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A COMPARATIVE STUDY OF SERUM ERRITIN LEVELS AND INSULIN RESISTANCE IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Introduction: Five to ten percent of women in the reproductive age range suffer with PCOS, one of the most common endocrine disorders. It is a diverse condition marked by hyperandrogenism and persistent anovulation. PCOS is linked to obesity and insulin resistance in addition to ovulatory dysfunction and hyperandrogenic characteristics.

Aims: To analyse the fasting serum levels of ferritin, insulin, iron, glucose and whole blood HbA1c in patients with PCOS and in normal women without PCOS. To measure the BMI, waist circumference and BP in the cases and control groups. To compare the parameters mentioned in cases and controls for any significant statistical differences.

Materials & Methods: Study type Case control study, Outdoor patient of Vani Vilas Hospital , Bangalore, study period from November, 2015 to September, 2017 and total sample size was 60

Result: In Cases Group, 6 (20.0%) patients were ≤25 BMI (kg/m2), 15 (50.0%) patients were 25-30 BMI(kg/m2), 9 (3.0%) patients were ≥30 BMI (kg/m2).In Controls Group, 20 (66.7%) patients were ≤25 BMI (kg/m2), 7 (23.3%) patients were 25-30 BMI(kg/m2), 3 (10.0%) patients were ≥30 BMI (kg/m2).Association of BMI (kg/m2) with cases and controls Group was statistically significant (p=0.0015)

Conclusion: Iron metabolism may be involved in the pathogenesis of PCOS, as indicated by elevated blood ferritin levels and their association with insulin resistance. To enhance metabolic outcomes for PCOS patients, more research is necessary to examine the mechanistic connection and assess treatment approaches that target iron metabolism.

Keywords: Insulin resistance**,** Polycystic Ovary Syndrome, BMI and hyperandrogenism

INTRODUCTION

Five to ten percent of women in the reproductive age range suffer with PCOS, one of the most common endocrine disorders. It is a diverse condition marked by hyperandrogenism and persistent anovulation. PCOS is linked to obesity and insulin resistance in addition to ovulatory dysfunction and hyperandrogenic characteristics [1]. Iron overload has been identified as a potential biological factor in insulin resistance. One of the main risk factors for type 2 diabetes mellitus (T2DM) and the ensuing cardiovascular disease is insulin resistance [2]. According to studies, the pathophysiology of insulin-resistant diseases such type 2 diabetes and metabolic syndrome frequently involves elevated body iron storage. Because iron buildup promotes insulin resistance and may lead to pancreatic β cell malfunction and diabetes mellitus, this participation seems to be reciprocal, as insulin resistance may also promote iron accumulation [3]. Because insulin may boost intestinal iron absorption by upregulating the activity of hypoxia-inducible factor-1α6, this hyperinsulinemia brought on by insulin resistance may also contribute to elevated body iron storage and serum ferritin levels.Long-term metabolic issues, including poor glucose tolerance, type 2 diabetes, and cardiovascular illnesses, may follow androgen production in PCOS, which has been thought to be caused by hyperinsulinemia [4]. Serum ferritin levels and insulin resistance in PCOS patients were analyzed in this study and compared to those of age and BMI-matched, seemingly healthy females. There aren't many studies on the relationship between IR and serum ferritin and iron levels in PCOS, especially in South Indian populations. More research is needed to validate these associations because PCOS and insulin resistance are more common in our group.Thus, the necessity of this research.

METERIALS AND METHODS

Study type: Case control study.
Place of study: Outdoor patient of Vani Vilas Hospital, Bangalore
Study period: November, 2015 to September, 2017
Sample size: 60

Inclusion criteria:

- Patients diagnosed with PCOS, ascertained by USG as per Rotterdam criteria.
- Age group: 15 to 45 years.
- Patients who give consent

Exclusion criteria:

1. Secondary etiologies of hyperandrogenism (clinically diagnosed)-
   - congenital adrenal hyperplasia
   - androgen secreting tumors
   - cushing‘s syndrome
2. Patients with hypertension, diabetes mellitus or any other chronic systemic diseases.
3. Pregnancy
4. Patients with haemoglobin <12g/dl
5. Those on any medications that affect the iron status and the menstrual cycles.

PARAMETERS STUDIED

The following parameters were taken for the present study:

Biochemical

1. Serum ferritin (ng/mL).
2. Serum insulin (µU/mL).
3. Serum fasting glucose (mg/dl) .
4. Serum iron (µg/dl).
5. Hba1c (%).

The level of Insulin resistance was determined by Homeostasis Model Assessment Index (HOMA-IR), and was calculated according to the following equation: [Fasting insulin(µU/mL) x Fasting glucose (mg/dl)] /405

Anthropometric
1. Waist circumference in centimeters(cm)
2. BMI (Kg/m2).

Statistical Analysis:
For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two- sample t-tests, which compare the means of independent or unpaired samples, were used to assess differences between groups. Paired t-tests, which account for the correlation between paired observations, offer greater power than unpaired tests. Chi-square tests (χ^2 tests) were employed to evaluate hypotheses where the sampling distribution of the test statistic follows a chi-squared distribution under the null hypothesis; Pearson's chi- squared test is often referred to simply as the chi-squared test. For comparisons of unpaired proportions, either the chi-square test or Fisher's exact test was used, depending on the context. To perform t-tests, the relevant formulae for test statistics, which either exactly follow or closely approximate a t-distribution under the null hypothesis, were applied, with specific degrees of freedom indicated for each test. P-values were determined from Student's t-distribution tables. A p-value ≤ 0.05 was considered statistically significant, leading to the rejection of the null hypothesis in favour of the alternative hypothesis.

RESULT

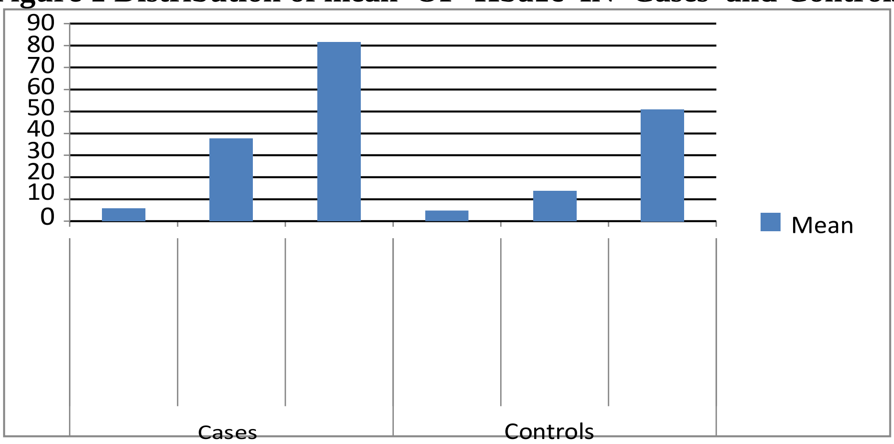
Table 1: Association between BMI in cases and controls

BMI(kg/m2)	Cases		Controls		P -value
	Number	%	Number	%	
<25	6	20	20	66.7	0.0015
25-30	15	50	7	23.3	
≥30	9	30	3	10	
Total	30	100	30	100	

Table2: Distribution of mean OF Hba1c IN Cases and Controls

Parameter	Cases	Controls	P- value
Hba1c (%)	5.747±0.6428	4.99±0.571	0.000011
INSULIN (µU/ml)	37.61±23.0305 2	13.63967±7.07873 2	<0.0001
FERRITIN(mg/ml)	81.50±63.98	50.83±39.92	0.02981

Figure 1 Distribution of mean OF Hba1c IN Cases and Controls



In Cases Group, 6 (20.0%) patients were ≤25 BMI (kg/m2), 15 (50.0%) patients were 25-30 BMI(kg/m2), 9 (3.0%) patients were ≥30 BMI (kg/m2).In Controls Group, 20 (66.7%) patients were ≤25 BMI (kg/m2), 7 (23.3%) patients were 25-30 BMI(kg/m2), 3 (10.0%) patients were ≥30 BMI (kg/m2).Association of BMI (kg/m2) with cases and controls Group was statistically significant (p=0.0015).In Cases, the mean Hba1c (%) (mean± s.d.) of patients was 5.747±0.6428.In Controls, the mean Hba1c (%) (mean± s.d.) of patients was 4.99±0.571. Distribution of mean Hba1c (%) with cases and controls Group was statistically significant (p=0.000011).In Cases, the mean INSULIN (µU/ml) (mean± s.d.) of patients was 37.61±23.03052.In Controls, the mean INSULIN (µU/ml) (mean± s.d.) of patients was 13.63967±7.078732. Distribution of mean INSULIN (µU/ml) with cases and controls Group was statistically significant (p<0.0001).In Cases, the mean FERRITIN (mg/ml) (mean± s.d.) of patients was 81.50±63.98.In Controls, the mean FERRITIN (mg/ml) (mean± s.d.) of patients was 50.83±39.92. Distribution of mean FERRITIN (mg/ml) with cases and controls Group was statistically significant (p=0.02981).

DISCUSSION

Women with PCOS diagnosed between the ages of 15 and 45 were the subjects of this study. Serum ferritin and insulin resistance levels in these patients and healthy controls were to be compared and evaluated. In this study, 30 women with PCOS were enrolled as cases, whereas 30 women without PCOS who were matched for age and BMI served as controls. Thirty patients with polycystic ovarian syndrome and their age-matched controls had their blood samples thoroughly analyzed. Clinical history and biochemical markers were used to study them, with particular attention paid to serum ferritin and insulin resistance (serum insulin and fasting blood glucose). The following lists the study's key findings. The Rotterdam European Society of Human Reproduction and embryology (ESHRE)/American Society for Reproductive Medicine (ASRM) criteria were used to diagnose polycystic ovarian syndrome in this study. The age range of the study population, which was also that of the controls, was 15–45 years old. The average age of the controls was 28.73±5.95 years, while the average age of the cases was 26.26±5.77 years.

The study also included two anthropometric measurements (waist circumference) in addition to biochemical markers. According to the data, the mean ± standard deviation for BMI and waist circumference was 28.16±4.63 kg/m2 and 90.83±28.53 cm for the patients and 24.6±3.60 kg/m2 and 78.2± 8.26 cm for the controls. Additionally, PCOS women had considerably greater levels of both than controls (p=0.001539 and 0.007247, respectively). These results are consistent with a prior study by Fahimeh Ramezani Tehran et al. that shown a relationship between PCOS and BMI and WC [5]. The average fasting blood glucose level in the patients was 119.43±35.0024 mg/dl, while the mean for the controls was 90.78±16.90831 mg/dl. According to the current study, people with PCOS had a substantially higher mean level of fasting blood glucose than healthy controls (p =0.000161). These results were consistent with Michael L. Traub's study, which found that PCOS patients had higher FBG than healthy controls. The homeostasis model assessment (HOMA) was used to measure insulin resistance.In cases, the mean ± standard deviation of insulin and insulin resistance was 37.61±23.03052 and 11.254±7.45, respectively, while in controls, the corresponding values were 13.63967±7.078732 and 3.029±1.90. Both insulin and insulin resistance had P values less than 0.00001.

As a result, it shown that, in comparison to the controls, PCOS patients had noticeably greater insulin resistance. These results are consistent with a study by Andrea Dunaif, who stated that insulin resistance is visible in PCOS patients who have anovulatory cycles and hyperandrogenism [6].The mean ± standard deviation of Hba1c in this study was 5.747 ± 0.6428 percent in cases and 4.99 ± 0.571% in controls. The mean in cases was substantially higher (p=0.000011). PCOS patients have higher levels of glycated hemoglobin, according to a study by Lerchbaum E, Schwetz V, Giuliani A, and Obermayer-Pettetsch B [7].

Serum iron mean ± standard deviation was 108.2667 ± 32.5798 µg/dl in patients and 96.83333 µg/dl in controls. When compared to the controls, it was shown that women with PCOS had higher mean serum iron concentrations; however, this difference was not statistically significant (p value 0.212496), while there was a positive link with serum ferritin. This result supports that of Fernandez-Real J M, who found that serum ferritin and iron were positively correlated in pre-diabetic people [8].

According to the data, the mean ± standard deviation of serum ferritin was 81.50867±63.98957 ng/ml for cases and 50.83567±39.9246 ng/ml for controls. Women with PCOS had significantly higher serum ferritin levels than controls (p=0.02981). Our results align with those of a prior study conducted by Manuel Luque Ramirez et al. [9]. They hypothesized that the elevated body iron reserves in PCOS are caused by insulin resistance and hyperinsulinemia.

According to this study, the mean serum ferritin levels of PCOS cases significantly increased, and there was a positive link between these levels and an increase in waist circumference (r=0.0172; p=0.007247). This study is supported by a study by Ilhan Tarkun et al. that found a link between ferritin and waist circumference [10]. Serum ferritin exhibits a negative association with Hba1c (r=-0.1398, p=0.000011) and BMI (r=-0.0018, p=0.001539), but a substantial positive correlation with FBG (r=0.0834, p=0.000161) and Insulin Resistance (r=0.1586, p<0.00001) in the current study. This is consistent with the research conducted by Sheu W H et al.who showed that serum ferritin, fasting blood glucose, and insulin are positively correlated [11].

The current study shows that women with PCOS have significantly elevated serum ferritin levels. All PCOS women with hyperandrogenism and a history of anovulation have insulin resistance. Insulin resistance may develop in hyperinsulinemia due to pancreatic β cell malfunction brought on by elevated iron levels. Conversely, insulin resistance may promote iron absorption by downregulating hepcidin expression and increasing the activity of hypoxia-inducible factor-1 α. The two processes may therefore be directed [12].

Iron metabolism is known to be influenced by insulin. Insulin reroutes transferrin receptors from an internal membrane compartment to the cell surface, causing fat cells to rapidly and noticeably increase their uptake of iron. Crucially, in the microsomal membranes of cultured adipocytes, transferrin receptors have been demonstrated to colocalize with insulin-responsive glucose transporters and insulin-like growth factor II receptors. This implies that insulin regulates iron uptake in tandem with its effects on glucose transport. Iron affects how glucose is metabolized. Iron prevents the hepatic glucose synthesis from being inhibited by insulin. Peripheral hyperinsulinemia results from decreased hepatic insulin extraction and metabolism caused by increased iron storage. In actuality, hepatic insulin resistance is the first and most prevalent anomaly observed in iron overload circumstances. Skeletal muscle, which is the primary effector of insulin action, has also been found to be impacted by iron excess [13].More research in the Indian population is necessary to support the current study, nevertheless, because the sample size is limited (30 cases and 30 controls).

CONCLUSION

We concluded that comparison to healthy controls, we found that women with PCOS have considerably higher serum ferritin levels and more insulin resistance. The found positive relationship between insulin resistance and serum ferritin raises the possibility that systemic inflammation and iron metabolism play a part in the pathogenesis of PCOS. The significance of keeping an eye on serum ferritin levels as a possible biomarker for metabolic abnormalities in PCOS patients is highlighted by these findings. More research is required to determine the precise mechanisms behind the relationship between ferritin and insulin resistance as well as to determine whether iron metabolism-focused therapy approaches could enhance metabolic results in the treatment of PCOS.

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