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Iron Status and Metabolic Syndrome in Women with Iron Deficiency Anemia: Findings from a Cross-sectional Study in Northern Iran

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Abstract

Background: The pathophysiology of iron deficiency anemia (IDA) and metabolic syndrome (MetS) involves inflammatory processes and disturbances in iron metabolism.

Objectives: This study aimed to determine whether hemoglobin and iron biomarkers were associated with MetS among female patients with IDA.

Methods: In this study, 196 women with IDA were recruited at a clinic affiliated with Mazandaran University of Medical Science. IDA was diagnosed based on the presence of anemia and serum ferritin < 30 ng/mL. MetS was diagnosed according to the NCEP ATP III/AHA-NHLBI criteria. Hemoglobin, serum iron, total iron binding capacity (TIBC), and serum ferritin levels were measured, and the association between these variables and MetS was estimated using a logistic regression model adjusted for age and Body Mass Index (BMI).

Results: Of the 196 participants, 63 (32.1%) were classified as MetS. Women who had MetS had a slightly higher median serum ferritin level compared to those who did not have MetS (10.0 vs. 9.0 ng/mL, P = 0.018). There was no significant difference in hemoglobin, serum iron or TIBC. Those who had 0, 1 - 2 or ≥ 3 components of MetS had increasing median ferritin levels (7.2, 9.0 and 10.0 ng/mL respectively), however there was no significant difference overall (P = 0.051). After adjustment for age and BMI there was no significant association between ferritin and MetS (OR = 1.100, 95% CI = 0.988 - 1.223, P = 0.081).

Conclusions: Serum ferritin levels were slightly higher in participants with MetS; however, ferritin was not significantly associated with MetS after adjustment for age and BMI. This suggests that markers of iron status may not be independently associated with metabolic syndrome, and further research is needed to clarify this relationship.

Keywords: Metabolic Syndrome, Anemia, Iron-Deficiency, Iron, Ferritins, Obesity, Body Mass Index

1. Background

Metabolic syndrome (MetS) is a prevalent and serious public health condition characterized by the clustering of abdominal obesity, elevated blood pressure, dysglycemia, hypertriglyceridemia, and reduced HDL-C (1). According to the latest information, the prevalence rate of MetS has increased from about 12% in 2000 to 28% in 2023 for the adult population globally (2). Anemia can be described as the reduction of hemoglobin levels to less than the established thresholds based on age and sex that cause reduced oxygen-carrying capacity of the blood (3). Iron deficiency anemia (IDA) is the most frequent type of anemia. The consequences of IDA may extend beyond the hematological system and manifest themselves in the development of disturbances in carbohydrate metabolism and changes in the functioning of pancreatic cells. It is reported that IDA is associated with several components of the metabolic syndrome. In addition, it has been found that improvement in iron status through the treatment of

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IDA may reduce insulin resistance in some populations (4, 5). Etiological factors that contribute to anemia among women with MetS are the onset of early diabetic nephropathy with defective erythropoietin production, oxidative stress causing premature destruction of red blood cells, and inadequate use of dietary micronutrients for iron absorption (6). Iron homeostasis is strictly controlled by hepcidin, a peptide hormone synthesized mainly in the liver, which regulates the iron exporter ferroportin. The inflammatory response increases hepcidin levels, mainly due to interleukin-6, decreasing the iron absorption from the intestine and its release from macrophages and other stores (7, 8). While serum ferritin is a reliable indicator of body iron stores, it is also an acute-phase reactant which can be elevated in patients with inflammation, infection and metabolic abnormalities. Such elevations in serum ferritin levels therefore may overestimate iron stores in individuals with obesity or MetS (9). In general, existing evidence suggests a multifactorial and contextual connection between metabolic syndrome and anemia, with the former being a result of inflammation-related iron regulation disorder and organ metabolic dysfunction (10). This is different from the previous studies reporting the role of ferritin or iron status in general or obese population. In addition, hemoglobin, serum iron, ferritin, and total iron-binding capacity were simultaneously measured in women with IDA and compared according to the presence or absence of MetS. Thus, it might help to elucidate if the metabolic abnormalities could affect the iron-status markers independent of the underlying IDA.

2. Objectives

In the present study, we investigated the association between iron-related biomarkers and metabolic syndrome among women with IDA.

3. Methods

Women with IDA who visited the Tooba Clinic, affiliated with Mazandaran University of Medical Sciences, during 2024 – 2025 were enrolled. Anemia was defined as a hemoglobin level < 12 g/dL in women, according to World Health Organization criteria. IDA was defined as anemia with serum ferritin levels below 30 ng/mL (9). Patients with cancer, autoimmune or inflammatory diseases, restricted food intake during the previous year, pregnancy, or iron supplement use were excluded. Demographic, clinical, anthropometric, hematological, and biochemical data were collected using a checklist and laboratory tests. MetS was defined according to the NCEP ATP III/AHA-NHLBI criteria as the presence of at least three of the following five components (11): waist circumference (WC) ≥88 cm for women; triglycerides (TG) ≥150 mg/dL; high-density lipoprotein (HDL)-C < 50 mg/dL; systolic blood pressure (SBP) ≥130 mmHg or diastolic blood pressure (DBP) ≥85 mmHg or treatment for hypertension; and fasting blood glucose (FBG) ≥100 mg/dL or treatment for diabetes.

3.1. Statistical Analysis

Continuous variables are presented as median (interquartile range), and categorical variables as frequencies (percentages). The Mann-Whitney U test was used to compare iron-related biomarkers in women with and without MetS. Iron-related biomarkers were also compared between women with 0 components, 1 – 2 components, or ≥ 3 components of MetS using the Kruskal-Wallis test. A separate binary logistic regression model was performed to determine the association between hemoglobin, serum iron, TIBC, and serum ferritin and MetS. Statistical analysis was carried out using IBM SPSS Statistics version 21.0. A two-sided $P < 0.05$ was considered statistically significant.

4. Results

A total of 196 women were included in the analysis. Of these, 63 (32.1%) fulfilled the diagnostic criteria for metabolic syndrome. The median age was 48 (IQR: 40 – 60) years, and the median BMI was 27.66 (IQR: 24.08 – 30.79) kg/m². The clinical, anthropometric, and iron-related characteristics of the study population are presented in Table 1.

Table 1. Clinical, Anthropometric, Metabolic, and Iron-related Characteristics of Women with Iron Deficiency Anemia [a]

Variables	Values
Age (y)	48 (40 – 60)
Height (cm)	159 (154 – 165)
Weight (kg)	70 (60 – 80)
BMI (kg/m²)	27.66 (24.08 – 30.79)
Waist circumference (cm)	88 (79 – 100)
Hip circumference (cm)	96.5 (85 – 109)
Hemoglobin (g/dL)	10.50 (9.33 – 11.20)
Serum iron (µg/dL)	37.50 (27 – 55.50)
Ferritin (ng/mL)	9.40 (7 – 11.90)
TIBC (µg/dL)	401 (367.25 – 439.25)

[a] Values are expressed as median (interquartile range). Abbreviations: BMI, Body Mass Index; TIBC, total iron-binding capacity.

Compared with women without MetS, women with MetS had a slightly higher median serum ferritin concentration ($P = 0.018$; 10.00 vs. 9.00 ng/mL). However,

Table 2. Iron-related Biomarkers According to Metabolic Syndrome Status [a]

Variables	Group		P-Value
	Without MetS (n = 133)	With MetS (n = 63)	
Ferritin (ng/mL)	9.00 (6.00 - 11.00)	10.00 (7.70 - 13.00)	0.018 [b]
Hemoglobin (g/dL)	10.40 (8.90 - 11.20)	10.60 (9.70 - 11.00)	0.662 [b]
Serum iron (µg/dL)	37.00 (25.00 - 55.00)	39.00 (29.00 - 57.00)	0.589 [b]
TIBC (µg/dL)	401.00 (363.50 - 438.50)	401.00 (375.00 - 451.00)	0.507 [b]

[a] Values are expressed as median (interquartile range). Abbreviations: MetS, metabolic syndrome; TIBC, total iron-binding capacity.

[b] P-value from the Mann-Whitney U test.

none of the other iron-related biomarkers showed statistically significant differences between the two groups. Hemoglobin (P = 0.662; 10.60 vs. 10.40 g/dL), serum iron (P = 0.589; 39.00 vs. 37.00 µg/dL), and TIBC (P = 0.507; 401.00 vs. 401.00 µg/dL) did not differ significantly between women with and without MetS (Table 2).

Women were divided into three groups based on the number of metabolic syndrome components. Median ferritin levels were 7.20, 9.00, and 10.00 ng/mL for those with no components, one or two components, and three or more components, respectively. Although ferritin levels showed a gradual increase, there was no significant difference between the groups (P = 0.051). Serum iron (P = 0.414), TIBC (P = 0.780), and hemoglobin (P = 0.076) levels also showed no significant differences between the three groups (Table 3).

None of the iron-related biomarkers was significantly associated with metabolic syndrome in separate logistic regression models adjusted for age and BMI. Ferritin had an adjusted OR of 1.100 (95% CI, 0.988 – 1.223; P = 0.081); hemoglobin had an adjusted OR of 1.021 (95% CI, 0.784 – 1.331; P = 0.876); serum iron had an adjusted OR of 0.999 (95% CI, 0.986 – 1.012; P = 0.917); and TIBC had an adjusted OR of 1.001 (95% CI, 0.995 – 1.007; P = 0.677) (Table 4).

5. Discussion

The principal finding of this study was that hemoglobin, serum iron, and TIBC levels did not differ significantly between female patients with and without MetS. Serum ferritin levels appeared to be significantly increased in women with MetS compared with those without MetS. This difference, however, was not significantly associated with MetS after adjustment for age and BMI.

The present study showed that the prevalence of MetS among 196 patients with IDA was 32.1%. An umbrella review recently indicated that the overall pooled prevalence of MetS in Iran was 30.4%; women also had a greater prevalence (33.05%) than men (27.57%) (12). Our observed prevalence is similar to previous estimates of MetS in Iranian women (33% based on ATP III/IDF criteria) reported in a systematic review (13). A recent Iranian cross-sectional study of 916 adults attending an obesity clinic also reported MetS in 30.7% of participants, with prevalence increasing from 18.1% in those with overweight to 38.7% in those with grade 3 obesity (14). The broadly comparable overall proportion should be interpreted cautiously because that cohort was selected on the basis of overweight or obesity and differed from our sample of women with confirmed IDA.

Women with MetS had a slightly higher median ferritin level than those without MetS (10.0 vs. 9.0 ng/mL); however, this finding should be interpreted with caution. Both groups had very low ferritin levels, indicating iron deficiency. The difference between the groups was small, and ferritin was not significantly associated with MetS in adjusted logistic regression models.

The component burden analysis provided additional insight. Median ferritin levels were higher in women with more MetS components (7.20 ng/mL for none vs. 9.00 ng/mL for one/two components vs. 10.00 ng/mL for three or more components). There was a clear trend toward increasing ferritin levels with an increasing number of components; however, this does not represent a dose-response relationship and does not indicate which components may be responsible. There was no significant difference in serum iron, TIBC, or hemoglobin between component burden groups.

Ferritin is an acute-phase protein, and metabolic disturbances have previously been associated with changes in iron regulation (15, 16). However, this study did not include inflammatory markers, such as CRP or hepcidin, so it is not possible to determine whether inflammation contributed to this difference. This finding should be interpreted as a small difference in ferritin distribution between the two groups; it does not indicate changes in iron stores or inflammation-induced changes in iron

Table 3. Iron Status Markers According to the Number of Metabolic Syndrome Components [a]

Variables	Number of MetS Components			P-Value
	0 (n = 20)	1 – 2 (n = 113)	≥ 3 (n = 63)	
Ferritin (ng/mL)	7.20	9.00	10.00	0.051 [b]
Serum iron (µg/dL)	34.00	38.00	39.00	0.414 [b]
TIBC (µg/dL)	410.50	399.00	401.00	0.780 [b]
Hemoglobin (g/dL)	9.35	10.60	10.60	0.076 [b]

[a] Values are expressed as median. Abbreviations: MetS, metabolic syndrome; TIBC, total iron-binding capacity.

[b] P-value from the Kruskal–Wallis test.

regulation in women with MetS. Our finding is consistent with several studies reporting a positive association between serum ferritin and MetS, although the populations and ferritin concentrations differed substantially. In a large analysis of 7,346 Korean adults from the 2007 – 2008 KNHANES, higher ferritin concentrations were associated with greater odds of MetS in women; compared with women in the lowest ferritin quartile, those in the highest quartile had an adjusted OR of 1.41 (95% CI, 1.06 – 1.88), although the association was attenuated after additional adjustment for insulin resistance (17). Supporting evidence comes from a case-control study conducted in 2026, which demonstrated elevated levels of CRP, leptin, and hepcidin in obese children and adolescents compared with controls, whereas ferritin and hemoglobin levels did not differ significantly. These data support an obesity-inflammation-hepcidin pathway in children; however, this finding cannot be directly applied to adult women with established IDA (18). The finding is further supported by studies conducted specifically among postmenopausal women. In a study of 959 Korean postmenopausal women, participants with MetS had significantly higher serum ferritin concentrations than those without MetS (74.7 vs. 59.6 ng/mL, $P < 0.001$), and ferritin was associated with several MetS components (19).

The non-significant findings are equally important. Serum iron did not differ between women with and without MetS, TIBC was also similar, and Hemoglobin showed no significant difference either. This is important since it suggests that the biologic relationship between obesity and iron deficiency is not necessarily reflected uniformly across all the conventional iron biomarkers. Previous literature has demonstrated that obesity may be associated with decreased availability of iron whilst ferritin remains normal or high due to inflammation rendering ferritin and serum iron potentially non concordant (20, 21).

The lack of a strong overall association should not be surprising given that the relation between iron status and MetS is heterogeneous. In a cohort study including 3271 adults followed up for 5.5 years, Kilani et al. found no significant association between ferritin or serum iron and incident MetS in men, but higher serum iron was inversely associated with incident MetS in women (22). Study on Ecuadorian women showed that MetS was related to a lower prevalence of iron deficiency and anemia compared to women without MetS, meaning that MetS was not associated with expected iron depletion and contradicting the belief that poor iron status accompanies greater metabolic dysfunction at the population level (23). Some findings of Ardekani et al. are comparable with the presented data. For instance, they found no statistically significant associations between serum iron content and triglycerides, HDL cholesterol, waist circumference, and oxidized LDL in patients with obesity and MetS. Furthermore, there was no statistically significant association between serum iron content and most of the metabolic syndrome markers in patients with obesity but without MetS and among the entire sample of patients with obesity. The only statistically significant association was found between serum iron and LDL cholesterol level in patients with obesity and MetS (24).

From a clinical perspective, this suggests that MetS should not be used to predict iron status or differences in hemoglobin, serum iron, or TIBC in women with pre-established IDA. Ferritin should be considered in conjunction with other hematological and biochemical parameters and the patient's clinical situation. The slight difference in median ferritin levels between groups in this study should not influence diagnostic criteria or iron replacement protocols.

This study has several limitations. First, it was cross-sectional; therefore, causality cannot be established. Second, subjects were selected by convenience sampling from one university-affiliated referral clinic in northern Iran, which may limit the generalizability of the findings to a broader population. Third, because CRP and hepcidin were not measured, we were unable to determine the

Table 4. Logistic Regression Analysis of Iron-related Biomarkers and MetS [a]

Variables	AOR [b]	95% CI	P-Value
Ferritin, per 1 ng/mL increase	1.100	0.988 – 1.223	0.081
Hemoglobin, per 1 g/dL increase	1.021	0.784 – 1.331	0.876
Serum iron, per 1 μg/dL increase	0.999	0.986 – 1.012	0.917
TIBC, per 1 μg/dL increase	1.001	0.995 – 1.007	0.677

[a] Each biomarker was entered in a separate binary logistic regression model. Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; MetS, metabolic syndrome; TIBC, total iron-binding capacity.

[b] Adjusted for age and BMI.

extent to which ferritin levels may be influenced by inflammatory and iron-regulatory factors. Fourth, because only a limited number of participants had no components of MetS (n = 20), the ability to compare the number of components was limited. Lastly, dietary intake, menopausal status, and physical activity were not systematically measured and therefore were not included in the analyses. This may have resulted in residual confounding. Lifestyle factors were not systematically assessed. An Iranian multicenter cross-sectional study of 284 adults who already had a diagnosis of MetS examined physical activity and Mediterranean diet adherence. Although MetS did not significantly correlate with these factors, this finding shows the importance of considering lifestyle in this population (25).

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Footnotes

AI Use Disclosure: ChatGPT was used to a limited extent for paraphrasing and translation in the Introduction section.

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Data Availability: The dataset presented in this study is available from the corresponding author upon request during submission or after publication. The data are not publicly available because of privacy and ethical considerations.

Ethical Approval: The study was approved by the Ethics Committee of Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1402.436).

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