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Cross-Sectional Study To Correlate Serum Ferritin Level with Insulin Resistance in women Suffering From Polycystic Ovarian Syndrome in the Department of Obstetrics and Gynaecology

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder associated with insulin resistance and metabolic dysfunction. Elevated serum ferritin levels in PCOS indicate iron overload, which may impair insulin signaling, contributing to hyperinsulinemia and metabolic imbalance. Understanding this relationship could guide improved therapeutic strategies.

Aim: to study the correlation of serum ferritin level with insulin resistance in women diagnosed with polycystic ovary syndrome.

Result: The study of 65 PCOS patients revealed a mean age of 26.03 ± 5.27 years, predominantly Hindu and urban middle-class. Mean serum ferritin was 52.02 ± 31.22 ng/mL and HOMA-IR 3.25 ± 1.87. A strong positive correlation ($r = 0.74$, $p < 0.0001$) was observed between serum ferritin and insulin resistance, indicating significant metabolic association.

Method: This prospective study was conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, including women aged 16–40 years diagnosed with PCOS using Rotterdam criteria. Detailed demographic, clinical, and biochemical evaluations were performed. Serum ferritin, fasting insulin, and glucose were measured to calculate HOMA-IR.

Correlations between serum ferritin, insulin resistance, and metabolic parameters were statistically analyzed to assess metabolic risk in PCOS.

Conclusion: In conclusion, elevated serum ferritin levels are significantly associated with increased insulin resistance in women with PCOS, independent of ovarian

morphology or anthropometric factors. Ferritin may serve as a valuable early marker for metabolic dysfunction, aiding in timely identification and management. Larger, multicentric studies are needed to validate these findings.

Keywords: Polycystic Ovary Syndrome, Serum Ferritin Levels, Serum Insulin, Ovarian Morphology, Anthropometric Factors.

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder characterized by hyperandrogenemia, insulin resistance, hyperinsulinemia, and chronic anovulation. It is the most common endocrine condition among women of reproductive age and is strongly associated with insulin resistance, impaired glucose tolerance, and an increased risk of type 2 diabetes. Studies suggest that serum ferritin levels are often elevated in women with PCOS, indicating mild iron overload.[1] This may result from reduced menstrual blood loss due to chronic anovulation, insulin resistance, and decreased hepcidin levels, which enhance iron absorption.[2]

Ferritin, an intracellular iron-storage protein, reflects total body iron stores and plays a vital role in maintaining iron homeostasis.[3] Excess iron acts as a pro-oxidant, generating oxidative stress that impairs insulin signaling and β-cell function, promoting insulin resistance and hyperinsulinemia. Early evidence linking iron overload to diabetes emerged from studies on hereditary hemochromatosis (HH) and transfusional iron overload. Jiang et al.[4] (2004) demonstrated that elevated ferritin levels increased the risk of type 2 diabetes, even among healthy women. Another study found that phlebotomy reduced glucose, cholesterol, and triglycerides while improving β-cell function and insulin sensitivity in diabetic patients. A 2016 pilot study by Wilson MS and Thompson EW showed that venesection, combined with oral therapy, may serve as an effective alternative to insulin in type 2 diabetes with elevated ferritin.

A 1997 cross-sectional study also linked mildly elevated ferritin to increased fasting insulin levels, indicating higher insulin demand to maintain normoglycemia. A meta-analysis and the 2008 study by Le et al.[5] supported ferritin as a potential early predictor of diabetes. Even slightly elevated iron stores can affect glucose homeostasis. However, this relationship is not yet reflected in diabetes management guidelines.

In PCOS, iron overload is associated with hyperandrogenism and menstrual irregularities. Impaired glucose transport increases free fatty acids, worsening insulin resistance and hyperinsulinemia. Elevated insulin enhances ovarian androgen synthesis via IGF-I and LH, disrupting follicular maturation. Assessing serum ferritin and insulin resistance markers may reveal ferritin's dual role in iron metabolism and inflammation in PCOS.

This study Aim's to study the correlation of serum ferritin level with insulin resistance in women diagnosed with polycystic ovary syndrome.

Materials and Methods

Study Type and Design: This hospital-based observational and analytical cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur, to evaluate the relationship between serum ferritin levels and insulin resistance in women with polycystic ovary syndrome (PCOS).

Study Duration: The study began in July 2023. Data collection commenced after obtaining ethical committee approval in October 2023 and continued until the

required sample size was achieved. An additional two months were allotted for data compilation and statistical analysis.

Study Population: The study included women aged 16–40 years diagnosed with PCOS based on the Rotterdam criteria. These criteria included oligo-anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries identified on ultrasound.

Ethical Clearance: Ethical approval was obtained from the institutional review board and the ethics committee of SMS Medical College before initiating the study. All participants provided written informed consent prior to enrollment.

Selection Criteria: Inclusion criteria comprised women aged 16–40 years diagnosed with PCOS, willing to participate, and not involved in any other study. Exclusion criteria included women with adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome, thalassemia, recent transfusion or iron therapy, chronic illnesses, or a history of smoking, alcohol, or drug use.

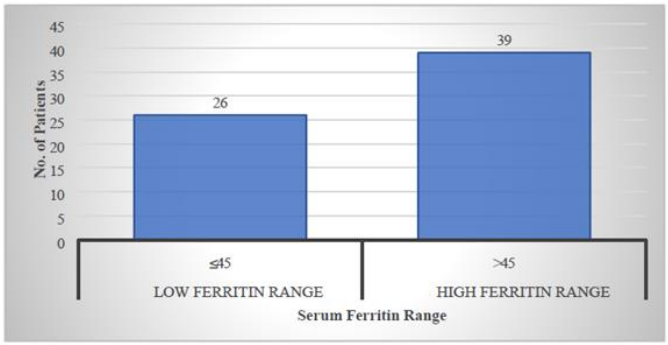
Sample Size: A total of 65 participants were included, with sample size calculated from a previous study on serum ferritin and insulin resistance in PCOS, ensuring 80% statistical power and 0.05 alpha error.

Methodology: Women attending the outpatient department meeting eligibility criteria provided written consent. Demographic, medical, and menstrual histories were recorded, and BMI was calculated. Laboratory tests included CBC, blood sugar, serum ferritin, hormones, lipid profile, HbA1c, and CRP. HOMA-IR was calculated as Fasting insulin × Fasting glucose / 22.5. Participants were classified by ferritin levels, and correlations with metabolic parameters were analyzed.

Results & Observations

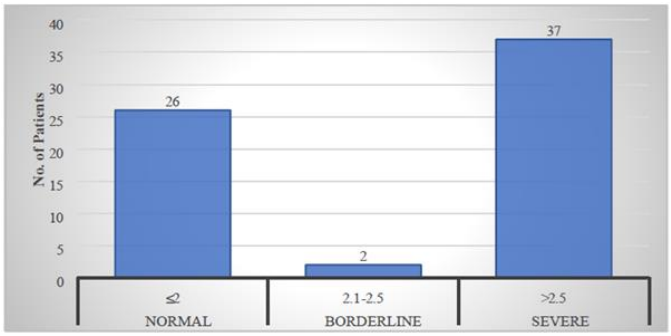
The majority of patients were aged 21–25 years, predominantly Hindu, and from urban middleclass backgrounds. Mean serum ferritin and HOMA-IR were 52.02 ± 31.22 ng/mL and 3.25± 1.87, respectively. Serum ferritin showed a strong positive correlation with HOMA-IR ($r = 0.74$, $p < 0.0001$), indicating that higher ferritin levels were significantly associated with increased insulin resistance in PCOS women.

Graph 1: Classification of serum ferritin range.



The distribution of patients based on serum ferritin levels categorized into low and high ranges. Out of 65 patients, 26 (40%) had low ferritin levels (≤45 ng/mL), while the majority, 39 patients (60%), had high ferritin levels (>45 ng/mL).

Graph 2: Classification of HOMA-IR.



The distribution of patients according to HOMA-IR range. Out of 65 patients, 40% had normal HOMA-IR values (≤2), while 3.08% fell into the borderline range (2.1–2.5). A majority of patients, 56.92%, exhibited severe insulin resistance with HOMA-IR values >2.5.

This indicates that more than half of the study population had significantly elevated HOMA-IR levels.

Table 1: Correlation of Age of Menarche with Serum Ferritin Levels

Age of Menarche	Low ferritin Group		High ferritin Group		Total		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	No. of Patients	Percentage	
12-13	12	46.15	13	33.33	25	38.46	<0.0001
13.1-14	11	42.31	19	48.72	30	46.15	
Total	26	100.00	39	100.00	65	100.00	
Mean±SD	13.09±0.81		12.66±0.38		12.83±0.62		

In the low ferritin group, 46.15% attained menarche at 12–13 years, while 42.31% at 13.1–14 years. In the high ferritin group, corresponding figures were 33.33% and 48.72%. The difference was statistically significant ($p < 0.0001$), with a mean age of 12.83 ± 0.62 years.

Table 2: Correlation of Dysmenorrhea with Serum Ferritin levels.

Dysmenorrhea	Low ferritin Group		High ferritin Group		Total		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	No. of Patients	Percentage	
Yes	5	19.23	7	17.95	12	18.46	0.003
No	21	80.77	32	82.05	53	81.54	
Total	26	100.00	39	100.00	65	100.00	

The presence of dysmenorrhea among patients in the low ferritin and high ferritin groups. In the low ferritin group (n=26), 19.23% reported dysmenorrhea, while 80.77% did not. Similarly, in the high ferritin group (n=39), 17.95% reported dysmenorrhea and 82.05% did not. The difference between the groups was statistically significant ($p = 0.003$). Overall, dysmenorrhea was present in 18.46% of patients and absent in 81.54%.

Table 3: Correlation of Fasting Serum Insulin with Serum Ferritin levels.

Fasting serum insulin (micro U/ml)	Low ferritin Group		High ferritin Group		Total		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	No. of Patients	Percentage	
≤5	9	34.62	0	0.00	9	13.85	<0.0001
5.1-10	17	65.38	0	0.00	17	26.15	
10.1-15	0	0.00	3	7.69	3	4.62	
15.1-20	0	0.00	21	53.85	21	32.31	
20.1-25	0	0.00	6	15.38	6	9.23	
26.1-30	0	0.00	9	23.08	9	13.85	
Total	26	100.00	39	100.00	65	100.00	
Mean±SD	5.72±2.24		20.57±4.67		14.63±8.28		

In the low ferritin group, most attained menarche between 12–14 years, while in the high ferritin group, a higher proportion attained it at 13.1–14 years. The difference was statistically significant ($p < 0.0001$), with an overall mean age of 12.83 ± 0.62 years.

Table 4: Correlation of Anthropometric Parameters with Serum Ferritin Levels and HOMA-IR.

Parameters	Serum ferritin(ng/ml)		HOMA-IR	
	r-value	p-value	r-value	p-value
BMI	0.1	0.42	-0.14	0.26
Waist/Hip ratio	0.04	0.75	-0.12	0.34
SBP	0.15	0.23	0.08	0.52

Correlation analysis showed no significant association of BMI, waist/hip ratio, or systolic blood pressure (SBP) with serum ferritin or HOMA-IR. For serum ferritin, the r-values were 0.10 ($p = 0.42$) for BMI, 0.04 ($p = 0.75$) for waist/hip ratio, and 0.15 ($p = 0.23$) for SBP. For HOMA-IR, the r-values were −0.14 ($p = 0.26$) for BMI, −0.12 ($p = 0.34$) for waist/hip ratio, and 0.08 ($p = 0.52$) for SBP.

Table 5: Correlation of Hormonal Parameters with Serum Ferritin Levels and HOMA-IR.

Hormonal Profile	Serum ferritin(ng/ml)		HOMA-IR	
	rvalue	p-value	rvalue	p-value
LH (mu/ml)	0.12	0.2	0.4	0.009
FSH(mu/ml)	0.39	0.001	0.41	0.009
TSH(mIU/L)	-0.02	0.87	-0.03	0.8
Testosterone (ng/dl)	0.03	0.81	-0.04	0.7
Prolactin (ng/ml)	0.15	0.23	0.1	0.4

Serum ferritin showed a significant positive correlation with FSH (r = 0.39, p = 0.001) but not with LH, TSH, testosterone, or prolactin. HOMA-IR correlated positively with LH (r = 0.40) and FSH (r = 0.41), indicating significant hormonal associations.

Discussion

This cross-sectional study on women with PCOS found that higher serum ferritin levels were significantly associated with increased insulin resistance, independent of ovarian morphology or anthropometric variations. Fasting glucose and hormonal levels, including LH and FSH, showed minor differences. Findings suggest ferritin as a potential marker of metabolic risk.

Among 65 patients, mean serum ferritin was 52.02 ± 31.22 ng/mL. Adamska A et al[6] found higher ferritin in PCOS women (47.3 ± 30.6 ng/mL) than controls (31.1 ± 22.4 ng/mL; p = 0.004). Similarly, Li Y et al[7] reported elevated ferritin in overweight PCOS women (~62 µg/L) versus BMI-matched controls (~49 µg/L; p < 0.05). HOMA-IR classification showed 40% normal (≤2), 3.08% borderline (2.1–2.5), and 56.92% severe insulin resistance (>2.5). Begum T et al[8] found a strong positive correlation between ferritin and HOMA-IR (r = 0.492, p < 0.001). Similarly, Adamska A et al[9] reported a positive association (r = 0.30, p = 0.01) in PCOS women.

In this study, mean menarche age was 13.09 ± 0.81 years in the low ferritin group and 12.66 ± 0.38 years in the high ferritin group. Maio D et al[10] found a positive correlation between menarche age and ferritin (r = 0.41, p = 0.005), with delayed puberty at higher iron levels. Similarly, Welt C K et al[11] reported earlier menarche in women with PCOS than controls.

In the present study, no significant correlation was found between age and serum ferritin levels (p = 0.61). Similarly, Sorensen E et al[12] observed that serum ferritin remained low during adolescence and reproductive years, rising post-menopause. Jensen J E B et al[13] also reported ferritin increasing with age—from ~38 µg/L at 30–40 years to ~84 µg/L at 60 years. In the present study, fasting serum insulin was significantly higher in the high ferritin group(20.57 ± 4.67 µU/mL) compared to the low ferritin group (5.72 ± 2.24 µU/mL; p < 0.0001).Similarly, Begum T et al8 found a strong positive correlation between serum ferritin and fasting insulin (r = 0.528, P < 0.001). Virtanen K et al[14] also reported a positive ferritin–insulin association in 1,918 women.

In the present study, LH (10.14 ± 4.84mU/mL) and FSH (6.16 ± 1.53mU/mL) were significantly higher in the low ferritin group compared to the high ferritin group (p = 0.04 and p = 0.0001, respectively). Similarly, Begum T et al8 reported mean LH of 8.27 ± 5.47 mU/mL and FSH of 5.78 ± 2.02mU/mL, with significantly higher LH in the low ferritin group (p = 0.022).

In the present study, HOMA-IR was significantly higher in the high ferritin group (4.58 ± 1.07) than in the low ferritin group (1.27 ± 0.62) (p < 0.0001), indicating greater insulin resistance with elevated ferritin. Similarly, Begum T et al[8] found a strong positive correlation between serum ferritin and HOMA-IR (r =

0.492, P < 0.001). Adamska A et al[9] also reported a positive ferritin– HOMA-IR association (r = 0.30, p = 0.01) in PCOS women.

Conclusion

This study shows a significant association between elevated serum ferritin and increased insulin resistance in women with PCOS. High ferritin correlated with greater fasting insulin and HOMA-IR, independent of ovarian morphology or BMI. LH and FSH were higher in the low ferritin group. Elevated ferritin may serve as a potential marker of metabolic dysfunction, warranting larger studies for confirmation.

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