Gazi Med J 2026;37(1):15-22

DOI: http://dx.doi.org/10.12996/gmj.2025.4502

Possible Relationships of Ferritin and Inflammatory Cytokines with Metabolic Syndrome: A Case Control Study

Ferritin ve Enflamatuvar Sitokinlerin Metabolik Sendrom ile Olası İlişkileri: Bir Olgu Kontrol Çalışması

Hatice Tuğçe Berberoğlu[1], Burcu Baba[2], Cem Onur Kıraç[3], Bahadır Öztürk[4], Aysun Hacışevki[5]

[1]Department of Nutrition and Dietetics, KTO Karatay University Faculty of Health Sciences, Konya, Türkiye
[2]Department of Medical Biochemistry, Yüksek İhtisas University Faculty of Medicine, Ankara, Türkiye
[3]Division of Endocrinology and Metabolism, Clinic of Internal Medicine, HG Hospital, Kahramanmaraş, Türkiye
[4]Department of Medical Biochemistry, Selçuk University Faculty of Medicine, Konya, Türkiye,
[5]Department of Biochemistry, Gazi University Faculty of Pharmacy; Health Sciences Institute, Sports Pharmacy Program, Gazi University, Ankara, Türkiye

ABSTRACT

Objective: Metabolic syndrome (MetS) is characterized by the coexistence of several risk factors, including abdominal obesity, elevated blood pressure, glucose intolerance, and dyslipidemia. MetS has become a significant public health concern worldwide, and its prevalence is steadily increasing in Türkiye. It has been suggested that serum ferritin concentrations are higher in individuals with MetS and that inflammation plays a crucial role in the pathogenesis of the syndrome. The aim of this study was to evaluate serum ferritin levels and inflammatory cytokine levels in individuals with and without MetS.

Methods: A total of 150 individuals who presented to the endocrinology unit were included in the study. According to the National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III) criteria, participants were divided into two groups: those with MetS (n = 75) and those without MetS (n = 75). Fasting serum ferritin, interleukin (IL)-1α, IL-10, and interferon (IFN)-γ levels were analyzed using commercial enzyme-linked immunosorbent assay (ELISA) kits. Demographic characteristics, anthropometric measurements, and biochemical parameters of the participants were also evaluated.

Results: Serum levels of ferritin, IL-1α, and IFN-γ were significantly higher in individuals with MetS than in the control group ($p < 0.05$). Although IL-10 levels were also higher in the MetS group, the difference was not statistically significant. Furthermore, fasting blood glucose, triglycerides, blood pressure, and waist circumference were

ÖZ

Amaç: Metabolik sendrom (MetS) abdominal obezite, artmış kan basıncı, glukoz intoleransı ve dislipidemi gibi risk faktörlerinden oluşan bir durum olarak tanımlanmaktadır. MetS dünya çapında önemli bir halk sağlığı sorunudur ve Türkiye'de MetS prevalansı giderek artmaktadır. Serum ferritin konsantrasyonunun MetS'li bireylerde daha yüksek ve enflamasyonun, MetS patogenezinde önemli bir rol oynadığı öne sürülmüştür. Bu çalışmanın amacı MetS olan ve olmayan bireylerde serum ferritin ve enflamatuvar sitokin düzeylerini değerlendirmektir.

Yöntemler: Endokrinoloji ünitesine başvuran 150 kişi, Ulusal Kolesterol Eğitim Programı/Yetişkin Tedavi Paneli (NCEP ATP III) MetS kriterleri temel alınarak her grupta 75 kişi olacak şekilde iki gruba ayrılmıştır. Açlık serum ferritin, interlökin (IL)-1α, IL-10 ve interferon (IFN)-γ düzeyleri ticari enzim bağlantılı immünosorbent test (ELISA) yöntemi ile analiz edilmiştir. Ayrıca demografik parametreler, antropometrik ölçümler ve biyokimyasal parametreler değerlendirilmiştir.

Bulgular: MetS'li bireylerde serum ferritin, IL-1α ve IFN-γ düzeyleri kontrol grubuna kıyasla anlamlı düzeyde yüksek bulunmuştur ($p < 0,05$). IL-10 düzeyleri hastalarda daha yüksek olmasına rağmen, bu artış istatistiksel olarak anlamlı bulunmamıştır. Ayrıca MetS grubunda, kontrol grubuna göre açlık kan şekeri, trigliserit, kan basıncı, bel çevresi değerleri anlamlı şekilde yüksek; yüksek yoğunluklu lipoprotein-kolesterol düzeyleri ise anlamlı şekilde düşük saptanmıştır.

Cite this article as: Berberoğlu HT, Baba B, Kıraç CO, Öztürk B, Hacışevki A. Possible relationships of ferritin and inflammatory cytokines with metabolic syndrome: a case control study. Gazi Med J. 2026;37(1):15-22

Address for Correspondence/Yazışma Adresi: Aysun Hacışevki, Department of Biochemistry, Gazi University Faculty of Pharmacy; Health Sciences Institute, Sports Pharmacy Program, Gazi University, Ankara, Türkiye
E-mail / E-posta: abozkir@gazi.edu.tr
ORCID ID: orcid.org/0000-0002-3844-5772

Received/Geliş Tarihi: 23.07.2025
Accepted/Kabul Tarihi: 29.08.2025
Publication Date/Yayınlanma Tarihi: 19.01.2026

ABSTRACT

significantly higher, whereas high-density lipoprotein cholesterol levels were significantly lower in the MetS group than in controls.

Conclusion: The findings suggest that inflammatory markers such as ferritin, IL-1α, and IFN-γ may serve as biomarkers for the diagnosis and management of MetS, thereby contributing to a better understanding of its pathogenesis and early detection. Further large-scale studies are required to validate these findings and clarify the roles of these parameters in MetS.

Keywords: Ferritin, inflammation, metabolic syndrome, interleukin-1alpha, interleukin-10, interferon-gamma

ÖZ

Sonuç: Bulgular, ferritin, IL-1α ve IFN-γ gibi enflamatuvar belirteçlerin MetS tanı ve yönetiminde potansiyel biyobelirteçler olarak hizmet edebileceğini, patogenezinin daha iyi anlaşılmasına ve erken teşhisine katkıda bulunabileceğini göstermektedir. Bu bulguların doğrulanması için bu değişkenlerin dikkate alındığı daha geniş örneklemli çalışmalara ihtiyaç duyulmaktadır.

Anahtar Sözcükler: Ferritin, enflamasyon, metabolik sendrom, interlökin-1alfa, interlökin-10, interferon-gama

INTRODUCTION

Metabolic syndrome (MetS) is a worldwide clinical challenge characterized by a cluster of risk factors, including abdominal obesity, insulin resistance, glucose intolerance, diabetes mellitus, dyslipidemia, and hypertension (1). According to the International Diabetes Federation, one-quarter of the global population has MetS (2). The Turkish Adult Risk Factor study reported that the prevalence of MetS among adults aged over 40 years in Türkiye was 53% (3). Obesity, low educational level, physical inactivity, hypertension, elevated total cholesterol levels, older age, and higher body mass index (BMI) are also strong risk factors for the development of MetS (4). Although the precise pathogenic pathways underlying MetS remain to be elucidated, the interaction among obesity, low-grade inflammation, and insulin resistance is considered to play a vital role in its development (5). The association between MetS and inflammation has not been fully explained; however, adipose tissue is thought to mediate the relationship between MetS and inflammation (6).

Obesity, an important risk factor for the development of MetS, is characterized by low-grade inflammation leading to adipose tissue dysfunction. Adipose tissue is an endocrine organ that secretes various bioactive substances, such as adipocytokines. An imbalance between the production of anti-inflammatory and pro-inflammatory adipocytokines in obese adipose tissue contributes to the pathophysiology of MetS (7). Ferritin, an acute-phase reactant, is a recognized biomarker of acute or chronic inflammation and is non-specifically elevated in various inflammatory conditions, including acute infection, malignancy, chronic kidney disease, rheumatoid arthritis, and other autoimmune disorders (8). Despite this, it remains unclear whether serum ferritin is involved in an inflammatory cycle or whether it causes or reflects inflammation (9). This study aimed to contribute to this growing area of research by exploring serum levels of ferritin, interleukin (IL)-1α, IL-10, and interferon (IFN)-γ as inflammatory markers and by examining the relationships among them in individuals with and without MetS.

MATERIALS AND METHODS

Study Population

Overweight or obese subjects were recruited from the Endocrinology and Metabolism Unit of Selçuk University Medical Faculty Hospital. This cross-sectional study was conducted in Konya Province, Türkiye, with 150 adults (114 women, 36 men) aged 19-65 yearsin Konya province, Türkiye. In this case-control study, 75 subjects diagnosed with MetS according to the National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III) criteria constituted the patient group (mean age 40.4 ± 1.5 years; mean BMI: 34.5 ± 0.8 kg/m^2), and 75 subjects without MetS constituted the control group (mean age 28.1 ± 1.0 years; mean BMI: 29.8 ± 0.6 kg/m^2). Individuals were excluded from the study if they met any of the following criteria: age outside the 19-65-year age range; use of antioxidants or specialized nutritional supplements; presence of inflammatory conditions (e.g., connective tissue diseases, cancer, infection, inflammatory bowel disease, rheumatoid arthritis, lupus, tuberculosis); diagnosis of any chronic or genetic disease other than diabetes mellitus or hypertension; pregnancy or lactation; or use of medications that affect nutritional status.

BMI was calculated as weight in kilograms divided by the square of height in metres (kg/m^2). BMI categories were defined as follows (10):

Normal weight: 18.5-24.9 kg/m^2

Overweight: 25-29.9 kg/m^2

Obesity: ≥30 kg/m^2

Obesity class I: 30-34.9 kg/m^2

Obesity class II: 35-39.9 kg/m^2

Obesity class III: ≥40 kg/m^2

The classification of MetS was based on the NCEP ATP III guidelines. According to the NCEP ATP III definition, a diagnosis of MetS requires the presence of at least three of the following five components: waist circumference >102 cm for men and >88 for women; triglycerides ≥150 mg/dL; high-density lipoprotein cholesterol (HDL)-C <40 mg/dL for men, and <50 mg/dL for women; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; and fasting glucose ≥110 mg/dL] (11).

Laboratory Analysis

Blood samples were collected after an overnight fast. Serum samples were separated by centrifugation at 3000 rpm for 10 minutes at room temperature and stored at -80 °C until analysis. Serum ferritin (DiaMetra, DK0039), IL-1α (Elabscience, E-EL-H0088), IL-10 (Elabscience, E-EL-H6154), and IFN-γ (Elabscience, E-EL-H0108) levels were analyzed using commercial enzyme-linked immunosorbent

assay (ELISA) kits. Biochemical parameters were analyzed at the Pharmaceutical Biochemistry Laboratory of Gazi University.

Blood pressure was measured twice on the participant's right arm using a mercury sphygmomanometer after a 20-minute rest. The mean of the two measurements was used for statistical analysis.

The study was approved by the Medical Ethics Committee of Selçuk University (approval number: 2016/304, dated: 21.12.2016). Written informed consent was obtained from all participants prior to study enrollment.

Statistical Analysis

Numerical variables were expressed as mean ± standard error and categorical variables as percentages. Unequal gender group sizes can affect test power when group variances are heterogeneous but have minimal impact when group variances are homogeneous. Therefore, Levene's test was used to assess the homogeneity of variances. When variances were not homogeneous, Welch's t test was applied; otherwise, Student's t-test or ANOVA was used for parametric variables. For nonparametric variables, the Mann-Whitney U test or the Kruskal-Wallis test was employed. Correlations were evaluated using either Pearson or Spearman correlation coefficients. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS (Statistical Package for the Social Sciences) version 24.0.

RESULTS

A total of 150 subjects participated in the present study. participants were divided into two subgroups based on the NCEP ATP III criteria for the diagnosis of MetS. The patient group included individuals with at least three MetS components: 31.3% (n = 47) had three components; 14.7% (n = 22) had four components; and 4% (n = 6) had all five components. The control group comprised individuals with no MetS components or with only one or two components: 7.3% (n = 11) had none; 17.3% (n = 26) had one component; and 25.3% (n = 38) had two components.

The general characteristics of the study participants, including age and BMI ranges, gender distribution, education level, smoking status, and alcohol consumption status, are summarized in Table 1.

Across the patient group (aged 40-65 years) and the control group (aged 18-24 years), the participation rate was 52% (n = 39). The mean ages of the patient and control groups were 40.4 ± 1.5 and 28.1 ± 1.0 years, respectively. Individuals diagnosed with MetS were significantly older than those without MetS (p=0.000; data not shown). Among patients, 33.3% (n = 25) had first-degree obesity, whereas among controls, 58.7% (n = 44) were overweight. BMI was significantly higher in patients than in controls (34.5 ± 0.8 and 29.8 ± 0.6, respectively; p < 0.001; data not shown). In terms of education, most patients (53.3%) were elementary school graduates, while most controls (48%) were high school graduates. The majority of participants reported never smoking and never consuming alcohol (77.3% and 91.3%, respectively).

Demographic characteristics, anthropometric measurements, biochemical data, and other measured parameters for each group are summarized in Table 2.

Anthropometric measurements, including hip circumference and mid-upper arm circumference, were significantly higher in patients than in controls (p = 0.000 for both). Biochemical analysis revealed that homeostatic model assessment-insulin resistance and levels of total cholesterol, alanine transaminase (ALT), urea, and insulin were significantly higher, whereas the estimated glomerular filtration rate (e-GFR) was significantly lower in patients compared with controls (p = 0.000, p = 0.001, p = 0.001, p = 0.000, p = 0.000, and p = 0.000, respectively). MetS components identified in patients included increased waist circumference, elevated fasting blood glucose, elevated systolic and diastolic blood pressure, elevated triglycerides, and reduced HDL-C levels. Recent evidence suggests that MetS accelerates eGFR decline, thereby increasing the risk of chronic kidney disease and end-stage renal disease (12). Although no prior study has specifically examined the relationship between urea and MetS, it is hypothesized that MetS may elevate serum urea levels by impairing renal function. Serum ferritin, IL-1α, IL-10, and IFN-γ levels for each group are presented in Table 3.

In the present study, serum levels of ferritin, IFN-γ, and IL-1α were significantly higher in patients than in controls. Although serum IL-10 levels were also higher in individuals with MetS, this difference did not reach statistical significance. The distribution of the measured parameters by gender is presented in Table 4.

This study revealed that serum ferritin concentrations were statistically significantly higher in men than in women in both the control and patient groups.

DISCUSSION

The main finding of this study was that the concentrations of serum ferritin, IL-1α, and IFN-γ were significantly higher in participants with MetS than in healthy controls. Although serum IL-10 levels were also higher in patients, the difference was not statistically significant. These results suggest that ferritin, IL-1α, and IFN-γ may serve as biomarkers for MetS.

Although the precise pathogenic mechanisms underlying MetS remain unclear, the interplay between obesity, low-grade inflammation, and insulin resistance is thought to play a vital role in its development (5). In particular, chronic low-grade inflammation is considered a central factor in the pathogenesis of MetS (13).

Ferritin plays a critical role in iron homeostasis and serves as a clinical biomarker for both iron deficiency and hemochromatosis (14). Recent studies have reported higher serum ferritin concentrations in individuals with MetS compared with healthy controls (13,15). This finding supports the idea that serum ferritin may serve as a marker for the development of MetS. Although the underlying mechanisms linking ferritin and MetS are not fully understood, several hypotheses have been proposed, including the Fenton reaction (16), the iron dysregulation and dormant microbes hypothesis (17), the lipolytic effect of excessive iron concentrations (18), and the increased hypersensitivity of pancreatic cells to reactive oxygen species (19). Nevertheless, some studies have reported conflicting results regarding the association between serum ferritin and MetS. These discrepancies have been attributed to small sample sizes, confounding factors, and differences in study populations (20).

Table 1. General characteristics of study participants.

		Total individuals n (%)	Patients n (%)	Controls n (%)
Age range	18-24 years	50 (33.3%)	11 (14.7%)	**39 (52%)**
	25-39 years	50 (33.3%)	25 (33.3%)	25 (33.3%)
	40-65 years	50 (33.3%)	**39 (52%)**	11 (14.7%)
Gender	Male	36 (24%)	23 (30.7%)	13 (17.3%)
	Female	114 (76%)	52 (69.3%)	62 (82.7%)
BMI range	Overweight	65 (43.3%)	21 (28%)	**44 (58.7%)**
	1st degree obesity	46 (30.7%)	**25 (33.3%)**	21 (28%)
	2nd degree obesity	26 (17.3%)	18 (24%)	8 (10.7%)
	3rd degree obesity	13 (8.7%)	11 (14.7%)	2 (2.7%)
Level of education	Literate	8 (5.3%)	4 (5.3%)	4 (5.3%)
	Elementary	57 (38%)	**40 (53.3%)**	17 (22.7%)
	High school	53 (35.3%)	17 (22.7%)	**36 (48%)**
	University	28 (18.7%)	12 (16%)	16 (21.3%)
	Postgraduate	4 (2.7%)	2 (2.7%)	2 (2.7%)
Smoking status	Current	20 (14%)	13 (17.3%)	7 (10.7%)
	Never	116 (77.3%)	54 (72%)	**62 (82.7%)**
	Former	13 (8.7%)	8 (10.7%)	5 (6.7%)
Alcohol consumption	Current	7 (4.7%)	3 (4%)	4 (5.3%)
	Never	137 (91.3%)	68 (90.7%)	**69 (92%)**
	Former	6 (4%)	4 (5.3%)	2 (2.7%)

BMI: Body mass index.

Adipose tissue, which is currently recognised as an endocrine organ (21), undergoes hypertrophy and hyperplasia in response to excessive caloric intake (22). This increase in adipose tissue mass leads to elevated adipokine production by pre-adipocytes and macrophages, thereby contributing to the development of inflammation (23). Therefore, the accumulation of visceral adipose tissue, a characteristic feature of MetS, may alter the vascular and lymphatic microenvironment, thereby creating lethal conditions for adipocytes that are distant from blood vessels. In addition, hypoxia and lipotoxicity may occur in adipocytes, thereby triggering the release of fatty acids and substrates that activate pro-inflammatory pathways in tissues (22). Although the pathogenesis of MetS has not yet been fully elucidated, it is hypothesised that an imbalance between antioxidant and pro-oxidant activities plays a vital role in its development (24). Furthermore, a chronic inflammatory state is considered the primary mechanism underlying MetS pathophysiology (21). Chronic low-grade inflammation, resulting from the accumulation of excess adipose tissue, is generally regarded as a key factor in the development of insulin resistance and may play an important role in the pathobiology of MetS (24,25).

Nicoară et al. (26) demonstrated the diagnostic value of the systemic immune-inflammatory response index for distinguishing MetS in obese children. Another study found a pronounced increase in pro-inflammatory cytokines in men with MetS and a decrease in anti-inflammatory adipokines in women with MetS (27). IFN-γ suppresses the expression of Sirtuin-1 (SIRT1), leading to metabolic dysfunction and the development of T2DM (28). Increased IFN-γ levels reduce insulin activity, disrupt metabolic homeostasis and insulin signaling in skeletal muscle, and induce tumor necrosis factor (TNF)-α and Nuclear Factor Kappa B (NF-kB). IFN-γ also contributes to T-cell modulation, diet-associated insulin resistance, T2DM, and obesity by activating the JAK-STAT pathway, ultimately leading to insulin resistance (28). IFN-γ cytokine levels were found to be significantly higher in individuals diagnosed with MetS than in healthy adults (29), and increased serum IFN-γ concentrations were associated with insulin resistance and MetS components in obese children (30). These findings indicate that elevated IFN-γ levels are related to insulin resistance and MetS in pediatric population. Therefore, IFN-γ concentration may serve as a clinical biomarker for MetS and T2DM development and is considered a potential therapeutic target for improving these pathologies (31). Similar to previous studies, we found that serum IFN-γ concentrations were significantly higher in patiens with MetS compared to healthy counterparts.

IL-1, which includes IL-1α, IL-1β, and IL-1 receptor, is produced and secreted by hepatocytes and various other cellss, including vascular smooth muscle cells, endothelial cells, and macrophages/monocytes (32). Elevated serum IL-1α concentrations have been identified as vital parameters in the development of MetS (29). Lower IL-1α concentrations were associated with reduced adiposity and improved glucose tolerance in diet-induced obese mice, suggesting that inhibition of IL-1α may help maintain glucose tolerance and protect against obesity-related comorbidities (33). In another study, IL-1α treatment was shown to impair insulin signaling (34) by increasing IL-6 production in 3T3-L1 adipocytes, thereby contributing to insulin resistance. Other mechanisms have been suggested, including disruption of insulin signalling via STAT phosphorylation, SOCS3

Table 2. Demographic, anthropometric, and clinical data of study participants.

	Patients mean ± SE	Controls mean ± SE	p-value
Age	40.4 ± 1.5	28.1 ± 1.0	**0.000***
BMI	34.5 ± 0.8	29.8 ± 0.6	**0.000***
Hip circumference (cm)	119.8 ± 1.6	112.5 ± 1.3	**0.000***
Mid upper arm circumference (cm)	37.9 ± 0.5	34.2 ± 0.5	**0.000***
Waist circumference (cm)	115.9 ± 1.8	99.8 ± 1.9	**0.000***
SBP (mmHg)	128.5 ± 2.4	110.8 ± 1.5	**0.000***
DBP (mmHg)	80.2 ± 1.4	72.7 ± 1.2	**0.000***
Fasting blood glucose (mg/dL)	118.5 ± 5.7	88.7 ± 0.9	**0.000***
Insulin (mU/L)	18.6 ± 1.3	12.7 ± 0.7	**0.000***
HOMA-IR	4.6 ± 0.3	2.8 ± 0.2	**0.000***
Total cholesterol (mg/dL)	200.5 ± 5.6	178.2 ± 3.9	**0.000***
Triglycerides (mg/dL)	203.5 ± 10.8	90.7 ± 4.1	**0.000***
HDL-C (mg/dL)	44.7 ± 1.1	53.6 ± 1.2	**0.000***
LDL-C (mg/dL)	117.2 ± 4.6	106.5 ± 2.9	0.051
e-GFR (mL/min)	117.6 ± 2.2	131.4 ± 1.6	**0.000***
ALT (U/L)	25.5 ± 1.5	19.5 ± 1.4	**0.001***
Creatinine (mg/dL)	0.73 ± 0.02	0.68 ± 0.01	0.178
Urea (mg/dL)	26.2 ± 0.9	22.3 ± 0.6	**0.000***
Vitamin B_{12} (ng/L)	292.0 ± 11.2	307.7 ± 13.5	0.684
TSH (mU/L)	2.1 ± 0.1	2.3 ± 0.2	0.403

*p < 0.05, HOMA-IR: Homeostatic model assessment-insulin resistance, SE: Standard error, BMI: Body mass index, SBP: systolic blood pressure, DBP: Diastolic blood pressure, HDL-C: High denstiy lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, ALT: Alanine aminotransferase, TSH: Thyroid-stimulating hormone.

Table 3. Evaluation of measured parameter levels in participants according to MetS status.

	Patients Mean ± SE	Controls Mean ± SE	p-value
Ferritin (ng/mL)	60.8 ± 4.2	37.1 ± 3.4	**0.000***
IL-1α (pg/mL)	3.3 ± 0.2	2.7 ± 0.1	**0.011***
IL-10 (pg/mL)	3.9 ± 0.1	3.7 ± 0.1	0.089
IFN-γ (pg/mL)	3.0 ± 0.1	2.8 ± 0.0	**0.001***

*p < 0.05.
IL-1α: Interleukin-1α, IL-10: Interleukin 10, IFN-γ: Interferon-γ, SE: Standard error.

induction (35), and downregulation of insulin receptor substrate-1 in the presence of IL-6 (28). Consistent with previous research (29), the present study found that serum IL-1α concentrations were significantly higher in patients than in controls.

IL-10, an anti-inflammatory cytokine, plays an important role in regulating the immune system and in inhibiting the production and expression of pro-inflammatory cytokines (25). IL-10 is produced by macrophages and lymphocytes and exerts its anti-inflammatory and insulin signalling-modulating effects by inhibiting kappa B inhibitor kinase activity, suppressing TNF-induced nuclear factor kappa B activation (36), inhibiting NADPH oxidase-mediated oxidative stress, and downregulating TNF-α and IL-6 concentrations (37). High circulating IL-10 levels help counter chronic inflammation in obesity and T2DM (38,39). Serum IL-10 has been found to be inversely associated with metabolic disorders, including elevated blood pressure, dyslipidemia, glucose intolerance (40), and MetS (25,38). Freitas et al. (41) reported that subjects with the IL-10 AA genotype, which is associated with lower IL-10 levels, had a higher risk of developing MetS. Serum IL-10 concentration has been linked to improvements in MetS and obesity by reducing BMI and body fat mass, reducing insulin resistance, and improving adipose tissue function in both human and animal models (42,43). Reduced IL-10 concentrations in adipose tissue and serum have been observed in subjects with obesity and type 2 diabetes (44,45). Interestingly, increased serum IL-10 concentrations have been found in obese women compared to non-obese women (38); this was attributed to a compensatory increase in IL-10 aimed at downregulating pro-inflammatory cytokines (38), as well as in children and adolescents (46). Some studies have also reported higher serum IL-10 concentrations in subjects with MetS compared with healthy counterparts (29,47). In our study, serum IL-10 concentrations were higher in patients; however, the difference between the two groups was not statistically significant. Although the underlying mechanism is not fully understood, a compensatory increase in IL-10 in response to the pro-inflammatory state may explain these findings (29). Additionally, genetic factors are thought to contribute to variability in cytokine production (48), and genetic differences

Table 4. Evaluation of measured parameters according to gender in controls and patient groups.

Measured parameters in controls	n	Meant ± SE	p-value
Ferritin			
Female	62	30.7 ± 2.1	**0.03***
Male	13	67.7 ± 14.6	
IL-1α			
Female	62	2.6 ± 0.1	0.317
Male	13	3.0 ± 0.3	
IL-10			
Female	62	3.7 ± 0.1	0.905
Male	13	3.7 ± 0.2	
IFN-γ			
Female	62	2.8 ± 0.0	0.413
Male	13	2.8 ± 0.0	
Measured parameters in patients			
Ferritin			
Female	52	52.7 ± 4.1	**0.011***
Male	23	79.2 ± 9.0	
IL-1α			
Female	52	3.2 ± 0.2	0.899
Male	23	3.4 ± 0.4	
IL-10			
Female	52	3.8 ± 0.1	0.140
Male	23	4.0 ± 0.1	
IFN-γ			
Female	52	3.1 ± 0.1	0.411
Male	23	3.0 ± 0.1	

*p < 0.05.
IL, IL-1α: Interleukin-1α, IL-10: Interleukin 10, IFN-γ: Interferon-γ, SE: Standard error.

among individuals in our study may account for the higher serum IL-10 concentrations observed in patients with MetS compared with those in the control group.

Gender is considered a significant factor that potentially influences differences in serum ferritin levels. A review of the literature has revealed that studies report inconsistent results (49). The discrepancies observed across studies may be attributed to differences in study population characteristics, sample size, and factors influencing serum ferritin levels. Physiologically, women tend to have lower serum ferritin concentrations than men due to iron loss through menstruation. In men, increased visceral adiposity and metabolic disorders may elevate serum ferritin levels by promoting the production of inflammatory cytokines. In our study, consistent with previous research (50), Levene's test indicated that variances across groups were not homogeneous. Therefore, Welch's t-test was applied, and only serum ferritin concentrations were higher in men than in women in both the patient and the control groups.

Study Limitations

Although this study was successfully completed, several limitations should be considered. First, the small sample size and the cross-sectional design of the study may limit the generalizability of the findings. Prospective studies with larger sample sizes are needed to clarify the causal relationships between serum ferritin, inflammatory cytokines, and MetS. Another limitation is that menopausal status was not considered, which may have influenced serum ferritin levels.

CONCLUSION

To the best of our knowledge, this is the first study in Türkiye to evaluate levels of serum ferritin and other inflammatory cytokines in individuals with and without MetS. The main finding was that serum concentrations of ferritin, IL-1α, and IFN-γ were significantly higher in participants diagnosed with MetS than in healthy controls. Although serum IL-10 levels were also higher in patients, the difference was not statistically significant. These findings indicate that individuals with MetS have elevated serum levels of pro-inflammatory cytokines and ferritin, which may be clinically relevant to the pathogenesis of the syndrome. Identifying new determinants of MetS could facilitate earlier diagnosis and more effective treatment. A better understanding of the roles of inflammation and ferritin in MetS may also contribute to improved prevention strategies. Prospective studies with larger cohorts are needed to further elucidate the relationship between cytokines and MetS.

Ethics

Ethics Committee Approval: The study was approved by the Medical Ethics Committee of Selcuk University (approval number: 2016/304, dated: 21.12.2016).

Informed Consent: Written informed consent was obtained from all participants prior to study enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.O.K., B.Ö., Concept: H.T.B., A.H.,

Design: H.T.B., A.H., Data Collection or Processing: H.T.B., C.O.K., B.Ö., Analysis or Interpretation: H.T.B., B.B., A.H., Literature Search: H.T.B., Writing: H.T.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: This study was supported by Gazi University Scientific Research Projects Unit (project no: 02/2017-17).

REFERENCES

1. Neeland IJ, Lim S, Tchernof A, Gastaldelli A, Rangaswami J, Ndumele CE, et al. Metabolic syndrome. Nat Rev Dis Primers. 2024; 10: 77.
2. International Diabetes Federation. The IDF consensus worldwide definition of the Metabolic Syndrome [Internet]. Brussels: IDF; 2023 [cited 2024 Jun 7]. Available from: https://idf.org/media/uploads/2023/05/attachments-30.pdf
3. Onat A, Yüksel M, Köroğlu B, Gümrükçüoğlu HA, Aydın M, Cakmak HA, et al. TEKHARF 2012: Turkish Adult Risk Factor Study survey 2012: overall and coronary mortality and trends in the prevalence of metabolic syndrome. Turk Kardiyol Dern Ars. 2013; 41: 373–8.

4. Mollaoğlu M, Kars Fertelli T, Özkan Tuncay F. The risk levels of metabolic syndrome and related factors among adults admitted at a village clinic. 2010; 18: 72–9.
5. Serbis A, Giapros V, Galli-Tsinopoulou A, Siomou E. Metabolic syndrome in children and adolescents: ıs there a universally accepted definition? Does it matter? Metab Syndr Relat Disord. 2020; 18: 462–70.
6. Hacışevki A, Berberoğlu HT. Activation of inflammatory signaling pathways in metabolic syndrome: changes in adipokines and cytokines. In: Yucel D, ed. Current Biochemical Studies. Ankara, Akademisyen Kitabevi; 2020: 15–36.
7. Coelho M, Oliveira T, Fernandes R. Biochemistry of adipose tissue: an endocrine organ. Arch Med Sci. 2013; 9: 191–200.
8. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: past, present and future. Biochim Biophys Acta. 2010; 1800: 760–9.
9. Mahroum N, Alghory A, Kiyak Z, Alwani A, Seida R, Alrais M, et al. Ferritin- from iron, through inflammation and autoimmunity, to COVID-19. J Autoimmun. 2022; 126: 102778.
10. Weir CB, Jan A. BMI classification percentile and cut off points. In: StatPearls [Internet]. Treasure island (FL): StatPearls Publishing; 2025 [cited 2025 Nov 05]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541070/.
11. National Cholesterol Education Program. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report [Internet]. Bethesda (MD): National Heart, Lung, and Blood Institute; 2002 [cited 2018 Jun 20]. Available from: https://www.nhlbi.nih.gov/files/docs/resources/heart/atp-3-cholesterol-full-report.pdf
12. Valizadeh A, Nikoohemmat M, Ebadinejad A, Soltani S, Tape PMK, Sohrabi A, et al. Metabolic syndrome as a risk factor for the development of kidney dysfunction: a meta-analysis of observational cohort studies. J Diabetes Metab Disord. 2023; 23: 215–27.
13. Srivastav SK, Mir IA, Bansal N, Singh PK, Kumari R, Deshmukh A. Serum ferritin in metabolic syndrome-mechanisms and clinical applications. Pathophysiology. 2022; 29: 319–25.
14. Heeney MM, Andrews NC. Iron homeostasis and inherited iron overload disorders: an overview. Hematol Oncol Clin North Am. 2004; 18: 1379–403.
15. Tran TN, Tran HD, Tran-Huu TT, Tran DM, Tran QN. A cross-sectional study of serum ferritin levels in vietnamese adults with metabolic syndrome. Diabetes Metab Syndr Obes. 2022; 15: 1517–23.
16. Shim YS, Kang MJ, Oh YJ, Baek JW, Yang S, Hwang IT. Association of serum ferritin with insulin resistance, abdominal obesity, and metabolic syndrome in Korean adolescent and adults: The Korean National Health and Nutrition Examination Survey, 2008 to 2011. Medicine (Baltimore). 2017; 96: e6179.
17. Kell DB, Pretorius E. No effects without causes: the ıron dysregulation and dormant microbes hypothesis for chronic, inflammatory diseases. Biol Rev Camb Philos Soc. 2018; 93: 1518–57.
18. Moore Heslin A, O'Donnell A, Buffini M, Nugent AP, Walton J, Flynn A, et al. Risk of ıron overload in obesity and ımplications in metabolic health. Nutrients. 2021; 13: 1539.
19. Eguchi N, Vaziri ND, Dafoe DC, Ichii H. The role of oxidative stress in pancreatic β Cell dysfunction in diabetes. Int J Mol Sci. 2021; 22: 1509.
20. Kilani N, Vollenweider P, Waeber G, Marques-Vidal P. Iron metabolism and incidence of metabolic syndrome. Nutr Metab Cardiovasc Dis. 2015; 25: 1025–32.
21. Dutta D, Maisnam I, Mukhopadhyay S, Raychaudhuri SK, Raychaudhuri SP. Systemic inflammation in psoriasis: sequel of metabolic syndrome. In: Mukhopadhyay S, Mondal S, eds. Metabolic syndrome: from mechanisms to interventions. Academic Press; 2024: 621-33. Available from: https://www.elsevier.com/books/metabolic-syndrome-from-mechanisms-to-interventions/mukhopadhyay/978-0-323-85732–1.
22. Debnath M, Agrawal S, Agrawal A, Dubey GP. Metaflammatory responses during obesity: Pathomechanism and treatment. Obes Res Clin Pract. 2016; 10: 103–13.
23. Guarner V, Rubio-Ruiz ME. Low-grade systemic inflammation connects aging, metabolic syndrome and cardiovascular disease. Interdiscip Top Gerontol. 2015; 40: 99–106.
24. Vona R, Gambardella L, Cittadini C, Straface E, Pietraforte D. Biomarkers of Oxidative Stress in Metabolic Syndrome and Associated Diseases. Oxid Med Cell Longev. 2019; 2019: 8267234.
25. Choi KM, Ryu OH, Lee KW, Kim HY, Seo JA, Kim SG, et al. Serum adiponectin, interleukin-10 levels and inflammatory markers in the metabolic syndrome. Diabetes Res Clin Pract. 2007; 75: 235–40.
26. Nicoară DM, Munteanu AI, Scutca AC, Mang N, Juganaru I, Brad GF, et al. Assessing the relationship between systemic immune-inflammation index and metabolic syndrome in children with obesity. Int J Mol Sci. 2023; 24: 8414.
27. Ter Horst R, van den Munckhof ICL, Schraa K, Aguirre-Gamboa R, Jaeger M, Smeekens SP, et al. Sex-specific regulation of inflammation and metabolic syndrome in obesity. Arterioscler Thromb Vasc Biol. 2020; 40: 1787–800.
28. Li P, Zhao Y, Wu X, Xia M, Fang M, Iwasaki Y, et al. Interferon gamma (IFN-γ) disrupts energy expenditure and metabolic homeostasis by suppressing SIRT1 transcription. Nucleic Acids Res. 2012; 40: 1609–20.
29. Mirhafez SR, Pasdar A, Avan A, Esmaily H, Moezzi A, Mohebati M, et al. Cytokine and growth factor profiling in patients with the metabolic syndrome. Br J Nutr. 2015; 113: 1911–9.
30. Pacifico L, Di Renzo L, Anania C, Osborn JF, Ippoliti F, Schiavo E, et al. Increased T-helper interferon-γ-secreting cells in obese children. Eur J Endocrinol. 2006; 154: 691–7.
31. Reinehr T, Roth CL. Inflammation markers in type 2 diabetes and the metabolic syndrome in the pediatric population. Curr Diab Rep. 2018; 18: 131.
32. Kamari Y, Werman-Venkert R, Shaish A, Werman A, Harari A, Gonen A, et al. Differential role and tissue specificity of interleukin-1alpha gene expression in atherogenesis and lipid metabolism. Atherosclerosis. 2007; 195: 31–8.
33. Almog T, Kandel Kfir M, Levkovich H, Shlomai G, Barshack I, Stienstra R, et al. Interleukin-1α deficiency reduces adiposity, glucose intolerance and hepatic de-novo lipogenesis in diet-induced obese mice. BMJ Open Diabetes Res Care. 2019; 7: e000650.
34. Ballak DB, Stienstra R, Tack CJ, Dinarello CA, van Diepen JA. IL-1 family members in the pathogenesis and treatment of metabolic disease: focus on adipose tissue inflammation and insulin resistance. Cytokine. 2015; 75: 280–90.
35. Uno T, He J, Usui I, Kanatani Y, Bukhari A, Fujisaka S, et al. Long-term interleukin-1alpha treatment inhibits insulin signaling via IL-6 production and SOCS3 expression in 3T3-L1 adipocytes. Horm Metab Res. 2008; 40: 8–12.
36. de Luca C, Olefsky JM. Inflammation and insulin resistance. FEBS Lett. 2008; 582: 97–105.

37. Srikanthan K, Feyh A, Visweshwar H, Shapiro JI, Sodhi K. Systematic review of metabolic syndrome biomarkers: a panel for early detection, management, and risk stratification in the West Virginian population. Int J Med Sci. 2016; 13: 25–38.
38. Esposito K, Pontillo A, Giugliano F, Giugliano G, Marfella R, Nicoletti G, et al. Association of low interleukin-10 levels with the metabolic syndrome in obese women. J Clin Endocrinol Metab. 2003; 88: 1055–8.
39. Barry JC, Shakibakho S, Durrer C, Simtchouk S, Jawanda KK, Cheung ST, et al. Hyporesponsiveness to the anti-inflammatory action of interleukin-10 in type 2 diabetes. Sci Rep. 2016; 6: 21244.
40. Kulshrestha H, Gupta V, Mishra S, Mahdi AA, Awasthi S, Kumar S. Interleukin-10 as a novel biomarker of metabolic risk factors. Diabetes Metab Syndr. 2018; 12: 543–7.
41. Freitas RS, de Souza Silva CM, Ferreira Fratelli C, Ramos de Lima L, Morato Stival M, Schwerz Funghetto S, et al. IL-10 and IL-1β serum levels, genetic variants, and metabolic syndrome: ınsights into older adults' clinical characteristics. Nutrients. 2024; 16: 1241.
42. Gao M, Zhang C, Ma Y, Bu L, Yan L, Liu D. Hydrodynamic delivery of mIL10 gene protects mice from high-fat diet-induced obesity and glucose intolerance. Mol Ther. 2013; 21: 1852–61.
43. Cintra DE, Pauli JR, Araújo EP, Moraes JC, de Souza CT, Milanski M, et al. Interleukin-10 is a protective factor against diet-induced insulin resistance in liver. J Hepatol. 2008; 48: 628–37.
44. Rodrigues KF, Pietrani NT, Bosco AA, Campos FMF, Sandrim VC, Gomes KB. IL-6, TNF-α, and IL-10 levels/polymorphisms and their association with type 2 diabetes mellitus and obesity in Brazilian individuals. Arch Endocrinol Metab. 2017; 61: 438–46.
45. Medeiros NI, Mattos RT, Menezes CA, Fares RCG, Talvani A, Dutra WO, Rios-Santos F, Correa-Oliveira R, Gomes JAS. IL-10 and TGF-β unbalanced levels in neutrophils contribute to increase inflammatory cytokine expression in childhood obesity. Eur J Nutr. 2018; 57: 2421–30.
46. Calcaterra V, De Amici M, Klersy C, Torre C, Brizzi V, Scaglia F, et al. Adiponectin, IL-10 and metabolic syndrome in obese children and adolescents. Acta Biomed. 2009; 80: 117–23.
47. Yeldu MH, Mus'ab A. Serum biochemical and inflammatory cytokines in a rat model of metabolic syndrome. Asian J Med Sci. 2020; 11: 46–52.
48. Westendorp RG, Langermans JA, Huizinga TW, Elouali AH, Verweij CL, Boomsma DI, et al. Genetic influence on cytokine production and fatal meningococcal disease. Lancet. 1997; 349: 170–3.
49. Alqahtani SAM, Alsaleem MA, Ghazy RM. Association between serum ferritin level and lipid profile among diabetic patients: A retrospective cohort study. Medicine (Baltimore). 2024; 103: e37631.
50. Badenhorst CE, Forsyth AK, Govus AD. A contemporary understanding of iron metabolism in active premenopausal females. Front Sports Act Living. 2022; 4: 903937.