Original Article

Evaluation Of Thyroid Function Status In Newly Diagnosed Poly Cystic Ovary Syndrome - An Analysis in a Tertiary Care Hospital

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ABSTRACT

Introduction: The most common endocrine disorder in reproductive age group women is Poly cystic ovary syndrome (PCOS) and hypothyroidism. Both these conditions play a vital role in the etiology of Diabetes, coronary artery disease and infertility. Their coexistence increases the morbidity and mortality of each other. Hyperestrogenism has been proposed as one explanation for the occurrence of increased autoimmune disorders like hypothyroidism in females. To determine the prevalence of hypothyroidism among PCOS, a study was conducted among newly diagnosed PCOS patients attending gynaecology outpatient department in a tertiary care hospital.

Aim of the study: To assess the thyroid function status in PCOS patients.

Materials & methods: 73 newly diagnosed PCOS women based on Rotterdam's criteria, were selected. Anthropometric measurements were measured and BMI, waist hip ratio were calculated. Thyroid function status was assessed with Thyroid Stimulating Hormone(TSH). TSH, Fasting Insulin and Total testosterone were estimated with Chemiluminescence Immuno Assay (CLIA) technique.

Results & Discussion: Among them, 21.9% had elevated TSH. The cut-off for diagnosing hypothyroidism was TSH >5µIU/mL. With this, they were divided into two groups. Euthyroid PCOS (Group 1) and Hypothyroid PCOS (Group 2). There was statistically significant difference between the two groups in BMI (P=0.026) and Total testosterone (P=0.023).

Conclusion: The prevalence of hypothyroidism among PCOS women is higher than in general population. This study emphasizes evaluating thyroid function status while treating PCOS women.

Keywords: Hypothyroidism, PCOS, Prevalence of hypothyroidism in Poly cystic ovary syndrome, TSH in PCOS.

INTRODUCTION

Poly Cystic Ovary Syndrome (PCOS) is the most common endocrine disorder in reproductive age group women and its prevalence in India is 5-10%[1,2]. Hypothyroidism, another very common endocrine disorder in women races with PCOS in the cause for female infertility. Prevalence of hypothyroidism in India in adult is ~ 10%[3]. Infertility and Menstrual irregularities are the psychological challenges faced by the modern era reproductive age group women. Many apparently healthy looking women were incidentally found to have hypothyroidism, either sub-clinically or overt and are diagnosed almost after developing complications. PCOS and Hypothyroidism either individually or together adds the risk for coronary artery disease by altering lipid metabolism apart from menstrual disorder and infertility. Studies have shown significant association between these two disorders and have

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affirmed that hypothyroidism is also a state of Insulin resistance (IR) and is one of the main etiology for PCOS[4]. Even though the exact definition is not known, the ultimate culprit in PCOS is hyperandrogenism which is aggravated in the presence of hypothyroidism. Considering the association of PCOS, Insulin resistance, the effect of thyroid hormone, and the sparsely available data in the hypothyroidism and PCOS, a cross sectional study was conducted to assess the thyroid function status in patients having Poly cystic ovary syndrome.

AIMS AND OBJECTIVES

1. To evaluate the thyroid function status in newly diagnosed polycystic ovary syndrome patients and estimate the prevalence of hypothyroidism in them.
2. To evaluate fasting Insulin and total Testosterone and compare between euthyroid PCOS and hypothyroid PCOS group.
3. To measure Body Mass Index (BMI) and waist hip ratio and compared between the two groups.

MATERIALS AND METHODS

Study Design:

Institutional Ethics committee approval was obtained at first. A cross sectional study was conducted in outpatient department of Gynaecology, Institute of Obstetrics & Gynaecology, attached to Madras medical college during March - September 2014. In this study, 73 newly diagnosed PCOS women were selected based on Rotterdam's criteria, 2003[5,6]. Those who were not on treatment between the age group of 15 - 45 yrs were chosen. The selection criteria was achieved with questionnaire to confirm the history of oligomenorrhoea / amenorrhoea, ultrasonogram to diagnose the poly cystic ovaries and their biochemical changes were confirmed with fasting Insulin and Total testosterone. As per American Thyroid association and UK Thyroid treatment guidelines the very first basic investigation to assess the thyroid function is Thyroid Stimulating Hormone (TSH). With this background, the thyroid function status of PCOS women was assessed with Thyroid Stimulating Hormone (TSH) by a highly sensitive technique Chemiluminescence Immunoassay (CLIA). Fasting Insulin and Total testosterone were also estimated by the same technique.

Anthropometric Measurements:

Height, Weight, Waist circumference, Hip circumference was measured (inch tape), Body Mass Index (BMI) & Waist Hip ratio was calculated.

Investigations:

After 10-12 hours of fasting, 3mL of venous blood sample was taken from the patients under strict aseptic precaution. Serum was separated and used to perform the analytes estimation. Fasting blood Glucose, 2 hrs post prandial glucose, Thyroid Stimulating Hormone (TSH), Fasting Insulin and Total Testosterone were measured. Glucose was done in fully automatic random access chemistry analyzer using Glucose Oxidase – Peroxidase (GOD-POD) method. Thyroid Stimulating Hormone, Fasting Insulin and Total Testosterone were done in SIEMENS ADVIA Centura XP with the principle Chemiluminescence Immunoassay technique.

Normal level of TSH was taken as 3.5–5μIU/mL and >5μIU/mL as hypothyroid state. Normal serum total testosterone as 14-76 ng/mL and >76 ng/mL as hyperandrogenic state.

STATISTICALANALYSIS :

The results were described as mean +/- SD. Significant results were reported with 95% Confidence Interval and Statistical analysis was done with SPSS software version 17.

Table:1 Various Parameters Among 73 Newly Diagnosed PCOS Patients

AGE			
<19 yrs no:9 (11%)	**= 20 yrs** no:65(89%)		
WAIST /HIP RATIO			
<0.8 no:23(32%)	**>0.8** no:50(68%)		
BODY MASS INDEX(BMI)			
=18.4 no:4 (5%)	**18.5 -24.9** no:19 (26%)	**25 -29.9** no:27(37%)	**=30** no: 23(32%)
SERUM TSH			
<5µU/mL no:57 (78%)	**>5µU/mL** no:16 (22%)		

Table:2 Comparison Of Anthropometric Measurements And Hormones Between Two Groups

PARAMETERS	GROUP:1 EUTHYROID-PCOS (Mean +/- SD)	GROUP:2 HYPOTHYROID-PCOS (Mean +/- SD)	SIGNIFICANT P VALUE(<0.05)
BMI	27.10(+/- 5.75)	30.71(+/- 4.9)	**0.026****
WAIST/HIP RATIO	0.84(+/- 0.05)	0.82(+/- 0.07)	0.28
FASTING BLOOD GLUCOSE (mg/dl)	90.01(+/-21.81)	83.81(+/-10.5)	0.27
2 HRS POST PRANDIAL GLUCOSE (mg/dl)	128.7(+/- 36.85)	119.75(+/- 24.2)	0.36
FASTING INSULIN (mIU/L)	24.85(+/-43.45)	27.24(+/- 16.16)	0.83
TESTOSTERONE (ng/ml)	52.95+/-28.06	70.08(+/- 16.93)	**0.023****

** SIGNIFICANT p-VALUE

RESULTS:

This study included 73 PCOS patients who attended Gynaecology OPD and various parameters for all of them were assessed and tabulated in Table:1. Among the 73 participants, 9 (11%) were below 19 yrs (teenage) and 65 (89%) were 20 yrs and above. BMI was < 18.4 for 4 (5%) participants, between 18.5- 24.9 for 19 (26%) individuals, between 25-29.9 for 27 (37%) participants and ⩾ 30 for 23 (32%) participants. Waist-Hip ratio was <0.8 for 23(32%) patients and >0.8 for 50 (68%) patients as in table:1.

Figure-I Prevalence Of Hypothyroidism In PCOS

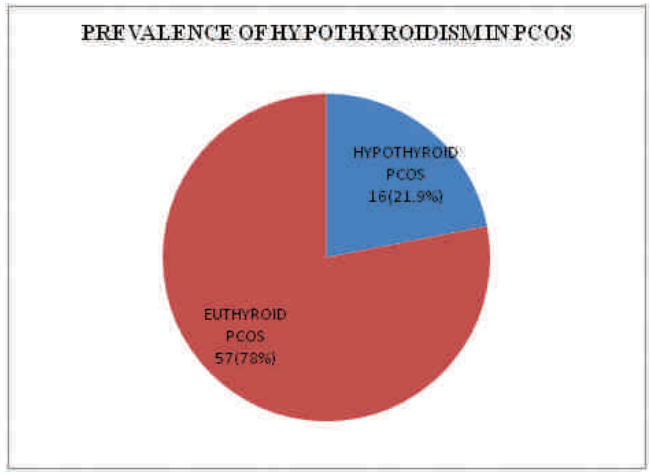
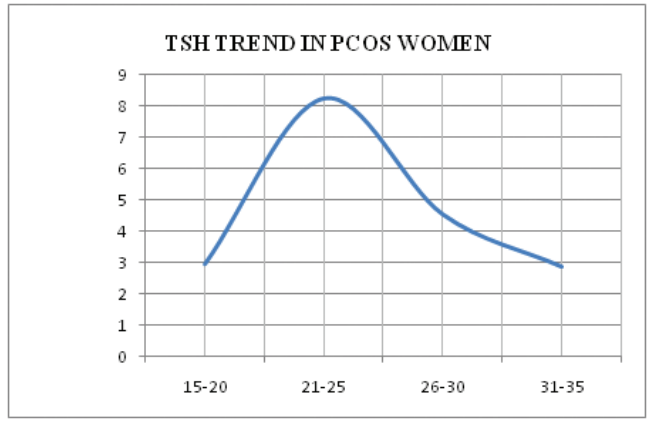
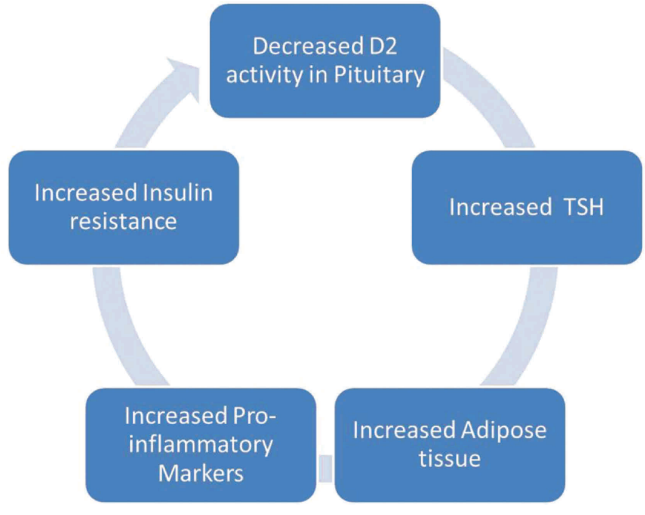


Figure-2 TSH Trend In PCOS Women



X-AXIS: AGE : Y-AXIS: MEAN TSH (µIU/dL)

Figure-3 Hypothesis Linking Adiposity And Raised Thyroid Stimulating Hormone



participants, 16 (21.9 %) had TSH ⩾ 5µIU/mL and 57 (88%) had TSH within normal range as shown in fig:1. Mean TSH was 2.93 for the age group 15 -20 yrs, 8.22 for 21 -25yrs, 4.52 for 26-30 yrs and 2.85 for 31 – 35yrs. The trend of TSH secretion in PCOS women is depicted in Fig:2 with a peak in the age group of 21-25yrs.

The PCOS patients were divided into two groups based on the TSH level as Group 1 (Euthyroid PCOS) and Group 2 (Hypothyroid PCOS). The mean BMI, WHR, Fasting Insulin and Total testosterone for the two groups were compared and tabulated in Table:2. There was no statistically significant difference between the two groups in waist hip ratio, fasting glucose, 2 hrs post prandial glucose, and fasting insulin. Total testosterone and BMI showed statistically significant difference.

DISCUSSION:

The prevalence of hypothyroidism in general population is 10-11% and in reproductive age group is 2-4%.This study showed the prevalence of hypothyroidism in PCOS as 21.9% (~ 22%) which is higher than in general. This observation is similar to Uma sinha etal study conducted in eastern part of India which showed 22.7%, Maryam etal and Janssen et al studies also showed 26.9% of autoimmune thyroiditis in PCOS women [9,10,11]. The high prevalence of hypothyroidism among PCOS women when compared to the general population indicates the strong association and some common factors among the two conditions. The pathophysiological pathway connecting these two disorders has not been clearly described as of now. The most obvious connection, perhaps, is the obesity and insulin resistance. Women with PCOS are more predisposed to autoimmune diseases as it is known to be a hyperestrogenic state. Hyperestrogenism has been proposed as one explanation for the occurrence of increased autoimmune diseases in females when compared to males[12]. Estrogen receptors have a proliferative action on B-lymphocytes and estrogen receptors are also present on T-cell as well as macrophages[13]. This explains the higher prevalence of hypothyroidism in PCOS women.

In this study, the serum TSH was measured for all women and it showed a trend with a peak in the age group between 21- 25 yrs. This shows that the young women have more hormonal dysfunction than other age group. This is similar to Cristina Laguna Benetti-Pinto etal result in which the mean age to have maximum thyroid dysfunction (SCH) in PCOS was 24yrs[14].

Among the 73 participants, 64 (88%) had menstrual irregularities and USG- polycystic ovaries, 53 (76.6%) had clinical features with USG findings, 19 (26%) had purely biochemical changes with USG findings, 44 (60%) satisfied all 3 criteriae of Rotterdam. So, the major complaint of the PCOS patients was menstrual irregularities which is similar to Najem et al and Carmina E lobo RA etal study who also showed 93% and 60-85% of PCOS presents with menstrual irregularity respectively[15,16].

This study showed 37% of PCOS patients were in over weight range and 32% were obese of various grade and was similar to Najem etal and Gomathi etal[15] studies. There was a statistically significant difference in BMI between euthyroid PCOS (27.1±5.75) and hypothyroid PCOS women (30.71±4.9). Increase in BMI is an integral part of PCOS and is seen in a large majority of these cases in general[17] .Obesity is associated with an altered milieu with increase in pro-inflammatory markers and increase in insulin resistance. This, through undefined mechanisms, leads to decreased deiodinase-2 activity at pituitary level resulting in

relative T3 deficiency and increase in TSH levels[18]. Increased leptin in obesity has been proposed to act directly on the hypothalamus resulting in increased TRH secretion[19]. Raised TSH levels, with any of these two pathways, act on adipocytes to increase their proliferation and is depicted in Fig:3. Muscogiuri et al studied 60 euthyroid subjects to find a correlation of TSH to either adipose tissue or insulin resistance. On univariate analysis, both adiposity and insulin resistance were significantly associated with raised TSH[18]. There is not enough evidence to suggest that this TSH lowering effect of metformin is mediated by lowering insulin resistance. A change in the affinity or in the number of TSH receptors; an increase in the central dopaminergic tone and direct effect of metformin on TSH regulation has been proposed as potential explanations[21]. Existence of insulin resistance among these two disorders is affirmed by Lupoli R etal who showed that TSH is lowered by metformin treatment in persons with clinical and subclinical hypothyroidism, but not in euthyroid people[22].

The leading hormonal cause for female infertility is PCOS and hypothyroidism and the expenditure for the child birth in India has risen tremendously. Thyroid hormone is essential for the synthesis of proteins in liver,that includes Sex Hormone Binding Globulin (SHBG), a major protein that binds testosterone in circulation. In hypothyroidism, synthesis of protein including SHBG production is reduced and that the free form of testosterone which is the biologically active form level is elevated[23]. There exists a cyclical association of PCOS and hypothyroidism from hypothalamus to ovary and vise-versa. Reduced circulating thyroid hormone (free T4) stimulates the thyroid gland and hypothalamus to secrete Thyroid Stimulating Hormone (TSH) and Thyrotropin Releasing Hormone (TRH) respectively. TRH from hypothalamus not only stimulates thyroid gland but also Prolactin (PRL) from hypothalamus leading to hyperprolactinemia and thereby reverses LH / FSH ratio. Hyperandrogenism due to increased free testosterone, along with hyperprolactinemia leads to anovulation and multiple cysts in ovaries in hypothyroidism. Thus these two endocrine disorders mutually increase the risk of infertility and other morbidities. This study explains the strong association between PCOS and hypothyroidism and the importance of treating both disorders. As a conclusion, this study emphasis mainly on evaluating thyroid function status among PCOS women while treating to reduce the morbidity and mortality of both disorders.

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