Thyroid Profile Status of Female Patients with Polycystic Ovary Syndrome (PCOS) in Western Rajasthan

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ABSTRACT
Background: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder in women with 6-7% prevalence in the world. PCOS produces symptoms in approximately 5% to 10% of women of reproductive age (12–45 years old). The heterogeneous disorder is associated with menstrual irregularities, hyperandrogenemia, obesity, increased insulin levels and insulin resistance. PCOS together with thyroid disorder create independent risks of ovarian malfunction as well as pregnancy associated problem. An abnormal thyroid concentration could trigger alterations in ovulation and then menstruation.

Objective: Assessment of serum Thyroid profile Levels in Female patients with Polycystic ovarian syndrome (PCOS) trying to find a correlation between Polycystic ovarian syndrome (PCOS) and the metabolic functions of Thyroid gland, as well as pregnancy associated problem.

Patients and Methods: 50 females were included in this study, they were divided into 2 groups, the first group included 25 PCOS female patients of age group (18-30yr) attending the Out Patient Department, Department of Obstetrics and Gynecology, Dr. S.N. Medical College and its associated group of hospitals, Jodhpur. The result will be compared with the second group in which age matched 25 healthy - control female subjects were included. Patients and controls were subjected to fill history taking, duration of the disease, the clinical course and any complications in relation to the disease were noted, measurement of body mass index and assessment of Serum thyroid hormones and Serum TSH level which was measured by using Enzyme Linked Fluorescent Assay Method.

Results: PCOS female patients were found with elevated Serum TSH level and Mean serum TSH values were highly significant as compared to healthy control subjects. While Serum T₃ and Serum T₄ levels were almost similar in both groups and there was a non-significant relationship.

Conclusion: The subclinical higher level of thyroid stimulating hormone in PCOS female patients may be associated with the development of the disease and may also implicated with other symptoms of the disease. As there is high prevalence of thyroid disorders in PCOS patients, thus all women in their reproductive age with and without PCOS, should have their thyroid function tests evaluated.

Keywords: PCOS, Ovarian Malfunction, Obesity, Subclinical Hypothyroidism.

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INTRODUCTION
Polycystic Ovarian Syndrome (PCOS) is one of the most common female endocrine disorder.¹ It is a complex, heterogeneous disorder of multifactorial etiology and there is strong evidence that it can be classified as a genetic disease.²,³ PCOS is thought to be one of the leading causes of female subfertility and the most frequent endocrine problem in women of reproductive age.⁴ This endocrine disorder was first identified in 1935 by Stein and Leventhal who noticed a condition in women characterized by irregular menstruation, obesity, and hirsutism, in addition to cysts on the women's ovaries and it is also known as Stein – Leventhal syndrome.⁵ Although PCOS is an endocrine disease, it affects many systems of the body resulting in reproductive, metabolic, and psychological consequences.⁶
Women with PCOS are at risk for weight gain.\textsuperscript{7-10} Obesity is a common finding of women with PCOS, but it is not part of the diagnostic criteria. Overweight or obesity affects approximately 60-80\% of PCOS patients.\textsuperscript{11} PCOS together with thyroid disorder create independent risks of ovarian malfunction as well as pregnancy associated problem. An abnormal thyroid concentration could trigger alterations in ovulation and then menstruation. Initial stages of thyroid malfunction can result in delicate modification in ovulation as well as endometrial receptivity, which consequently may have drastic influence on fertility.\textsuperscript{12,13} 

Evaluation of thyroid function must be undertaken in any woman presenting with menstrual irregularities.\textsuperscript{14}

The most obvious connection between these two disorders (Thyroid and PCOS) is the increased BMI and insulin resistance. Increase in BMI is an integral part of PCOS and is seen in large majority (54-68\%) of these cases.\textsuperscript{15} PCOS is believed to be a heterogeneous dysfunction of multifactorial etiology. It can also be linked to primary hypothyroidism in 6.3\% of PCOS patients.\textsuperscript{16,17} Thyroid gland dysfunction manifested as hypothyroidism is a common disorder has been reported in PCOS patients. The clinical features of hypothyroidism also include weight gain, menstrual irregularities and infertility.\textsuperscript{11} Most of the times hypothyroidism is subclinical and diagnosed first time during evaluation of PCOS.\textsuperscript{7,14}

The main pathophysiological components of PCOS are gonadotropin dysfunction and insulin resistance. It has been found that both of these components are related to BMI.\textsuperscript{19-21}

\textbf{MATERIALS and METHODS}

\textbf{Study Design and Population}

The present study represents a case-control study. The study was carried out in 25 cases, between the age group (18-30 year) and 25 age and gender matched controls who attended the Out Patient Department, Department of Obstetrics and Gynaecology, Dr. S.N. Medical College and its associated group of hospitals, Jodhpur, Rajasthan, India.

The institutional ethical committee approved the study protocol. Informed consent was obtained from all the participants. A through clinical and symptomatic examination of all the patients was done with the help of treating clinicians and was recorded to rule out and confirm the presence of disease by evidence of symptoms. The detailed information regarding family background, personal history, dietary habits and physical activity of each subject was recorded. Family history for obesity and hypothyroidism was taken.

\textbf{Methods}

Informed consent was taken from patients and controls. A pre-structured Performa was used to collect the data. Baseline data including age, gender, BMI (kg/m\textsuperscript{2}), detailed medical history, clinical examinations. Sample was collected from women patients between the age group 18 – 30years, during 2\textsuperscript{nd} or 3\textsuperscript{rd} day of menstrual cycle, venous blood sample was drawn from antecubital vein of each subject by using aseptic techniques. Blood samples were collected in vial was allowed to clot. The serum was separated from the clotted specimen by centrifugation at 3000 rpm for 10 minutes and serum was estimated for T\textsubscript{3}, T\textsubscript{4} and TSH by using Enzyme Linked Fluorescent Assay Method.

\textbf{Statistical analysis}

The data assembled for different anthropometric and biochemical parameters were subjected to suitable statistical analysis to compute central tendencies (mean) and accompanying measures of variability statistics (standard deviation) etc for all the groups. The magnitude of inter group differences for each of the parameters was quantified by using students ‘t’ test values (Student’s ‘t’ test). On the basis of t-values, ‘p’ values (probability) were determined to make out significance of variance between the mean values of individual parameters among the groups of subjects studied.

\begin{table}[h!]
\centering
\caption{Mean BMI (kg/m\textsuperscript{2}) of the subjects studied}
\begin{tabular}{lcc}
\hline
S. No. & Group studied & BMI (Mean ± S.D.) [Range] \\
\hline
1 & Healthy Control (25) & 22.18 ± 1.97 [20.06-26.84] \\
2 & PCOS patients (25) & 25.19 ± 1.14 [22.72-27.11] \\
\hline
\end{tabular}
\end{table}

\begin{table}[h!]
\centering
\caption{Statistical analysis of BMI among the groups studied}
\begin{tabular}{ll}
\hline
S. No. & Group Compared & Healthy Control v/s PCOS patients \\
\hline
1 & t – value & 6.61 \\
2 & p – value & <0.0001 (HS) \\
\hline
\end{tabular}
\end{table}

\begin{table}[h!]
\centering
\caption{Mean Serum Thyroid Profile of the subjects studied}
\begin{tabular}{llll}
\hline
S.No. & Thyroid profile Tests & Healthy Control (25) & PCOS patients (25) \\
\hline
1. & Serum T\textsubscript{3} & Mean ± S.D. & Range \\
 & 1.53 ± 0.29 nmol/L & 1.04-2.02 & 1.64 ± 0.33 nmol/L & 1.10-2.26 \\
2. & Serum T\textsubscript{4} & Mean ± S.D. & Range \\
 & 93.05 ±9.75nmol/L & 78.59-113.87 & 97.82±17.67nmol/L & 60.98-123.12 \\
3. & Serum TSH & Mean ± S.D. & Range \\
 & 2.15 ± 0.84 µU/mL & 1.19-3.78 & 5.06 ± 1.21 µU/mL & 3.51-7.87 \\
\hline
\end{tabular}
\end{table}
RESULTS

The mean Body Mass Index (BMI) of the healthy control subjects was 22.18 ± 1.97; which varies from 20.06 to 26.84 kg/m². It was 25.19 ± 1.14 in PCOS patients which varies from 22.72 to 27.11 kg/m². (Table 1)

A statistically high-significant difference (p =< 0.0001) was observed in BMI of PCOS patients (t = 6.61) when results were compared with the healthy control subjects. (Table 2)

Serum triiodothyronine (T3) level varies from 1.04 to 2.02 nmol/L in healthy control subjects and 1.10 to 2.02 nmol/L in PCOS patients. Mean triiodothyronine was 1.53± 0.29 in healthy controls and 1.64± 0.33 in PCOS patients. (Table 3) Mean serum triiodothyronine (T3) values were non-significant (t=1.25, p=0.2167) in PCOS patients, as compared to healthy control subjects. (Table 4)

Serum tetraiodothyronine (T4) level varies from 78.59 to 113.87 nmol/L in healthy control subjects and 60.98 to 123.12 nmol/L in PCOS patients. Mean serum tetraiodothyronine (T4) level was 93.05± 9.75 nmol/L in healthy controls and 97.82± 17.67 in PCOS patients. (Table 2) Mean serum tetraiodothyronine (T4) were non-significant (t=0.24, p=1.18) in PCOS patients, as compared to healthy control subjects. (Table 4)

The serum TSH levels varied from 1.19-3.78 µIU/mL in healthy control subjects and 1.30-7.87 µIU/mL in PCOS patients. Mean serum TSH level was 2.15±0.84 µIU/mL in healthy control subjects and 4.00±1.86 in PCOS patients. (Table 3) Mean serum TSH values were highly significant (t=4.53, p<0.001) in PCOS patients, as compared to healthy control subjects. (Table 4)

DISCUSSION

Polycystic ovarian syndrome (PCOS) is an intense problem which manifests later as infertility, obesity, insulin resistance, dyslipidemia, endolthal dysfuncion and overt diabetes mellitus. PCOS is often associated with abnormalities of other endocrine glands. Women with PCOS may be four times more likely to suffer from hypothyroidism.22

In our study, we found that the BMI values in the cases were significantly higher than in the control group. Thatapadi S et al (2014) observed a statistically high-significant difference (p<0.0001) in BMI of PCOS patients as compared to healthy control subjects.23 Ibraheem NJ et al (2015) also observed a statistically highly significant difference (p=0.02) in BMI of PCOS patients (25.19 ± 1.14) which in turn contribute to PCOS symptoms like infertility, polycystic ovaries, hirsutism, male pattern hair loss and acne. If hypothyroidism is diagnosed and treated early, some of PCOS symptoms may diminish.25

Our study showed that the mean TSH level were significantly higher in the cases than those in the control group which was consistent with Janssen OE et al (2004). This study did not show a statistically significant difference between cases and controls regarding T3 and T4 levels which was consistent with study by Shirsath A et al (2015).27

Mean serum TSH values were highly significant (t=4.53, p<0.001) in PCOS patients in our study. Similar result was obtained by Janssen OE et al (2004) in his study, which demonstrated a threefold higher prevalence of hypothyroidism in patients with PCOS.

In fewer other studies same results obtained, like Baul SN et al (2013) observed a statistically highly-significant relation (p<0.05) in serum TSH levels between normal individuals (2.67± 3.11 µIU/ml) and PCOS patients (4.55± 2.66 mIU/ml).28 Shirsath A et al (2015) also reported a highly significant relation (p<0.05) in Thyroid stimulating hormone (TSH) levels (µU/mL) between normal individuals (1.26±0.45) and PCOS patients (7.13±1.60).27

The study also evaluated that there is no relationship between thyroid hormones and PCOS disease which is similar with few old literatures. Shirsath A et al (2015) reported a non-significant relation (p>0.05) in triiodothyronine (T3) levels (ng/ml) between normal individuals (1.26 ± 0.21) and PCOS patients (1.30±0.16).27 Abdeisalam A and Ibrahim W (2015) also observed a non-significant relation (p>0.05) in triiodothyronine (T3) levels between normal healthy subjects and PCOS patients. Our findings of serum triiodothyronine (T3) levels were in accordance with the above studies.29

Shirsath A et al (2015) reported a non-significant relation (p>0.05) in tetraiodothyronine (T4) levels (µg/dl) between normal individuals (7.52±1.82) and PCOS patients (7.87±1.38).27

CONCLUSION AND RECOMMENDATIONS

The positive correlation between serum TSH levels and the presence of higher BMR in our study threw bright light that female patients with PCOS must be investigated for the presence of Subclinical hypothyroidism which is proved to be metabolic risk factors. As there is high prevalence of thyroid disorders in PCOS patients, all women in their reproductive age with and without PCOS, should have their thyroid function tests evaluated. Secondly correcting subclinical hypothyroidism will lead to improvement of overall hormonal and metabolic health of these females.
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