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Original Research Article

Association of Serum Ferritin and Inflammatory Markers with Insulin Resistance in Non-Obese Adults: A Cross-Sectional Study

Khushboo Raj[1], Santosh Kumar[2], Prabhakar[3], Ashok Kumar[4]

[1]Senior resident, Department of Biochemistry, All India Institute of Medical Sciences, Patna, Bihar, India
[2]Senior Resident, Department of General Medicine, Patna Medical College & Hospital, Patna, Bihar, India
[3]Senior Resident, Department of Emergency Medicine, Patna Medical College & Hospital, Patna, Bihar, India
[4]Professor, HOD, General Medicine, Patna Medical College & Hospital, Patna, Bihar, India

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Corresponding Author: Ashok Kumar
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Abstract:

Insulin resistance is a central pathophysiological mechanism underlying the development of type 2 diabetes mellitus and other metabolic disorders. Although obesity is a well-established contributor, insulin resistance is increasingly recognized in non-obese individuals, suggesting the involvement of additional metabolic factors. Serum ferritin, a marker of body iron stores, and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) have been implicated in impaired insulin sensitivity. This cross-sectional analytical study was conducted among 102 non-obese adults (BMI <25 kg/m²) attending a tertiary care hospital to evaluate the association between serum ferritin, inflammatory markers, and insulin resistance. Fasting glucose and insulin were measured, and insulin resistance was calculated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), with a cut-off value of ≥2.5. Insulin resistance was observed in 40.2% of participants. Individuals with insulin resistance had significantly higher serum ferritin (214.7 ± 64.8 vs 137.9 ± 58.6 ng/mL; p <0.001), CRP (4.1 ± 1.2 vs 2.6 ± 1.1 mg/L; p <0.001), and ESR (21.4 ± 5.8 vs 15.1 ± 4.9 mm/hr; p <0.001) compared to insulin-sensitive individuals. Serum ferritin (r = 0.48), CRP (r = 0.52), and ESR (r = 0.39) demonstrated significant positive correlations with HOMA-IR (all p <0.001). On multivariate analysis, serum ferritin (β = 0.31, p = 0.002) and CRP (β = 0.36, p <0.001) remained independently associated with insulin resistance after adjusting for age, sex, and BMI. These findings indicate that elevated iron stores and low-grade systemic inflammation are significantly associated with insulin resistance in non-obese adults, highlighting the importance of evaluating non-traditional metabolic risk factors beyond obesity.

Keywords: Serum ferritin; Inflammatory markers; Insulin resistance; Non-obese adults; HOMA-IR; C-reactive protein.

Introduction

Insulin resistance represents a fundamental metabolic abnormality characterized by reduced biological responsiveness of peripheral tissues to insulin action. It plays a pivotal role in the pathogenesis of type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease [1]. Although obesity remains the most prominent risk factor for insulin resistance, a substantial proportion of non-obese individuals also exhibit insulin resistance, indicating the involvement of alternative pathogenic mechanisms [2,3].

Iron metabolism has emerged as a significant modulator of glucose homeostasis. Serum ferritin, a widely used surrogate marker of body iron stores, has been shown to influence insulin sensitivity through mechanisms involving oxidative stress, hepatic insulin extraction, and pancreatic β-cell dysfunction [4–6]. Elevated ferritin levels have been associated with impaired glucose tolerance and increased risk of diabetes, even in individuals without overt obesity [7,8].

Chronic low-grade inflammation is another key contributor to insulin resistance. Inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate reflect systemic inflammatory activity that may interfere with insulin signaling pathways [9–11]. Pro-inflammatory cytokines are known to impair insulin receptor signaling and glucose uptake, thereby promoting insulin resistance independent of adiposity [12,13].

In the Indian population, insulin resistance is often observed at lower body mass indices compared to Western populations, suggesting a unique metabolic phenotype [14,15]. Despite this, limited data are available regarding the combined role of iron status and inflammatory markers in non-obese Indian adults. This study was undertaken to evaluate the association between serum ferritin, inflammatory markers, and insulin resistance in non-obese adults, thereby contributing to a better understanding of early metabolic risk factors beyond obesity.

Materials and Methods

Study Design and Setting: This was a cross-sectional study conducted at Patna Medical College and Hospital (PMCH) over a period of six months, from March 2025 to August 2025.

Study Population: A total of 102 non-obese adults attending the outpatient department were enrolled in the study. Non-obesity was defined as body mass index (BMI) <25 kg/m² according to WHO Asian population criteria.

Inclusion Criteria

- Adults aged 18 years and above
- Non-obese individuals
- Willingness to participate and provide informed consent

Exclusion Criteria

- Known diabetes mellitus
- Obesity
- Chronic inflammatory or infectious diseases
- Liver disease, renal disease, or hematological disorders
- Current iron supplementation or steroid therapy

Data Collection: Demographic details, clinical history, and anthropometric measurements were recorded using a structured proforma. Blood samples were collected after an overnight fast for biochemical analysis.

Laboratory Parameters: Serum ferritin was measured using chemiluminescent immunoassay (CLIA). C-reactive protein (CRP) was estimated using immunoturbidimetric method, and erythrocyte sedimentation rate (ESR) was measured using the Westergren method. Fasting plasma glucose was measured by glucose oxidase-peroxidase method, and fasting insulin was estimated using chemiluminescent immunoassay. Insulin resistance was calculated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) formula:

HOMA-IR = [Fasting insulin (μIU/mL) × Fasting glucose (mg/dL)] / 405.

A HOMA-IR value ≥2.5 was considered indicative of insulin resistance.

Ethical Considerations: The study was approved by the Institutional Ethics Committee, and informed written consent was obtained from all participants prior to enrollment.

Statistical Analysis: Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation. Independent t-test was used for comparison between groups. Pearson correlation coefficient was used to assess associations between variables. Multiple linear regression analysis was performed to determine independent predictors of insulin resistance. A p-value <0.05 was considered statistically significant.

Results

A total of 102 non-obese adults were included in the final analysis. The mean age of participants was 36.8 ± 9.4 years. Among them, 56 (54.9%) were males and 46 (45.1%) were females. The mean body mass index (BMI) was 22.4 ± 1.8 kg/m².

Baseline Clinical and Biochemical Characteristics: The mean fasting plasma glucose was 94.6 ± 10.8 mg/dL, and the mean fasting insulin level was 11.8 ± 4.6 μIU/mL. The calculated mean HOMA-IR was 2.74 ± 1.18. The mean serum ferritin level was 168.5 ± 72.3 ng/mL. Mean C-reactive protein (CRP) was 3.2 ± 1.4 mg/L and erythrocyte sedimentation rate (ESR) was 17.6 ± 6.3 mm/hr. Baseline characteristics are shown in Table 1.

Prevalence of Insulin Resistance: Using HOMA-IR ≥2.5 as the cut-off for insulin resistance, 41 participants (40.2%) were classified as insulin resistant, while 61 (59.8%) were insulin sensitive. The distribution is illustrated in Figure 1.

Comparison Between Insulin Resistant and Insulin Sensitive Groups.

Participants with insulin resistance had significantly higher:

- Serum ferritin (214.7 ± 64.8 vs 137.9 ± 58.6 ng/mL; $p < 0.001$)
- CRP levels (4.1 ± 1.2 vs 2.6 ± 1.1 mg/L; $p < 0.001$)
- ESR (21.4 ± 5.8 vs 15.1 ± 4.9 mm/hr; $p < 0.001$)

No significant difference was observed in BMI between groups ($p = 0.09$). Detailed comparison is shown in Table 2.

Correlation Analysis: Pearson correlation analysis showed:

- Serum ferritin positively correlated with HOMA-IR ($r = 0.48$, $p < 0.001$)
- CRP positively correlated with HOMA-IR ($r = 0.52$, $p < 0.001$)
- ESR positively correlated with HOMA-IR ($r = 0.39$, $p < 0.001$)

Correlation plots are shown in Figure 2, Figure 3, and Figure 4.

Multivariate Analysis: Multiple linear regression analysis was performed with HOMA-IR as dependent variable.

After adjusting for age, sex, and BMI:

- Serum ferritin remained independently associated with HOMA-IR ($\beta = 0.31$, $p = 0.002$)
- CRP remained independently associated ($\beta = 0.36$, $p < 0.001$)

Regression model summary is shown in **Table 3**.

Table 1: Baseline Characteristics of Study Participants (n=102)

Parameter	Mean ± SD
Age (years)	36.8 ± 9.4
BMI (kg/m²)	22.4 ± 1.8
Fasting glucose (mg/dL)	94.6 ± 10.8
Fasting insulin (µIU/mL)	11.8 ± 4.6
HOMA-IR	2.74 ± 1.18
Serum ferritin (ng/mL)	168.5 ± 72.3
CRP (mg/L)	3.2 ± 1.4
ESR (mm/hr)	17.6 ± 6.3

Table 2: Comparison Between Insulin Sensitive and Insulin Resistant Groups

Parameter	Insulin Sensitive (n=61)	Insulin Resistant (n=41)	p-value
BMI (kg/m²)	22.1 ± 1.7	22.8 ± 1.9	0.09
Ferritin (ng/mL)	137.9 ± 58.6	214.7 ± 64.8	<0.001
CRP (mg/L)	2.6 ± 1.1	4.1 ± 1.2	<0.001
ESR (mm/hr)	15.1 ± 4.9	21.4 ± 5.8	<0.001
HOMA-IR	1.89 ± 0.42	3.98 ± 0.76	<0.001

Table 3: Multiple Linear Regression Analysis for Predictors of HOMA-IR

Variable	β coefficient	p-value
Age	0.12	0.18
BMI	0.14	0.11
Serum Ferritin	0.31	0.002
CRP	0.36	<0.001

$R^2 = 0.42$
Model $p < 0.001$

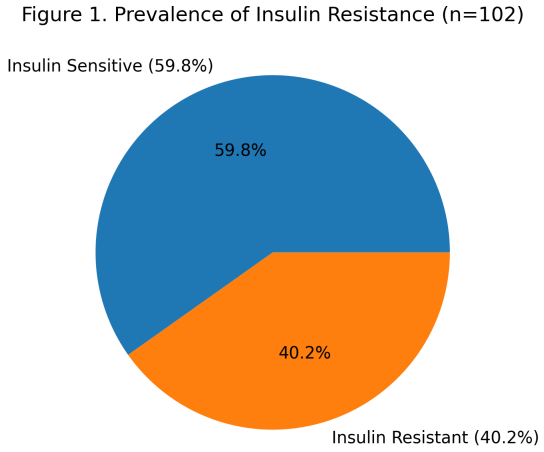

Figure 1: Prevalence of Insulin Resistance

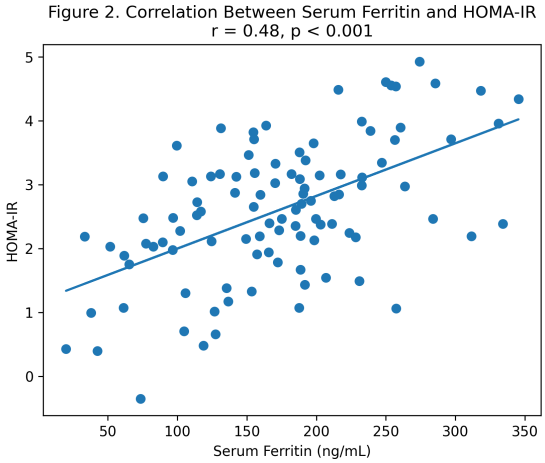

Figure 2: Correlation Between Serum Ferritin and HOMA-IR

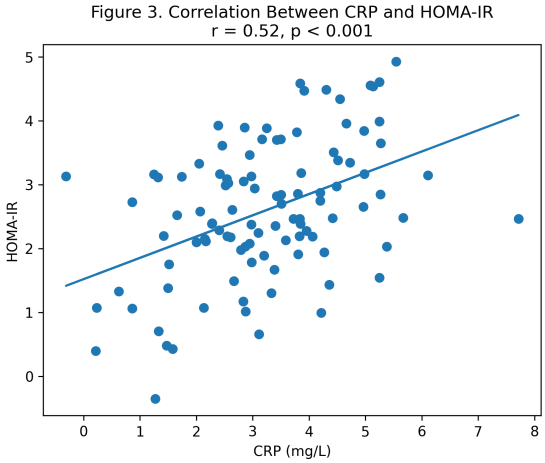

Figure 3: Correlation Between CRP and HOMA-IR

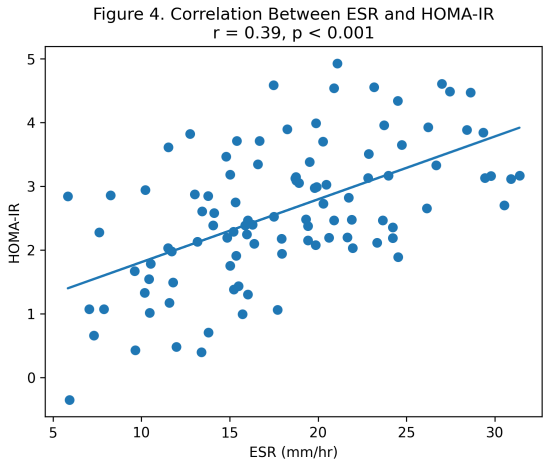

Figure 4: Correlation Between ESR and HOMA-IR

Discussion

The present study highlights the association between serum ferritin, inflammatory markers, and insulin resistance in non-obese adults. These findings support the concept that insulin resistance is not exclusively linked to obesity and may arise due to metabolic and inflammatory factors even in individuals with normal body weight [1–3].

Elevated serum ferritin levels observed among insulin-resistant participants are consistent with previous studies demonstrating a relationship between increased iron stores and impaired insulin sensitivity [4–6]. Excess iron is believed to induce oxidative stress, which disrupts insulin signaling and contributes to β-cell dysfunction [7,8]. These mechanisms may explain the presence of insulin resistance in non-obese individuals with elevated ferritin levels.

The association between inflammatory markers and insulin resistance observed in this study aligns with existing literature emphasizing the role of chronic low-grade inflammation in metabolic dysregulation [9–11]. Inflammatory mediators interfere with insulin receptor activity and glucose transport, thereby promoting insulin resistance independent of adiposity [12,13].

In the Indian context, metabolic abnormalities often manifest at lower body mass indices, reinforcing the importance of evaluating non-traditional risk factors such as iron status and inflammation [14,15]. Similar associations have been reported in both population-based and clinical studies, underscoring the global relevance of these findings [16–19].

The results of this study suggest that serum ferritin and inflammatory markers may serve as early indicators of metabolic risk in non-obese adults. Early identification of such individuals could facilitate timely lifestyle and therapeutic interventions aimed at preventing progression to overt metabolic disease [20–22]. From a public health perspective, these findings emphasize the need to broaden screening strategies beyond obesity-centric models [23–25].

Conclusion

Serum ferritin and inflammatory markers show a significant association with insulin resistance in non-obese adults. These findings highlight the role of altered iron metabolism and low-grade inflammation in the pathogenesis of insulin resistance independent of obesity. Incorporating these parameters into routine metabolic assessment may aid in early identification of at-risk individuals.

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