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Original Research Article

Drawing Association between Thyroid Function and Auto Immune Status in Female Patients with Polycystic Ovarian Syndrome

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Abstract

Background: Thyroid disorder and PCOS are considered as two of the most common endocrine disorder among general population and share many common features. As per the clinical analysis, increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. Only small numbers of genes are responsible for the endocrine and metabolic symptoms. Apart from this, the environmental risk factors during the prenatal or postnatal period convert PCOS into a clinically manifest syndrome.

Aim: The study aims to draw an association between thyroid function and auto immune status in female patients with polycystic ovarian syndrome.

Method: The samples were collected from PCOS patients diagnosed according to Rotterdam criteria, ascertained by ultrasonography, attending the OPD in the department of Obstetrics and Gynecology, Rajarajeshwari Medical college and Hospital, Bangalore from December 2014 to May 2016. Seventy-five cases of PCOS patients in the age group of 20-40 years, and seventy-five age-matched healthy women (control) with regular menstrual cycle were selected.

Results: The mean age for case was 30.13 years (SD=5.32) and control was 28.54 years (SD=6.78). Pearson's correlation coefficient for the relationships between anti TPO and T3, T4, TSH, FBS, WT, HT, BMI and WC for cases was determined. Serum T4 and TSH had significant positive correlation with anti TPO in cases. However, there was no significant correlation between anti TPO and T3, FBS, WT, HT, BMI and WC in cases.

Conclusion: Positivity for Anti TPO antibodies is more common in PCOS subjects. Euthyroid PCOS cases with anti TPO positivity should be considered as at risk for hypothyroid disorders. Moreover, thyroid disorder is more common among patients with PCOS as compared to normal population.

Keywords: Autoimmunity, Leptin, Obesity, Polycystic Ovary Syndrome, Thyroid.

Background

There are various health issues that influence the health of an individual and lead to many complications. According to clinical analysis, improvement in endocrine dysfunctions leads to association of Polycystic Ovary Syndrome (PCOS) and auto immune thyroid disease [1]. Although, the causality of this association is uncertain, the two conditions share a bidirectional relationship. In addition to this, both syndromes share certain common characteristics, risk factors and patho-physiological abnormalities [2]. Further, adiposity, increased insulin resistance, high leptin, and evidence of deranged autoimmunity are present in both disease states and play a complex role in connecting these two disorders [3].

Thyroid disorders and PCOS are considered as two of the most common endocrine disorder among the general population. As per the clinical analysis, increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism [4]. Moreover, thyroid disorder is common among the patients with PCOS as compared to normal population. The prevalence of PCOS among premenopausal women is reported to range between 6-10% globally and 4-10% in India. Only small numbers of genes are responsible for the endocrine and metabolic symptoms. Apart from this, the environmental risk factors during the prenatal or postnatal period convert the PCOS into a clinically manifest syndrome [5].

The key characteristics of PCOS are inappropriate gonadotropin secretion which is a cause of ovarian dysfunction. In addition to this, improvement in the plasma testosterone level is also a consistent biochemical feature of PCOS. Thyroid hormones are primary determinants of glucose homeostasis and changes in their level can affect the insulin agonist as demonstrated in muscles or antagonistic as demonstrated in liver [6]. Autoimmune thyroid disorders are characterized by the presence of thyroid auto-antibodies (Abs), particularly anti-Thyroid peroxidase (anti-TPO) antibody an autoantibody. Thyroid autoimmunity (TAI) is the most common autoimmune disorder in women of reproductive age, with a prevalence varying between 5 and 15%. It is five- to ten-times more common in women than in men and can be present without thyroid dysfunction, thus remaining undiagnosed [7].

Clinical studies suggest that thyroid dysfunction and PCOS have profound effects on the reproductive system and fertility quality of the women. Moreover, thyroid disorder initiate, maintain or worsen the syndrome and vice versa. The cause of polycystic ovary syndrome remains unknown, although, like most complex heterogeneous diseases, both environmental and genetic factors are implicated [8]. With time and technological advances, focus has shifted from the ovary to the hypothalamic–pituitary axis, to some primary defects of insulin activity as the primary pathological cause of the syndrome. Genetic factors like familial aggregation of polycystic ovary syndrome has been recognised for many years but since Polycystic ovary syndrome does not show clear Mendelian inheritance, it is regarded as a complex disorder, and poses unique challenges to geneticists [9].

Aim

The study aims to draw association between thyroid function and auto immune status in female patients with polycystic ovarian syndrome.

Method and material

The samples were collected from PCOS patients attending the OPD in the department of Obstetrics and Gynecology, Rajarajeshwari Medical college and Hospital, Bangalore from December 2014 to May 2016. Seventy-five cases of PCOS

patients in the age group of 20-40 years, diagnosed according to Rotterdam criteria, ascertained by ultrasonography, and seventy-five age matched healthy women (control) with regular menstrual cycle in the age group of 20-40 years were selected.

Inclusion Criteria

1. 75 women diagnosed with PCOS ascertained by USG – as per Rotterdam Criteria in the age group of 20 – 40 years attending OPD of Department of OBG at RRMCH were included in the study.
2. 75 age-matched, healthy women attending the OBG OPD as control groups (with menstrual regularities)

Exclusion Criteria

1. Other etiologies of hyperandrogenism (Clinically diagnosed)
2. Congenital adrenal hyperplasia
3. Androgen secreting tumors
4. Cushings syndrome
5. Subjects with known thyroid diseases
6. Women with regular mensuration in cases

Method of Collection of Data:

Patients satisfying the inclusion criteria were enrolled in the study after obtaining written informed consent. A thorough medical history and detailed physical examination was performed for everyone. A pre-structured and pre-tested proforma was used to collect the data.

Method of Collection of Sample:

Under full aseptic precautions, 5ml of venous whole blood sample was collected from the cubital vein from both study and control group, in clot activator containing vacuum evacuated tubes and were properly labelled. Precautions were taken to prevent hemolysis. Samples were brought to Clinical Biochemistry laboratory and centrifuged after clotting and retraction at room temperature. Clear serum was collected and subsequently analyzed.

The following investigations were performed by fully automated analyzer

a) Anti TPO Ab by — Chemiluminescence immune assay
b) T3, T4, TSH by – Chemiluminescence immune assay
c) Fasting blood glucose -- Glucose oxidase-peroxidase (GOD-POD) method

Statistical Analysis

The data was entered in Microsoft Excel and analyzed in SPSS V28. Mean and standard deviation for quantitative variables were calculated for the study population. Difference in the group means of quantitative variables was compared by two tailed student t-test at 95% significance level.

Results

Table 1: Case and Control age distribution

Age Group	Cases (n=75)	Control (n=75)	Total
20 - 25	15(20%)	31(41.33%)	47(31.33%)
26 - 30	29(38.66%)	21(28%)	50(33.33%)
31 - 35	13(17.33%)	9(12%)	22(14.66%)
36 - 40	18(24%)	14(18.66%)	32(21.33%)
Total	**75(100%)**	**75(100%)**	**150(100%)**
Mean± SD	**30.13 ± 5.32**	**28.54 ± 6.78**	**29.33 ±6.05**

According to analysis of table 1, mean age for case was 30.13 years (SD=5.32) and control was 28.54 years (SD=6.78).

Table 2: Pearson's correlation coefficient between Anti-TPO and other parameters in cases

Parameters	r	P-Value
T3 (ng/dl)	-0.070	0.553
T4 (µg/dl)	-0.262	0.023*
TSH (µIU/dl)	0.544	<0.001*
FBS (mg/dl)	-0.052	0.658
Weight (Kgs)	0.043	0.715
Height (cms)	-0.006	0.962
BMI(kg/m^2)	0.043	0.716
WC	0.166	0.155

Table 2 shows Pearson's correlation coefficient for the relationships between anti TPO and T3, T4, TSH, FBS, WT, HT, BMI, and WC for cases. The serum T4 and TSH had significant positive correlation with anti TPO. However, there was no significant correlation between anti TPO and T3, FBS, WT, HT, BMI and WC. Although a significant correlation is obtained between anti TPO and T4, TSH but we did not get a linear scatter plot due to the data. Also correlation cannot be taken as causation.

Table 3: Pearson's Correlation between Anti TPO and other parameters in Controls

Parameter	R	P-Value
T3 (ng/dl)	-0.068	0.564
T4 (µg/dl)	-0.158	0.175
TSH (µIU/dl)	0.105	0.372
FBS (mg/dl)	-0.223	0.054
Weight (Kgs)	0.215	0.064
Height (cms)	0.140	0.231
BMI (kg/m^2)	0.130	0.267
WC (cm)	0.220	0.057

Table 3 shows Pearson's correlation coefficient for the relationships between anti TPO and T3, T4, TSH, FBS, WT, HT, BMI, and WC for controls. There was no significant correlation found between anti TPO and T3, T4, TSH, FBS, WT, HT, BMI, and WC.

Table 4: Association between T3 and groups

T3	Cases		Controls		χ^2	P-Value
	N	%	N	%		
Below Normal (<69)	7	9%	1	1%	1.007	0.316
Normal (69 - 215)	66	88%	72	96%		
Increase (>215)	2	3%	2	3%		
Total Count	**75**	**100%**	**75**	**100%**		

According to table 4, there was no significant association observed between T3 and the groups (p> .05).

Table 5: Association between T4 and groups

T4	Cases		Controls		χ^2	P-Value
	N	%	N	%		
Below Normal (<5.2)	8	11%	2	3%	2.238	0.327
Normal (5.2 - 12.7)	65	87%	71	95%		
Increased Volume (>12.7)	2	3%	2	3%		
Total Count	**75**	**100%**	**75**	**100%**		

According to table 5, there was no significant association observed between T4 and the groups (p> .05).

Table 6: Association between Anti TPO and groups

Anti TPO	Cases		Controls		χ^2	P-Value
	N	%	N	%		
Normal (<30)	59	79%	66	88%	1.885	0.170
Increased Volume (>30)	16	21%	9	12%		
Total Count	**75**	**100%**	**75**	**100%**		

According to table 6, there was no significant association observed between anti TPO and the groups (p>.05).

Table 7: Association between FBS and groups

FBS	Cases		Controls		χ^2	P-Value
	N	%	N	%		
Below Normal (<70)	0	0%	0	0%	-	-
Normal (70-110)	75	100%	75	100%		
Increased Volume (>110)	0	0%	0	0%		
Total Count	**75**	**100%**	**75**	**100%**		

According to table 7, there was no association observed between FBS and the groups as all the participants of both groups were in normal range.

Table 8: Association between TSH and groups

TSH	Cases		Controls		$\chi 2$	P-Value
	N	%	n	%		
Hyperthyroid Clinical values (<0.1)	0	0%	0	0%	4.256	0.235
Hyperthyroid Sub clinical values (0.1 - 0.39)	5	7%	2	3%		
EU Thyroid (Normal values) 0.4 - 4.5	55	73%	65	87%		
Sub clinical Hypothyroid values (4.6 - 10)	11	15%	6	8%		
Clinical Hypothyroid (>10)	4	5%	2	3%		
Total Count	**75**	**100%**	**75**	**100%**		

According to table 8, there was no significant association observed between TSH and groups (p> .05).

Discussion

Thyroid disorder and PCOS are considered as two of the most common endocrine disorder among the general population and share many common features. As per the clinical analysis, increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. Moreover, thyroid disorder is common among the patients with PCOS as compared to the normal population.

Thyroid hormones are primary determinants of glucose homeostasis and changes in their level can affect the insulin agonist as demonstrated in muscles or antagonistic as demonstrated in liver. Autoimmune thyroid disorders are characterized by the presence of thyroid auto-antibodies (Abs), particularly anti-thyroid peroxidase (TPO) an Auto-Abs.

According to analysis of current study, mean age for case was 30.13 years (SD=5.32) and control was 28.54 years (SD=6.78). Serum T4 and TSH had a significant positive correlation with anti TPO in case group. However, there was no significant correlation between anti TPO and T3, FBS, WT, HT, BMI and WC.

As per the study outcome of Artini et al., (2013) [10] the significance of anti TPO positivity in euthyroid PCOS subjects may be explained by the fact that nearly all PCOS patients have high serum levels of antibodies against one or more thyroid antigens, particularly anti TPO antibodies. Approximately 10% of asymptomatic individuals have elevated levels of anti-TPO Ab that may suggest a predisposition to thyroid autoimmune disease. Also autoimmune thyroid disease (AITD) is the most frequent cause of hypothyroidism in young women and it may be present without thyroid dysfunction for many years; thus, often ignored resulting in hypothyroidism later in life. Another study by Ozdemir et al. (2011) [11] found that 37.8% of 107 patients with PCOS had positive anti-TPO. The study has also shown significantly higher prevalence of autoimmune thyroiditis in PCOS patients than that in control subjects.

Apart from this, the Chi square test has shown no significant association. Uma Sinha et al. (2013) [12] found the mean values of anti TPO more in cases than controls (28.037 ± 9.138 vs 25.72 ± 8.27, p=0.035; respectively) and was statistically significant. A study done by Hefler-Frischmuth et al. (2014) [13] also revealed the same with anti TPO. They got the mean values as (10 ± 18 for controls vs 123 ± 328 for cases, p<0.001) respectively. [14]

Conclusion

PCOS subjects are prone for thyroid disorders, particularly Hypothyroidism. Autoimmunity as Autoimmune thyroiditis is more prevalent in PCOS subjects. Positivity for Anti TPO antibodies is more common in PCOS subjects. Euthyroid PCOS cases with anti TPO positivity should be considered as at risk for hypothyroid disorders. Thus should be evaluated for thyroid status periodically.

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