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Serum PRL, TSH and Insulin Have Any Association with Insulin Resistance in Females with Polycystic Ovary Syndrome

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ABSTRACT

Background & Objective: One of the main public health issues in India that has medical repercussions is polycystic ovarian syndrome. As a result of its several etiological factors, including menstruation disruption, dyslipidemia, insulin resistance, obesity, and infertility. Hence, the main objective of the study is to evaluate the levels of serum PRL, TSH, FBG, Insulin and find out its association with HOMA-IR in females with PCOD.
Method: - The cross-sectional study was conducted at SGT Medical College and Hospital, Gurgaon where a total of 200 females participated in the study, out of which 100 were considered as a study group and 100 were considered as a healthy control group between the age group of 18-45 years. Fasting blood samples were drawn to assess the levels of serum PRL, serum Insulin, TSH, FBS and were sent to laboratory.
Result: A significant increase in the level of PRL, TSH, FBG, Insulin and HOMA-IR ($p<0.001$) were found in patients with PCOS in comparison with controls. Significant correlation was found between Serum Insulin and HOMA-IR. Further, no significant correlations were found between serum prolactin, TSH, FBG and HOMA-IR.
Conclusion: Elevated levels of PRL, TSH and Insulin indicates the possibility of developing Insulin Resistance among patients of PCOS. Insulin Resistance may be helpful in diagnosing number of comorbidities that may lead to metabolic syndrome, hypertension, dyslipidaemia, glucose intolerance, and diabetes.

Keywords: Prolactin, Thyroid Stimulating Hormone, Fasting Blood Glucose, Homeostatic Model Assessment for Insulin Resistance, Polycystic Ovary Disorder

INTRODUCTION

One of the most common endocrine disorders in women of reproductive age is polycystic ovary syndrome (PCOS), also known as Stein-Leventhal syndrome. It is characterised by increased ovarian and adrenal androgen secretion, hyper androgenic metabolic syndrome symptoms like hirsutism, acne, and/or alopecia, irregular menstruation, and polycystic ovaries.[1] It has been seen that between 5% and 10% of women in the reproductive age group have PCOS. 20–25% of women have polycystic ovary disease alone.[2] The presence of PCOS increases a woman's risk of experiencing infertility, endometrial cancer, obesity, type 2 diabetes,

dyslipidaemia, hypertension, and cardiovascular disease (CVD).[3] Although the pathogenesis of PCOS is not entirely known, insulin resistance and obesity, particularly central obesity, have been linked to the disease. The vast majority of PCOS women are insulin-resistant and exhibit metabolic abnormalities.[4,5]

Prolactin (PRL) is a multifunctional polypeptide that promotes beta-cell survival and proliferation as well as insulin secretion.[6] Circulating PRL is said to increase hepatic insulin sensitivity and 5-hydroxytryptamine and serotonin production, which can enhance islet development. Additionally, multiple studies have shown that PRL impacts the metabolism through the control of important enzymes and transporters linked to insulin resistance, hypertension, or coronary syndrome.[7-12] Prolactin (Prl) is a pituitary hormone that functions as a single-chain polypeptide in a variety of ways, including lactation, luteal function, reproduction, hunger, fertility suppression, homeostasis, osmotic balance, immunity, and coagulation. Prolactin has been identified as a powerful lipogenic and diabetogenic agent, influencing energy balance and fuel metabolism.[13]

Women with PCOS are more likely to have increased levels of thyroid-stimulating hormone (TSH), which may contribute to their phenotype.[14] Hypothyroidism is a disorder in which glucose absorption in muscle and adipose tissue becomes insulin resistant, causing high insulin levels in these patients.[15]

It has been noted in various research that fasting insulin and insulin sensitivity are correlated with plasma levels of thyroid-stimulating hormone (TSH).[16]

Hence, the purpose of the study is to evaluate the levels of serum PRL, TSH, FBG, Insulin and find out its association with HOMA-IR in females with PCOD.

MATERIAL AND METHOD

The present study was done in Departments of Biochemistry and Gynecology & Obstetrics of Faculty of Medicine and Health Sciences, SGT University, Budhera, Gurugram. The study includes 100 clinically diagnosed cases of PCOS between the age group of 18-45 years attending Obstetrics & Gynecology OPD of SGT Hospital.

Selection of study group was done on the basis of their History, Physical examination, laboratory and radiological investigation.

The following radiological criteria will be used on ultrasonography findings:

- Number of follicles ≥ 12 having diameter 2-9 mm diameter.
- The volume of each ovary > 10cc with peripheral volume of follicles.

100 age matched healthy volunteers from general population was taken as control. After explaining the purpose details of the study to all the subjects of both the groups, a written and informed consent was taken. Ethical clearance was taken from the Institutional Ethical Committee before starting of collection of samples.

Women with irregular menses and radiologically confirmed for PCOD were included in the study while women with other endocrinal disorder, on Vitamin D drugs, Pregnant women and having any other chronic diseases were excluded from the study.

A pre-structured and pre-tested proforma was used to collect the data. Baseline data including age, BMI, detailed medical history, clinical examinations and relevant investigations were included as part of the methodology. Serum prolactin (PRL), Thyroid stimulating Hormone (TSH), Insulin, Insulin Resistance (IR), Fasting Blood Glucose (FBG) levels were measured. The blood samples were obtained from peripheral veins between the 3rd and 9th days of the menstrual cycle, or 60 days after the last menstrual period, following a fasting period of at least 12 hours.

Glucose levels were measured using ERBA EM360, Serum PRL, TSH, Insulin was analysed by Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI. Insulin Resistance will be calculated by HOMA-IR according to the formula: fasting insulin (µU/L) x fasting glucose (nmol/L)/22.5.

The subject is considered to have insulin resistance if HOMA-IR value is more than 2.7.

STATISTICS ANALYSIS

SPSS software version 22.0 was used for statistical analysis. Correlation analysis of Serum prolactin, Serum TSH and Serum Insulin with Insulin resistance were done using Pearson correlation coefficients where P value < 0.005 was considered statistically significant.

RESULT

Results were presented as Mean ± SD. Table 1 depicts the basic characteristics and mean distributions of biochemical parameters in both cases and controls. The concentration of fasting serum PRL, TSH, Insulin, fasting plasma glucose, and HOMA-IR in controls are 6.7 ± 1.4 ng/mL, 3.05 ± 0.51 mg/dL, 6.651± 2.92 µIU/ml, 86.796± 7.793 mg/dL, 1.42 ± 0.674 respectively; in PCOS cases they are 12.6 ± 5.1 ng/mL, 10.65 ± 1 mg/dL, 21.0610 ± 8.62 µIU/ml, 103.13 ± 23.464 mg/dL, and 5.349 ± 2.745 respectively. It was observed that the mean levels of serum PRL, Insulin, TSH and HOMA-IR were higher in subject group as compared to the healthy controls and their levels were found to be statistically significant. (P<0.005)

Table-1: Mean distribution of biochemical parameters in PCOS cases and controls.

Parameters	Controls (n = 100)	Cases with PCOS (n=100)	p value
SERUM PRL (ng/mL)	6.7 ± 1.4	12.6 ± 5.1	<0.001
SERUM TSH (mg/dL)	3.05 ± 0.51	10.65 ± 1	<0.001
INSULIN (µIU/ml)	6.651± 2.92	21.0610 ± 8.62	<0.0001
FBG (mg/dL)	86.796± 7.793	103.13 ± 23.464	<0.0001
HOMA-IR	1.42 ± 0.674	5.349 ± 2.745	<0.0001

Table-2 Shows the correlation between all the parameters with HOMA-IR. No significant correlation was found between PRL and HOMA-IR (P= 0.3), TSH and HOMA-IR (P= 0.460), FBG and HOMA-IR (P=0.05). Further, a significant positive correlation was observed between Serum Insulin and HOMA-IR (P= 0.00).

FIGURE 1: OF HYPOTHYROIDISM AMONG THE STUDY GROUP

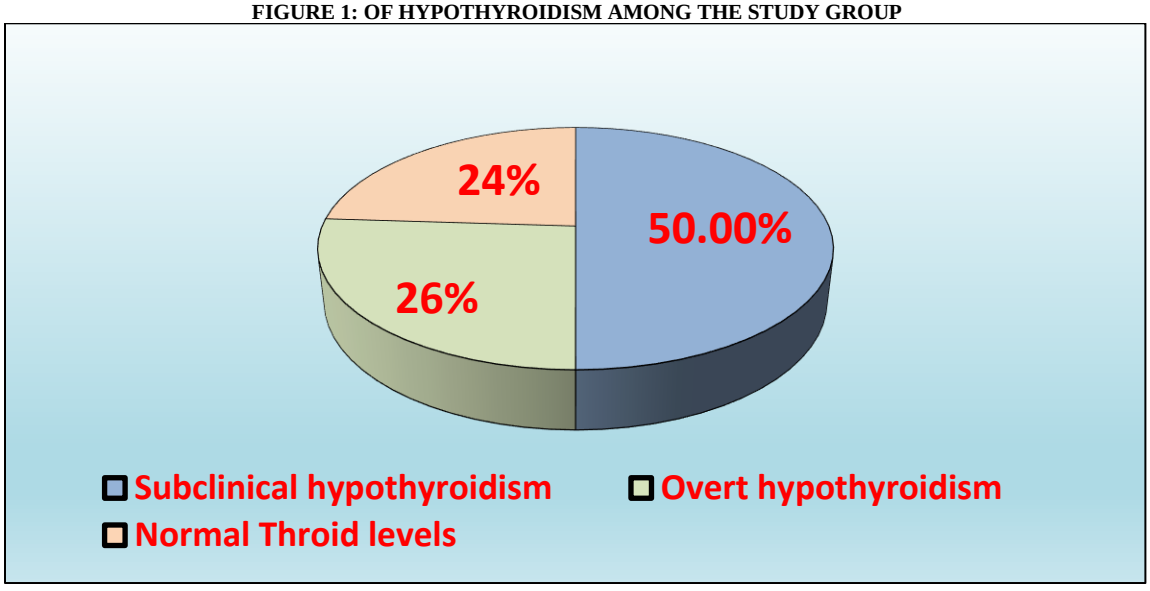

Figure 1 shows of the total 100 patients in the study, 76 of them Hypothyroidism (76%), most of whom 50 (50%) had subclinical hypothyroidism while 26 (26%) of them had overt hypothyroidism with the TSH levels in the higher range.

Table-2: Correlation between various parameters

Parameters	Cases with PCOS (r)	p value
PRL and HOMA-IR	-0.1047	0.3
TSH and HOMA-IR	- 0.1411	0.16
INSULIN and HOMA-IR	0.877	<0.00
FBG and HOMA-IR	-0.1917	0.05

DISCUSSION

Polycystic ovarian syndrome (PCOS) is a diverse illness with uncertain causes that affects 5-10% of reproductive-age women. It is a condition that affects reproductive, endocrine, and metabolic systems and is the most common cause of prolonged anovulation, which leads to infertility.[17, 18] Obesity, insulin resistance, dyslipidemia, and endothelial dysfunction are also connected with it.[19] In the current study, PCOS women had higher mean prolactin levels than controls, and the differences between cases and controls were statistically significant (P<0.001). This finding is in agreement with the study given by Roy George K et. al. which states that serum insulin and prolactin levels are considerably higher in PCOS women. This elevated prolactin may enhance adrenal androgen output by inhibiting 3beta-hydroxysteroid dehydrogenase activity or, less frequently, by selective impact on DHEA sulfation in adrenal or extra-adrenal locations. Prolactin, on the other hand, inhibits FSH-induced ovarian aromatase, resulting in intraovarian hyperandrogenemia.[20]

In our study, there was no a significant correlation between prolactin and HOMA-IR in PCOS patients (p= 0.3). Similarly, no significant relationship was identified between serum TSH and HOMA-IR in PCOS patients (p= 0.460). The effect of prolactin on glucose metabolism and insulin resistance is proportional to its circulating levels.

Thyroid dysfunction is frequent in women of reproductive age, with increased TSH levels ranging from 4 to 9%. [21, 22] Recently, there has been a surge of interest in the link between thyroid function, weight, and metabolic condition. According to Reinehr and Andler, thyroid function is similarly connected to weight status, with elevated TSH levels in obese women. Our study showed higher mean TSH levels 10.65 ± 10 mg/dl in PCOD group, compared to the healthy control group 3.05 ± 0.51 mg/dl. Similar, results were observed in studies given by Ram Babu et. al.[23]

These results corroborate the fact that there is a strong association between PCOS and thyroid dysfunction. This connection may be related to the obesity and Insulin resistance. There were 50% patients in the study group who had subclinical hypothyroidism while 26% patients had overt hypothyroidism. This condition may be worsening the risk of PCOS in women which m ay elevate the risk of infertility. A study by Sinha et al reported subclinical hypothyroidism in 22.5% while clinical hypothyroidism in only 2.5% of the cases.[24]

A. Muller[25] showed the association between TSH increasing IR in women with PCOS. However, in our study there was no significant correlation was found among TSH and HOMA-IR and their Pearson correlation coefficient was (P=0.460). Many studies have been found showing positive correlation of TSH and IR with the reason that in certain women with PCOS, IR may be exacerbated by disrupted thyroid function, as seen by higher TSH levels.

A number of studies have found that hyperinsulinemia may play a key role in the development of hyperandrogenism in PCOS patients.[26] The impairment of insulin's ability to induce glucose uptake and utilization results in insulin resistance, a metabolic disorder. [27] In studies given by Seow et al. discovered that IR in PCOS involves both receptor and post-receptor problems, such as deficits in

phosphatidylinositol 3-kinase and the GLUT-4 glucose transporter.[28]

In our study, Higher mean Serum Insulin and HOMA-IR were recorded in PCOS subject group as compared to healthy control and their difference found to be statistically significant (P<0.01). Similar investigations published by Kundu D. et al. discovered that the mean fasting Serum Insulin and HOMA_IR values were greater in PCOS subjects compared to healthy controls and were statistically significant, indicating that insulin resistance played a critical role in the etiology of PCOS.[29] Similar results were also given by Shou-Kul Xiang et. al. as they discovered that the HOMA-IR of PCOS women was considerably greater than that of age-matched healthy women, implying that insulin resistance played a critical role in the etiology of PCOS. [19]

Further, the results of our study showed mean fasting blood glucose in normal healthy women (controls) as 86.796± 7.793 mg/dl and in PCOS women (cases) it was 103.13 ± 23.464 mg/dl. There was very highly significant statistical difference in the mean fasting blood glucose values (P<0.0001).

CONCLUSION- The current study offers more proof that the PCOD group had considerably higher PRL, TSH, fasting insulin and HOMA levels, which are indicators of the presence of IR. IR in the PCOS group may be able to predict the development of dysglycemia in PCOS-afflicted females. Because of the disturbed metabolism females may get effected more and develop severe morbidities such as infertility, irregular periods, obesity, Diabetes and CVD. So, a large-scale clinical trial with subjects suffering from polycystic ovarian syndrome should be undertaken for evaluating risk of metabolic and endocrine disorders may be undertaken.

Abbreviations: PCOS; Polycystic Ovarian Syndrome, FBG; Fasting Blood Sugar, IR; Insulin Resistance, HOMA; Homeostasis Model Assessment

Declaration by Authors

Ethical Approval: Approved by Institutional ethical committee

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