et al also observed to have hirsutism.[19,20]

In this study BMI and waist circumference was also significantly higher in group A than that of group B,68.8% of participants were overweight (BMI>25) (Table III). This is similar to the findings of the findings of Pasquali et al and Kiddy et al.[21,22] But findings of this study differed from that of Alnakash et al.[23] The explanation for higher frequency of obesity and overweight in this study may be attributed to the food habits, lack of exercise in Bangladeshi women.

The fundamental markers of thyroid autoimmunity are anti-thyroid peroxidase antibodies (Anti-TPO Ab) and antithyroglobulin antibodies (Anti-Tg Ab). Poppe et al has conducted a study and he demonstrated that thyroid auto antibodies are significantly higher in infertile patients.[24] In PCOS patients, thyroid hormones follow up are considered important because of medically treatable infertility.[25] In developed countries, 10 15% of couples suffer from infertility.[26] Thyroid autoimmunity is related to recurrent miscarriages as well as primary and secondary infertility.

In Bangladesh, recently Mustari et al. found that 21% of PCOS patients have thyroid dysfunction.[27] There is an association between PCOS and autoimmune diseases such as Anti-Nuclear (ANA) and anti-TPO and different autoantibodies have been documented in PCOS. Thus, it is suspected that there are autoantibodies that may affect the long term clinical treatment in these patients.[28]

The exact prevalence of Autoimmune Thyroid Diseases (AITD) in PCOS in the Bangladeshi population is unknown. PCOS is the most common reason for medically treatable anovulatory dysfunction and infertility.[25] In addition, PCOS is one of the causes of infertility but the association with AITD is also a known cause of infertility. Therefore, the association of PCOS with AITD may increases the rate of infertility and consequently the adverse outcome of the patient.

Limitations

This study has certain limitations which include:

i) Sample size in the present study was small that may not reflect generalization of the findings to that of reference population

ii)This study was conducted in a single center

iii) Cross sectional study lowered its strength

iv) The anthropometric measurements were done once and certain error cannot be excluded.

Conclusion

From this study, it can be concluded that serum antithyroid antibodies (Anti-TPO Ab, anti-Tg Ab) are significantly increased in PCOS patients. Due to high prevalence of thyroid autoimmunity in euthyroid PCOS patients, there is importance of screening not only thyroid hormone levels but also levels of antithyroid antibodies during the investigation of PCOS of reproductive women. So, the assessment of antithyroid antibodies (Anti-TPO Ab, anti-Tg Ab) in Polycystic Ovary Syndrome (PCOS) may give a baseline information regarding early diagnosis and management of infertility associated with PCOS.

Recommendations

● Multicenter study with large sample size should be done to get a broader concept.

● More researchers may be forwarded to formulate baseline investigations regarding association of thyroid autoimmunity with PCOS.

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Contribution of authors

S A- Conception, design, acquisition of data, data analysis, drafting and final approval.

N T- Interpretation of data, critical revision and final approval.

M H I-Interpretation of data, critical revision and final approval.

P A-Data analysis, critical revision and final approval.

P K- Interpretation of data, drafting and final approval.

U S- Acquisition of data, critical revision and final approval.

Disclosure

All the authors declared no competing interests.

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