Ankara Eğt. Arş. Hast. Derg., 2021 ; 54(1) : 102-106

Özgün Çalışma / Original Article **DOI: 10.20492/aeahtd.826939**

IS SERUM FERRITIN LEVEL DIFFERENT BETWEEN HEALTHY INDIVIDUALS AND NEWLY DIAGNOSED PATIENTS WITH TYPE 2 DIABETES MELLITUS? A CASE-CONTROL STUDY

SERUM FERRİTİN DÜZEYİ SAĞLIKLI BİREYLERLE YENİ TANI TİP 2 DİYABET HASTALARINDA FARKLI MIDIR? VAKA KONTROL ÇALIŞMASI

Veli SUNAR[1], Engin SENNAROĞLU[2]

ABSTRACT

AIM: This study aims to evaluate whether serum ferritin levels differ between recently diagnosed patients with type 2 diabetes mellitus (DM) and healthy controls, and to assess the relationship between serum ferritin level, insulin resistance and metabolic control in patients with type 2 DM.

MATERIAL AND METHOD: This study included 40 patients with recently diagnosed type 2 DM and 40 healthy controls. The Homeostasis Model Assessment of insulin resistance (HOMA-IR) score was used for evaluation of insulin resistance. HOMA-IR scores ≥2.7 were accepted as insulin resistance. The patient and control groups were compared in terms of age, gender, body mass index (BMI), serum ferritin, insulin, HbA1c, and HOMA-IR scores. The correlation between ferritin levels and other parameters were assessed in the patient group. Furthermore, patients with good (HbA1c<7%) and poor glycemic control (HbA1c≥7%) were compared regarding serum ferritin level.

RESULTS: Ninety percent (n=36) of the patient group and 27.5%(n=11) of the controls had HOMA-IR scores ≥2.7. Serum ferritin levels were significantly higher in the patient group (153.57±150.01 vs62.83±53.18; p=0.003). There were significant positive correlations between serum ferritin and fasting plasma glucose levels (r=0.419 p=0.007), HbA1c (r=0.410, p=0.009) and HOMA-IR score (r=0.320, p=0.044) in the patient group. Mean serum ferritin level of patients with poor metabolic control (201.20±170.67) was significantly higher than the ones with good metabolic control (91.92±71.39) among patients with type 2 DM (p=0.047).

CONCLUSION: Serum ferritin levels were found to be higher in patients with type 2 DM than controls and there was positive correlation between serum ferritin levels and insulin resistance.

Keywords: *ferritin, diabetes mellitus, insulin resistance*

ÖZET

GİRİŞ: Bu çalışmanın amacı yeni tanı tip 2 DM hastaları ile sağlıklı bireyler arasında serum ferritin düzeyi açısından fark olup olmadığını değerlendirmek, ayrıca tip 2 DM hastalarında serum ferritin düzeyinin insulin direnci ve metabolik kontrol ile ilişkisini araştırmaktır.

GEREÇ VE YÖNTEM: Çalışmaya 40 yeni tanı tip 2 DM hastası ile 40 sağlıklı kişiden oluşan control grubu dahil edildi. İnsülin direncini değerlendirmek için Homeostasis Model Assessment of Insulin resistance (HOMA-IR) skoru kullanıldı. HOMA-IR skorunun ≥2.7olması insulin direnci olarak Kabul edildi. Hasta ve control grubunu oluşturan bireyler yaş, cinsiyet dağılımı, Vücut kitle indeksi (VKİ), serum ferritin düzeyi, insulin düzeyi ve HOMA-IR skoru açısından karşılaştırıldı. Hasta grubundaki bireylerin ferritin düzeyi ile diğer parametreler arasındaki ilişki incelendi. Ayrıca iyi glisemik kontrollü (HbA1c<%7) ve kötü glisemik kontrollü (HbA1c≥%7) hastaların serum ferritin düzeyleri karşılaştırıldı.

BULGULAR: Hasta grubunun %90'ında (n=36), kontrol grubunun %27,5'inde (n=11) HOMA-IR skoru ≥2.7 olarak tespit edildi. Hasta grubunun ferritin düzeyi kontrol grubuna göre anlamlı olarak yüksek saptandı (153.57±150.01'e 62.83±53.18; p=0.003). Hasta grubunda ferritin düzeyi ile açlık kan şekeri (r=0.419 p=0.007), HbA1c (r=0.410, p=0.009) ve HOMA-IR skoru (r=0.320, p=0.044) arasında pozitif bir korelasyon tespit edildi. Tip 2 DM hastalarında kötü glisemik kontrollü hastaların ortalama ferritin düzeyleri (201,20±170.67) iyi glisemik kontrollü hastaların ortalama ferritin düzeylerine (91.92±71.39) göre anlamlı olarak daha yüksek saptandı (p=0.047).

SONUÇ: Tip 2 DM hastalarında serum ferritin düzeyi sağlıklı bireylere göre yüksek saptanmış olup serum ferritin düzeyi ile insulin direnci arasında pozitif bir ilişki bulunmuştur.

Anahtar kelimeler: *ferritin, diyabet mellitus, insülin direnci*

[1] Department of Medical Oncology, Aydın Atatürk State Hospital, Aydın, Turkey
[2] Department of Internal Medicine, University of Krenia, Krenia, Turkish Republic of Northern Cyprus

Geliş Tarihi / Submitted : Kasım 2020 / November 2020 Kabul Tarihi / Accepted : Ocak 2021 / January 2021

Sorumlu Yazar / Corresponding Author:
Veli SUNAR
Department of Medical Oncology, Aydın Atatürk State Hospital, Aydın, Turkey
Gsm: +90 555 560 80 24 **Fax:** +90 256 212 92 22
E-mail: velisunar@gmail.com

Yazar Bilgileri /Author Information:
Veli SUNAR (ORCID: 0000-0003-4672-4621),
Engin SENNAROĞLU (ORCID: 0000-0001-6191-0583)

The ethics approval was obtained from Ankara Numune Training and Research Hospital Scientific Research Evaluation Committee (date: 29.02.2012, decision number: 2012-338).

INTRODUCTION

Diabetes mellitus (DM) is one of major causes of death worldwide (1). The prevalence of type 2 DM has been increasing in the last two decades (2). The prevalence of type 2 DM in adults is predicted to be 6.4% ranging between 3.8-10.2% regionally (3). Type 2 DM accounts for approximately 90% of all diabetic patients. It can lead to serious complications including myocardial infarction, stroke, end stage renal disease, retinopathy, and foot ulcers (4). The pathogenesis of DM has not been clearly depicted yet which occur due to a complex interaction between genetic and environmental factors (5-7). Decreased insulin release and insulin resistance are independent risk factors for development of type 2 DM (8). Several studies have focused on the role of inflammation in pathogenesis of type 2 DM (9, 10). There are studies reporting correlations between incidence of type 2 DM and certain inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), plasminogen activator inhibitor-1 (PAI-1), tumor necrosis factor-alpha (TNFα) and white blood cell numbers (WBC) (11-14).

Identification of the relationship between body iron stores and obesity, dyslipidemia, and atherosclerosis has led to much research whether serum ferritin has a role in the pathogenesis of insulin resistance (15-17). Iron is known to have active role in several processes including oxidative stress, formation of toxic free radicals, lipid peroxidation, and endothelial dysfunction (18). Cross sectional studies report that body iron stores are directly related to insulin resistance and the risk of developing type 2 DM is higher among healthy patients with high serum ferritin levels compared to ones with normal serum ferritin levels (19, 20). Moreover, there are papers suggesting that decreasing iron stores by phlebotomy in patients with type 2 DM and high ferritin levels lead to improvement in metabolic control (21, 22). This study aims to compare patients with recent-onset type 2 DM and healthy individuals and to evaluate the relationship between serum ferritin level, insulin resistance and metabolic control.

MATERIAL AND METHOD

This case control study involved 40 patients with recent-onset type 2 DM diagnosed according to American Diabetes Association (ADA) criteria and 40 healthy controls applying to Ankara Numune Training and Research Hospital between January to December 2012. The ethics approval was obtained from Ankara Numune Training and Research Hospital Scientific Research Evaluation Committee (date: 29.02.2012, decision number: 2012-338).

The inclusion criteria were being recently diagnosed with type 2 DM and not having received any treatments for diabetes previously, and being above 18 years old. Patients with anemia (hemoglobin < 13 g/dl in males and 12 < g/dl in females), patients who received iron, vitamin B12, and folic acid treatments or history of blood transfusion before, ones with comorbid systemic diseases (cancer, liver or kidney failure, neurologic, or other endocrine diseases), acute or chronic inflammatory or infectious diseases, disorders in iron metabolism, major cardiovascular events in last 6 months, smokers and patients who consume alcohol were excluded. The control group consisted of hospital staff and patients' accompanies.

A detailed medical history was obtained from all patients and healthy controls. Gender, age, height, and weight of all participants were recorded. Complete blood count, liver and kidney function tests, fasting plasma glucose (FPG), Glycated Hemoglobin A1c (HbA1c), serum insulin and ferritin levels were also recorded. Ferritin levels were determined by electrochemiluminescence immunoassay (ECLIA) in central biochemistry laboratory of our hospital. (Reference for male: 30-400 ng/ml, for female:13-150 ng/ml). Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) score was used for evaluation of insulin resistance. HOMA-IR score is calculated as[Fasting serum insulin (μlU/mL) x Fasting plasma glucose (mg/dL)]/405 (23). Patients with HOMA-IR score ≥2.7 were considered to have insulin resistance while ones with HOMA-IR score<2.7 did not have (24). Body mass index (BMI) was calculated from the formula: (kg)/ (height)^2 (m). The patients and controls were compared in terms of age, gender, BMI, serum ferritin, insulin levels, and HOMA-IR scores. Correlations between ferritin and other parameters were evaluated in patients' group. Patients were divided into two groups with good (HbA1c<%7) and poor glycemic control (HbA1c≥%7) according to glycated hemoglobin A1c. Patients and control groups were compared in terms of serum ferritin levels.

Descriptive statistics were summarized as mean, standard deviation, and percentages. Chi square test was used for comparison of categorical variables and Student's t test was used for comparing continuous parameters with normal distribution. Mann Whitney U test was employed for comparison of continuous variables without normal distribution. Spearman's correlation test was used to assess correlations. $p<0.05$ was considered statistically significant.

RESULTS

The age of participants ranged between 29 and 67 years, and of the patients 29 (36.25%) were males while 51 (63.75%) were females. Characteristics of patients and controls were presented in **Table 1.**

Patients and controls did not differ in terms of gender, age, and BMI ($p>0.05$). The mean FPG was higher in patients' group as expected ($p<0.001$). The mean insulin level was also higher in patients with type 2 DM ($p=0.006$).

When two groups were compared in terms of HOMA-IR scores, patients' group had significantly higher

scores (p<0.001). HOMA-IR score was ≥2.7 in 90% (n=36) of patients and 27.5% (n=11) of controls. Furthermore, the mean ferritin level was higher in the patient group (153.57±150.01ng/ml vs 62.83±53.18ng/ml; p=0.003) **(Table1).**

When relationships between serum ferritin and other parameters were considered, mean serum ferritin levels were significantly lower in females. In patients group, there were significant positive correlations between ferritin, FPG (r=0.419 p=0.007), HbA1c (r=0.410, p=0.009), and HOMA-IR scores (r=0.320, p=0.044). There were not any statistically significant correlations between mean serum ferritin levels and age, BMI, and mean insulin levels (p>0.05) **(Table 2).** Of the diabetic patients, 37.5% (n=15) had good glycemic control and 62.5% (n=25) had poor glycemic control. Mean serum ferritin levels were significantly higher among patients with poor glycemic control (201.20±170.67 ng/ml) compared to ones with good glycemic control (p=0.047) **(Table 3).** Of the diabetic patients, 90% (n=36) had insulin resistance according to HOMA-IR, while 10% (n=4) did not have. When patients with and without insulin resistance were compared in terms of serum ferritin levels, patients with insulin resistance had significantly higher ferritin levels than others (167.02±152.35 ng/ml vs 32.50±4.72 ng/ml, p=0.038) **(Table 4).**

Table2. The relationship between ferritin and other parameters in patients with type 2 DM

Parameter	Ferritin level	
	r	*p*
Age (years)	0.112	0.493
BMI (kg/m^2)	0.158	0.359
FPG (mg/dl)	0.419	**0.007**
Insulin (µlU/ml)	0.065	0.688
HOMA-IR score	0.320	**0.044**
HbA1c	0.410	**0.009**

BMI: Body Mass Index FPG: fasting plasma glucose
HOMA-IR: Homeostasis Model Assessment of insulin resistance
HbA1c: Glycated Hemoglobin A1c *r:* correlation coefficient

DISCUSSION

We enrolled 40 patients with recently diagnosed type 2 DM and 40 healthy controls. We evaluated if ferritin levels differed between patients and controls and whether there were associations between serum ferritin levels, insulin resistance, and metabolic control. We detected that serum ferritin levels were significantly higher in patients with type 2 DM compared to controls. Moreover, we found that patients with poor metabolic control had higher serum ferritin levels than patients with good control. We also detected that patients with insulin resistance according to HOMA-IR score

Table1. The comparison of patients with type 2 DM and controls

	Type 2 DM (n=40)	Control Group (n=40)	*p*
Gender (F/M), number (%)	24(%60)/16(%40)	27(%67.5)/13 (%32.5)	>0.05
Age (years)*	51.85±10.52	48.43±10.63	>0.05
BMI (kg/m^2)*	26.81±5.35	25.43±34.20	>0.05
FPG (mg/dl) *	201.90±82.87	92.5±5.48	**<0.001**
Insulin (µlU/ml) *	14.23±10.62	9.19±4.11	**0.006**
HOMA-IR score*	6.95±6.02	2.16±1.16	**<0.001**
Ferritin (ng/ml) *	153.57±150.01	62.83±53.18	**0.003**

*: mean ± standard deviation F/M: female/male BMI: body mass index FPG: fasting plasma glucose HOMA-IR: Homeostasis Model Assessment of insulin resistance

Table 3. Comparison of serum ferritin levels in patients with good and poor glycemic control

Group	n	Ferritin level (ng/ml), Mean± SD	p
Patients with good glycemic control	15	91.92±71.39	0.047
Patients with poor glycemic control (HbA1c≥7)	25	201.20±170.67	

Table 4. Comparison of serum ferritin levels in patients with and without insulin resistance

Group	n	Ferritin level(ng/ml), Mean± SD	*p*
Patients with insulin resistance (HOMA-IR≥2.7)	36	167.02±152.35	0.038
Patients without insulin resistance (HOMA-IR<2.7)	4	32.50±4.72	

HOMA-IR: Homeostasis Model Assessment of insulin resistance

had higher ferritin levels than ones without insulin resistance. These findings suggest that body iron stores may be associated with insulin resistance and metabolic control in type 2 DM.

Various results have been reported in different studies comparing ferritin levels among patients with type 2 DM and healthy controls (25-27). Hernandez et al. reported higher ferritin levels in diabetic patients compared to healthy individuals (28). Kim et al. did not detect statistically significant difference between patients with type 2 DM and controls (29). In a cross-sectional study by Ford et al., the relationship between serum ferritin level and the risk of DM development was assessed on a total of 9486 persons. In this study, serum ferritin levels were the highest in diabetic group followed by patients with impaired glucose tolerance and non-diabetic patients respectively. They concluded that increased serum ferritin level has an association with increased diabetes risk (19). In our study, we also detected significantly higher ferritin levels in patients with newly-diagnosed type 2 DM compared to healthy controls. We may propound that our results match up with results of this large cross-sectional study.

The importance of insulin resistance in pathogenesis of type 2 DM has been assessed in several studies and has been assumed an independent risk factor for development of type 2 DM (8, 30, 31). The positive correlation between increased body iron store, the prevalence of metabolic syndrome, and insulin resistance have led to studies questioning if ferritin has a role in pathogenesis of insulin resistance (16). Chen et al. evaluated 2786 persons in Chinese population and reported positive correlations between serum ferritin level, insulin resistance, and metabolic syndrome. They also stated that increased serum ferritin levels and the prevalence of metabolic syndrome were associated (32). In NHANES-3 study on 5959 non-diabetic healthy individuals, serum ferritin, WBC, CRP, and uric acid levels were higher in patients with insulin resistance determined according to HOMA-IR score (20). Fernandez et al. reported that serum ferritin level was a positive predictor for insulin sensitivity and HbA1c (33). We also detected positive correlations between serum ferritin levels and FPG, HbA1c, and insulin resistance determined by HOMA-IR score in diabetic patients.

In a recent study investigating the association of ferritin levels with insulin resistance according to gender and menopausal state, reported that increased serum ferritin levels had significant relationship with insulin resistance in men and post-menopausal women, but not in pre-menopausal women (34). Similarly, in a nationwide population-based study from Korea, serum ferritin levels were found to be positively associated with insülin resistance in postmenopausal women (35). However, due to small number of participants in the current study we could not perform a sub-group analysis to reveal such an association.

It is considered that an association may be existent between body iron stores and glycemic control in patients with type 2 DM. On discovering the role of iron stores in the pathogenesis of diabetes, it was researched if decreasing body iron stores may help in improving the glycemic control (17, 21). Dymocke et al. reported improvement in glucose tolerance with therapeutic phlebotomy in patients with diabetes secondary to hemochromatosis (22). It was reported that frequent blood donation leads to improvements in postprandial hyperinsulinemia and insulin sensitivity having a preventive role against development of type 2 DM by decreasing body iron stores (36-38). We also detected that type 2 diabetic patients with poor glycemic control had significantly higher serum ferritin levels compared to ones with good glycemic control.

The most important limitation of our study is low number of patients. The other limitation is the role of ferritin as an inflammatory acute phase reactant reflecting an inflammatory conditions well as being a biomarker of body iron stores. Although we have excluded the patients with known inflammatory and infectious diseases, other inflammatory markers such as CRP or fibrinogen have not been investigated in our study.

Consequently, serum ferritin levels of diabetic patients have been detected to be higher compared to healthy individuals, and a positive correlation was found between ferritin levels and insulin resistance in diabetic patients.

REFERENCES

1.)Classification and Diagnosis of Diabetes. Diabetes care. 2017;40,S11-s24.
2.)Engelgau MM, Geiss LS, Saaddine JB, et al. The evolving diabetes burden in the United States. Annals of internal medicine. 2004;140:945-50.
3.)Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. The New England journal of medicine. 2010;362:1090-101.
4.)Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. Jama. 2003;289:76-9.
5.)Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. Lancet (London, England). 2005;365:1333-46.
6.)Carter JS, Pugh JA, Monterrosa A. Non-insulin-dependent diabetes mellitus in minorities in the United States. Annals of internal medicine. 1996;125:221-32.
7.)Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes care. 1998;21:518-24.
8.)Haffner SM, Miettinen H, Gaskill SP, et al. Decreased insulin secretion and increased insulin resistance are independently related to the 7-year risk of NIDDM in Mexican-Americans. Diabetes. 1995;44:1386-91.
9.)Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. The Journal of clinical investigation. 2006;116:1793-801.
10.)Vandanmagsar B, Youm YH, Ravussin A, et al. The NLRP3 inflammasome instigates obesity-induced inflammation and

insulin resistance. Nat Med. 2011;17:179-88.
11.)Duncan BB, Schmidt MI, Pankow JS, et al. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes. 2003;52:1799-805.
12.)Pradhan AD, Manson JE, Rifai N, et al. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. Jama. 2001;286:327-34.
13.)Vozarova B, Weyer C, Lindsay RS, et al. High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes. 2002;51:455-61.
14.)de Rekeneire N, Peila R, Ding J, et al. Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition study. Diabetes care. 2006;29:1902-8.
15.)Merkel PA, Simonson DC, Amiel SA, et al. Insulin resistance and hyperinsulinemia in patients with thalassemia major treated by hypertransfusion. The New England journal of medicine. 1988;318:809-14.
16.)Jehn M, Clark JM, Guallar E. Serum ferritin and risk of the metabolic syndrome in U.S. adults. Diabetes care. 2004;27:2422-8.
17.)Iwasaki T, Nakajima A, Yoneda M, et al. Serum ferritin is associated with visceral fat area and subcutaneous fat area. Diabetes care. 2005;28:2486-91.
18.)Emerit J, Beaumont C, Trivin F. Iron metabolism, free radicals, and oxidative injury. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2001;55:333-9.
19.)Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. Diabetes care. 1999;22:1978-83.
20.)Chen J, Wildman RP, Hamm LL, et al. Association between inflammation and insulin resistance in U.S. nondiabetic adults: results from the Third National Health and Nutrition Examination Survey. Diabetes care. 2004;27:2960-5.
21.)Williams R, Smith PM, Spicer EJ, et al. Venesection therapy in idiopathic haemochromatosis. An analysis of 40 treated and 18 untreated patients. The Quarterly journal of medicine. 1969;38:1-16.
22.)Dymock IW, Cassar J, Pyke DA, et al. Observations on the pathogenesis, complications and treatment of diabetes in 115 cases of haemochromatosis. The American journal of medicine. 1972;52:203-10.
23.)Ascaso JF, Pardo S, Real JT, et al. Diagnosing insulin resistance by simple quantitative methods in subjects with normal glucose metabolism. Diabetes care. 2003;26:3320-5.
24.)Tang Q, Li X, Song P, et al. Optimal cut-off values for the homeostasis model assessment of insulin resistance (HOMA-IR) and pre-diabetes screening: Developments in research and prospects for the future. Drug discoveries & therapeutics. 2015;9:380-5.
25.)Touitou Y, Proust J, Carayon A, et al. Plasma ferritin in old age. Influence of biological and pathological factors in a large elderly population. Clinica chimica acta; international journal of clinical chemistry. 1985;149:37-45.
26.)Woo J, Mak YT, Law LK, et al. Plasma ferritin in an elderly population living in the community. Journal of medicine. 1989;20:123-34.
27.)Dinneen SF, O'Mahony MS, O'Brien T, et al. Serum ferritin in newly diagnosed and poorly controlled diabetes mellitus. Irish journal of medical science. 1992;161:636-8.
28.)Hernandez C, Lecube A, Carrera A, et al. Soluble transferrin receptors and ferritin in Type 2 diabetic patients. Diabetic medicine : a journal of the British Diabetic Association. 2005;22:97-101.
29.)Kim NH, Oh JH, Choi KM, et al. Serum ferritin in healthy subjects and type 2 diabetic patients. Yonsei Med J. 2000;41:387-92.
30.)Chen KW, Boyko EJ, Bergstrom RW, et al. Earlier appearance of impaired insulin secretion than of visceral adiposity in the pathogenesis of NIDDM. 5-Year follow-up of initially nondiabetic Japanese-American men. Diabetes care. 1995;18:747-53.
31.)Weyer C, Bogardus C, Mott DM, et al. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. The Journal of clinical investigation. 1999;104:787-94.
32.)Chen L, Li Y, Zhang F, et al. Association of serum ferritin levels with metabolic syndrome and insulin resistance in a Chinese population. Journal of diabetes and its complications. 2017;31:364-8.
33.)Fernandez-Real JM, Ricart-Engel W, Arroyo E, et al. Serum ferritin as a component of the insulin resistance syndrome. Diabetes care. 1998;21:62-8.
34.)Ma H, Lin H, Hu Y, et al. Serum ferritin levels are associated with insulin resistance in Chinese men and post-menopausal women: the Shanghai Changfeng study. The British journal of nutrition. 2018;120:863-71.
35.)Cho MR, Park JK, Choi WJ, et al. Serum ferritin level is positively associated with insulin resistance and metabolic syndrome in postmenopausal women: A nationwide population-based study. Maturitas. 2017;103:3-7.
36.)Facchini FS. Effect of phlebotomy on plasma glucose and insulin concentrations. Diabetes care. 1998;21:2190.
37.)Hua NW, Stoohs RA, Facchini FS. Low iron status and enhanced insulin sensitivity in lacto-ovo vegetarians. The British journal of nutrition. 2001;86:515-9.
38.)Ascherio A, Rimm EB, Giovannucci E, et al. Blood donations and risk of coronary heart disease in men. Circulation. 2001;103:52-7.

Ankara Eğt. Arş. Hast. Derg. (Med. J. Ankara Tr. Res. Hosp.), 2021 ; 54(1) : 102-106

The ethics approval was obtained from Ankara Numune Training and Research Hospital Scientific Research Evaluation Committee (date: 29.02.2012, decision number: 2012-338).