

Frequency and Pattern of Thyroid Dysfunction in Patients with Polycystic Ovary Syndrome

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ABSTRACT

Objective: To determine the frequency and pattern of thyroid dysfunction in patients with polycystic ovary syndrome.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Endocrinology, Jinnah Hospital, Lahore Pakistan, from Jan to Jun 2017.

Methodology: Seventy-seven patients diagnosed with PCOS, based on Rotterdam criteria, were enrolled in the study. Thyroid function status was evaluated using measurement of serum thyroid-stimulating hormone (TSH), free T₃, T₄ and anti-thyroperoxidase (anti-TPO) antibodies.

Results: The mean age of the study population was 29.0±9.2 years. Out of 77 females with PCOS, 63(81.8%) were euthyroid, five (6.5%) patients were diagnosed with primary hypothyroidism, and nine (11.7%) were found to have subclinical hypothyroidism. Anti-TPO antibodies were detected in 18 patients (23.4%), including 12(19.0%) euthyroid females.

Conclusion: Thyroid dysfunction was found among patients with PCOS. Evidence of autoimmunity was seen even in euthyroid patients.

Keywords: Anti-TPO, Polycystic ovarian syndrome, Thyroid autoimmunity, Thyroid dysfunction.

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a common multifactorial, heterogeneous endocrine disorder often associated with clinical and biochemical hyperandrogenism due to ovarian dysfunction.¹ Biochemical and hormonal abnormalities play a crucial role in making this syndrome a major cause of anovulatory menstrual cycles leading to infertility.²

Hyperinsulinemia and insulin resistance are the two major factors responsible for the pathophysiology of PCOs.³ About 75% of affected females with PCOS were observed to have insulin resistance and hyperinsulinemia, and approximately 50% have high levels of luteinizing hormone (LH).⁴ Insulin resistance accompanied by compensatory hyperinsulinemia leads to early luteinizing hormone sensitivity of the follicle, which in turn leads to ovarian stimulation resulting in excess adrenal and ovarian androgen production.⁵ This hyperandrogenism is responsible for anovulation and certain clinical features of PCOS.

It is well known that thyroid hormones affect several aspects of human reproduction. The role of thyroid hormones is crucial in the maturity and development of human reproductive organs. Not only is thyroid hormone development critical for the appropriate functioning of the female reproductive organs,

Thyroid dysfunction, but either hyperthyroidism or hypothyroidism also has a significant effect on oestrogen and androgen metabolism.⁵ Thyroid dysfunction can present with menstrual abnormalities, subfertility, fertility, miscarriages, pre-eclampsia, intrauterine growth restriction, preterm labour, mental retardation in the foetus and increased risk of postpartum thyroiditis in females.^{6,7} Being a reproductive endocrine disorder, patients with PCOS are adversely affected by associated thyroid dysfunction. Both are independent risk factors for ovarian failure and pregnancy-related complications. Commonly seen thyroid abnormalities in females include primary hypothyroidism, subclinical hypothyroidism, and hyperthyroidism. The most common cause of hypothyroidism in adolescence and females during their reproductive age is autoimmune thyroiditis. In the general population, the prevalence of subclinical hypothyroidism has been reported at around 4-10%, but relatively low in reproductive years, estimated around about 3-6%.^{7,8}

Similarly, recent studies have highlighted a relationship between PCOs and thyroid abnormalities. It is emphasized that there is an increased incidence of thyroid dysfunction, especially autoimmune thyroiditis, in patients with PCOS. The potential pathogenic link responsible for developing thyroid dysfunction in females with PCOS is not fully understood. However, similar factors like genetic susceptibility and autoimmunity contribute to developing thyroid dysfunction in females with PCOs.⁹⁻¹⁰ It is important to diagnose

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thyroid abnormalities early in patients with PCOS to minimize the chances of complications related to both disorders, especially in females who want to get pregnant. The rationale of the study was that early detection and treatment of thyroid dysfunction in patients with PCOS leads to improve quality of life by reversing menstrual irregularities and improving fertility. Therefore, we conducted this study to determine the prevalence and pattern of thyroid dysfunction in our patients with PCOS.

METHODOLOGY

This cross-sectional study was conducted at the Department of Clinical Endocrinology and Diabetes, Jinnah Hospital, Lahore Pakistan, for six months, from January to July 2017. The study was conducted following the principles of ethical medical practice, as laid down in the Declaration of Helsinki, after formally approved by the Institutional Ethical Review Board of Allama Iqbal Medical College (34thB 22/ERB, 22.11.2016), Jinnah Hospital, Lahore Pakistan. A sample size of 77 cases was calculated using a 95% confidence level and 10% absolute precision and taking the expected frequency of goitre to be 27.5% in patients.⁹

Inclusion Criteria: Patients aged between 16 to 45 years were in following Rotterdam criteria for a diagnosis of PCOS. PCOS was diagnosed if the patient fulfilled two out of the following three criteria: presence of oligomenorrhea/amenorrhea, signs of hyperandrogenism (hirsutism, acne, male pattern baldness) and polycystic ovaries on ultrasonography (polycystic ovaries; multiple cysts >12 number and ranging in size from 2-9 mm).¹¹

Exclusion Criteria: Patients with a history of any diagnosed autoimmune disease and a history of diabetes mellitus, were excluded from the study.

Seventy-seven patients fulfilling the inclusion criteria were enrolled in the study after obtaining written informed consent through non-probability, consecutive sampling. Clinical features like menstrual irregularities, acne, hirsutism, male pattern baldness and ultrasound (pelvis) were recorded. In addition, a blood sample was drawn under sterilized conditions and sent to evaluate TSH, free T3 and fT4 and anti-TPO antibodies. Thyroid dysfunction Tietz criteria was shown in the Table-I.¹²

We also performed a hormonal profile of the patients, which included serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone and prolactin levels.

Table-I: Tietz Criteria for Assessment of Thyroid Dysfunction

	TSH (mIU/L)	FT4 (pmol/L)	FT3 (pg/ml)	T3 (ng/dl)
Normal values	0.3-5.5	7.8-14.4	2.5-3.9	80-200
Primary Hypothyroidism	>5.5	<7.8	Not required	Not required
Primary hyperthyroidism	<0.3	>14.4	Not required	>200
Subclinical primary hypothyroidism	>5.5	7.8-14.4	Not required	Not required
Subclinical primary hyperthyroidism	<0.3	7.8-14.4	Not required	80-200
T3 Thyrotoxicosis	<0.3	7.8-14.4	Not required	>200

The information was analyzed using Statistical Package for the social sciences (SPSS) version 23:00. Mean±SD deviation (SD) were calculated for quantitative variables. Qualitative variables were calculated as frequency and percentages. The chi-square and t-test were used to calculate statistical significance taking *p*-value ≤0.05 as statistically significant.

RESULTS

The results of the study showed that the mean age of patients was 29.0±7.9% (range: 16-45) years. In patients with PCOS, the major presenting clinical feature was menstrual irregularity, 74(96.1%) followed by hirsutism 56(72.7%) and acne 41(53.2%). On ultrasonography, polycystic ovaries were found in 77(100%) patients, as shown in Table-II.

Table-II: Percentage of Various Symptoms in Patients with PCOS (Multiple Response) (n=77)

Symptoms	Frequency (%)
HIRSUTISM	56 (72.7)
ACNE	41 (53.2)
Menstrual irregularities	74 (96.1)
Polycystic ovaries	77 (100.0)

Thyroid dysfunction was found in 14(18.5%) patients. Of 77 females with PCOS, 63(81.8%) were euthyroid. While out of 14 females with thyroid dysfunction, 5(6.5%) patients had primary hypothyroidism (6.5%), and 9(12%) patients had subclinical hypothyroidism. No case of hyperthyroidism was observed in this study.

Anti-thyroperoxidase antibodies were observed in 18(23.4%) patients. Interestingly twelve euthyroid patients tested were also positive for anti-TPO. Out of nine patients with subclinical hypothyroidism, only 2(22.2%) patients were Anti-TPO positive and out of

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five patients with primary hypothyroidism, 4(80.0%) patients were anti-TPO positive. Results of the study showed a considerable number of females with thyroid dysfunction, primary hypothyroidism and subclinical hypothyroidism and also a considerable number of positive cases with thyroid autoimmunity as expressed by the presence of positive anti-TPOs in females with PCOs with either thyroid dysfunction or euthyroid patients with a significant p -value = 0.008 (Table-III).

lation. Sinha *et al.* conducted a case-control study in which she compared 80 PCOS females with 80 controls and found subclinical hypothyroidism in PCOS patients compared with controls (22.5% vs 8.75%).⁹ A meta-analysis and systemic review in 2017 showed that 10% to 25% of patients with PCOS had subclinical hypothyroidism.¹⁵ In the present study, 5 out of 77 patients (6.4%) with PCOS had primary hypothyroidism, according to another study that reported clinical

Table-III: Frequency of Anti-Thyroperoxidase Antibodies in Polycystic Ovarian Syndrome Patients (n=77)

Anti-Thyroperoxidase Antibodies	Thyroid Disease Status Frequency (%)			p - value
	Euthyroid (n=63)	Primary Hypothyroidism (n=5)	Subclinical Hypothyroidism (n=9)	
Present	12 (19.0)	4 (80.0)	2 (22.2)	0.008
Absent	51(81.0)	1 (20.0)	7 (77.8)	

DISCUSSION

We observed thyroid abnormalities in 18.5% of the patients with PCOS. The major thyroid dysfunction was found to be primary hypothyroidism and subclinical hypothyroidism. Besides, several euthyroid patients were also anti-TPO positive, showing evidence of autoimmunity in these patients. Therefore, the study showed autoantibodies and thyroid autoimmunity in patients with thyroid dysfunction and in euthyroid females, emphasizing that most PCOS patients were potential candidates for future monitoring of thyroid dysfunctions for early detection and management of thyroid dysfunction and its related complications.

In our study, the major presenting feature was menstrual irregularities, followed by hirsutism and acne. A previous study on PCOS reported hirsutism in 92% and 75% sub-clinically hypothyroid and euthyroid patients respectively.¹³ Another study from India reported hirsutism in 44.1% of euthyroid and 44.4% of hypothyroid patients. Acne has been reported in 21.6% euthyroid and 11.1% hypothyroid PCOS patients.¹⁴

The presence of anti-TPO indicates autoimmunity against the thyroid gland, and these patients are more prone to overt thyroid dysfunction in the future and need zealous observation. The study also showed autoantibodies in patients with thyroid dysfunction and in euthyroid females, emphasizing that these females are also candidates for regular thyroid function evaluation in the future for a better quality of life and fertility outcomes.

We observed subclinical hypothyroidism to be a predominant thyroid abnormality in our study popu-

lation. Out of 5 patients with primary hypothyroidism, four were anti-TPO positive, showing under-lying pathogenic elements of autoimmunity. Therefore, we presumed that this hypothyroidism was due to underlying autoimmune thyroiditis. Novias *et al.* showed that serological markers of autoimmunity and various systemic and organ-specific antibodies were recognized in patients with PCOS.¹⁶

In the present study, thyroperoxidase antibodies were present in 23.4% of females suffering from PCOS. Our findings are closely related to the results of a study from Germany that reported a prevalence of anti-TPO antibodies to be 26.9% in PCOS patients.¹⁷ A study from Turkey reported an even higher prevalence of 30.5% of positive anti-TPO antibodies in PCOS patients.¹⁸ Out of 63 euthyroid patients, 12(19%) had positive results for anti-TPO, while 2 out of 9 patients with subclinical hypothyroidism tested positive for anti-TPO antibodies. A study in Syria revealed that 19.6% of euthyroid patients with PCOS had anti-TPO antibodies. It has been reported that euthyroid patients with anti-TPO are more likely to develop thyroid dysfunction later in life.¹⁹ Therefore, we recommend monitoring these patients carefully over fixed intervals of time to detect any impending overt thyroid dysfunction and treat that at an early stage.

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LIMITATIONS OF STUDY

The main limitation of the study was that the study population only represented patients enrolled in the Endocrinology Department. Secondly, we could not recruit a healthy control group in our study to compare the results of PCOS patients with those without PCOS for thyroid dysfunction. Therefore, we recommend future studies on a case-control model to determine the statistical significance between the two groups. Lastly, we recommend conducting multi-centre trials in our country involving endocrinologists and gynaecologists to develop unanimous guidelines on the holistic management of these two disorders together.

CONCLUSIONS

The current study concluded that thyroid dysfunction is significantly prevalent in PCOS patients. In addition, our study showed a higher frequency of primary hypothyroidism and subclinical hypothyroidism.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

KAK & AU: Critical review, drafting the manuscript, approval of the final version to be published.

MTR & KMN: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

IH: Data acquisition, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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