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Original Article

Iron Levels and Dysfunctional Adipose Index in Women

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ABSTRACT

Objective: The intricate connection between serum iron levels, adipose tissue, and metabolic parameters has been the subject of many clinical studies. In this direction, the aim of this study was to evaluate the relationship between the Dysfunctional Adiposity Index (DAI) and serum iron status.

Methods: This single-center retrospective study included 32 women with iron deficiency (ID) as a patient group and 45 women without ID as a control group. The individuals' demographic data, laboratory tests, height, weight, and waist circumference (WC) measurements were obtained from our hospital's records. DAI was calculated by the following formula: [WC/[24.02 + [2.37 * Body Mass Index (BMI)]] * [triglyceride (mmol/L) / 1.32] * [1.43 / high-density lipoprotein (mmol/L)]].

Results: We found statistically significant differences between the two groups in terms of hemoglobin values and iron parameters, such as ferritin, total iron-binding capacity, and transferrin saturation ($p<0.001$). While there was a statistically significant difference in waist circumference between the groups ($p<0.001$), the other DAI components did not differ. We also detected a negative correlation among DAI and serum iron, ferritin levels, and transferrin saturation ($r=-0.321$, $p=0.004$; $r=-0.416$, $p<0.001$; $r=0.359$, $p=0.001$, respectively).

Conclusion: This study tries to add information to the current literature on the interaction between serum iron parameters and DAI as a metabolic risk marker. The results of our study emphasize the close relationship between iron deficiency and increased waist circumference, which are very common and constitute global health problems, and underline the importance of the interaction of these two entities in clinical evaluation. However, the contradictory results of the existing literature highlight the complexity of this relationship, pointing to the need for larger, well-designed prospective studies to provide a more detailed understanding of the role of serum iron parameters, especially among individuals with high waist circumference and DAI levels.

INTRODUCTION

According to the World Health Organization report[1] published in 2024, 16% of the adult population is obese (over 890 million), while those with overweight increased up to 43% (2.5 billion). The most often used tool for determining excess body weight is the body mass index (BMI). Nonetheless, a number of researchers have cast doubt on the reliability of BMI and suggested that assessing the morpho-functional features of adipose tissue (AT) may be a more effective way to determine the risk of developing metabolic disorders.[2-4] Given that metabolic abnormalities are detected in one-fifth of individuals with normal body weight and approximately one-fourth of overweight or obese subjects are metabolically healthy, several clinical markers, such as the visceral adiposity index and the body adiposity index, have been proposed to identify metabolic abnormalities that may reflect AT functionality.[5-7]

The process of adipose tissue dysfunction involves several steps. Initially, hypertrophic adipocytes are produced when subcutaneous AT is unable to preserve energy appropriately. This leads to inflammation and visceral AT fat deposition. Subcutaneous and visceral AT dysfunction eventually results in impaired systemic metabolism.[8,9]

Iron deficiency (ID) and iron deficiency anemia (IDA) are global health problems. IDA accounts for 66.2% of all anemias and affects approximately 825 million women. It is approximately twice as common in the female sex as in men. In developing societies, the most common cause is inadequate intake, whereas in developed societies, there are different causes depending on age, gender, and region.[10]

Iron plays a crucial role in many biological processes in the body and is also essential for maintaining the homeostasis

of adipose tissue. For adipocyte differentiation, especially brown fat tissue production, endocrine function, energy supply, and other physiological processes, iron is vital.[11] On the other hand, fat tissue accumulation and obesity also affect many steps of iron metabolism.[12] Numerous chronic metabolic diseases, including obesity, type 2 diabetes mellitus, and non-alcoholic fatty liver disease, are influenced by iron homeostasis. ID is linked to obesity in adipose tissue, primarily as a result of systemic inflammation.[13-15]

This intricate connection between iron and fat tissue is the subject of many clinical studies. In the present study, we aimed to evaluate the association between ID and the dysfunctional adiposity index (DAI), which is a clinical measurement linked to the morpho-functional traits of AT (leptin, adiponectin, and adipocyte area) and is simply measured by using BMI, waist circumference, triglycerides, and high-density lipoprotein cholesterol.

MATERIALS AND METHODS

Study Design and Measurements

This retrospective study included 32 women with ID and 45 women as a control group who were applied to the internal medicine outpatient clinic of our hospital. This study excluded those who were pregnant and had autoimmune, oncological, or chronic diseases. The determination of all participants was summarized in Figure 1 as a flow chart.

Participants' demographic data, height, weight, and waist circumference (WC) measurements, and laboratory test results were obtained from our hospital's electronic records. The following formula was used to calculate the DAI: [WC / [24.02 + [2.37 * Body mass index (BMI)]] * [triglyceride (mmol/L) / 1.32] * [1.43 / high-density lipoprotein (mmol/L)]].[9] WC was measured via non-extensible tape at the midpoint between the upper iliac crest and the inferior costal edge. The subjects were measured when they were standing with their feet together, their arms swinging loosely at their sides, and breathing regularly. BMI is derived from height and weight measurements as kg/m².

Statistical Analysis

Due to the retrospective nature of the study, a formal power analysis could not be performed at the study design phase. The statistical software SPSS 26.0 was used for all of the analyses (Chicago, IL, IBM Corp.). The Kolmogorov-

Table 1. Demografic and clinical features and laboratory findings of groups

	Group 1 n=32	Group 2 n=45	p
Age, years	33 (23-41)	40 (29-45)	0.06
Body weight, kg	66.8 (55.2-68.2)	65 (54-75)	0.681
Blood pressure, mmHg			
-Systolic	112 (110-120)	110 (106-124)	0.247
-Diastolic	75 (70-80)	70 (68-82)	0.473
Smoking status, %			
-No-smoker/current	71.9/28.1	84.4/15.6	0.231
Iron, mg/dL	20 (9.5-29.7)	102 (70-108)	<0.001
Ferritin, ug/L	7 (5.2-9.1)	36 (24-61)	<0.001
TIBC, mg/dL	377 (333-427)	310 (297-349)	<0.001
Transferrin saturation, %	5.25 (2.82-7.32)	30 (20.4-39.1)	<0.001
Hemoglobin, g/dL	10.9 (9.9-11.3)	12.8 (12.25-13.4)	<0.001
Leukocyte, 10^3/uL	6.86 (5.84-7.8)	6.71 (5.7-7.48)	0.266
Platelet, 10^3/uL	273 (240-299)	258 (233-286)	0.153
CRP, mg/L	0.86 (0.6-1.86)	1.54 (0.6-2.62)	0.129
Blood glucose, mg/dL	90 (88-94)	89 (86-97)	0.567
Creatinine, mg/dL	0.65 (0.57-0.7)	0.64 (0.61-0.7)	0.727
eGFR, ml/min/1.73m^2	120 (109-125)	111 (103-119)	0.012
ALT, U/L	13 (9-17)	11 (9-21)	0.379
LDL, mg/dL	101 (83-120)	106 (85-123)	0.322
Uric acid, mg/dL	3.6 (3.1-4.1)	3.9 (3.4-4.6)	0.184
Vitamin B12, µg/L	315 (275-438)	289 (247-394)	0.434
Folic acid, µg/L	7.63 (6.47-9.95)	7.2 (6.06- 8.88)	0.632
TSH, mIU/L	1.62 (1.2-2.19)	1.7 (1.15-2.35)	0.868

TIBC: total iron binding capacity, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, ALT: alanin aminotransferase, LDL: low density lipoprotein, TSH: thyroid stimulating hormone.

Table 2. Demografic and clinical features and laboratory findings of groups

	Group 1 n=32	Group 2 n=45	p
Waist circumference (cm)	81 (75-91)	75 (69-81)	0.001
Body mass index (kg/m²)	24.4 (20.3-27.8)	25.9 (20.1-30. 1)	0.795
HDL (mg/dL)	64 (54-72)	67 (54-74)	0.445
Tryglyceride (mg/dL)	85 (95-104)	72 (52-90)	0.068
DAI	1.4 (1.19-1.8)	1.01 (0.74- 1.53)	0.07

BMI: body mass index; HDL: high density lipoprotein; DAI: dysfunctional adipose index.

Smirnov test determined the distributions of variables. The variables that were not normally distributed were expressed as the median. Categorical parameters were indicated as percentages. The Kruskal-Wallis test was used to assess significance among study groups. Additionally, the correlations between serum iron, ferritin, and hemoglobin levels and DAI were determined with the Spearman correlation test. The statistical significance cut-off value was deemed to be $p<0.05$.

RESULTS

As shown in Table 1, no differences were observed between the groups in terms of demographic data and clinical features. There were statistically significant differences between the values of hemoglobin, ferritin, total iron-binding capacity, and serum iron in the biochemical data.

Table 2 unveils statistical disparities in DAI and its components across the delineated groups. The difference between the groups in terms of waist circumference reached the $p<0.001$ significance level. Other DAI components, including BMI, HDL, and triglycerides, showed no differences.

Concurrently, correlation analysis, as outlined in Table 3, unearthed a robust negative correlation between serum ferritin levels, transferrin saturation, and DAI ($r=-0.416$, $p<0.001$; $r=0.359$, $p=0.001$, respectively). There was also a significant negative correlation between serum iron level and DAI ($r=-0.321$, $p=0.004$).

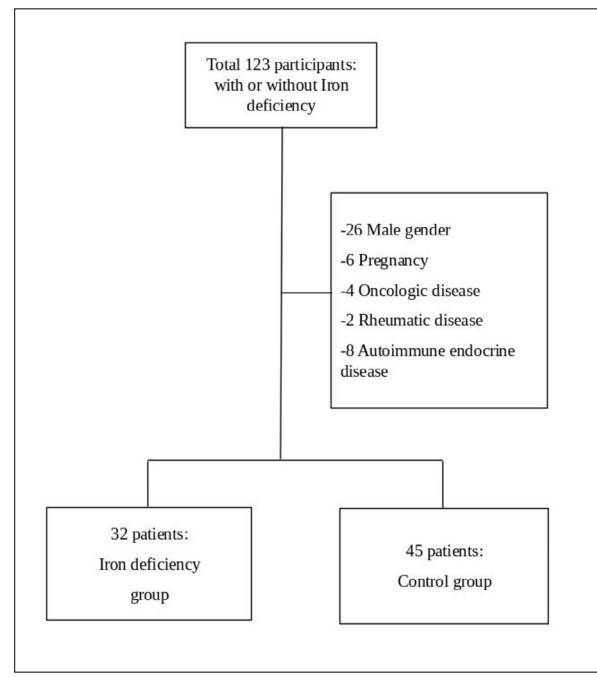

Figure 1. The determination of all participants.

DISCUSSION

In the present retrospective study, we assessed the relationships between serum iron parameters and DAI. We found statistically significant differences between the values of hemoglobin and iron parameters such as ferritin and TIBC. While there was a statistically significant difference in waist circumference between the groups, the other DAI components did not differ. We also detected negative correlations among serum iron, ferritin, transferrin saturation levels, and DAI.

Several studies have shown close relationships between

Table 3. Correlation analysis between DAI and anemia parameters.

	Serum iron	Serum ferritin	TS	Hb
DAI				
r	-0.321	-0.416	-0.359	-0.197
p	0.004	<0.001	0.001	0.86

DAI: Dysfunctional adipose index; TS: Transferrin saturation; Hb: Hemoglobin.

iron status, body weight status, and adipose tissue. Chambers et al.[16] found a negative correlation between serum iron and BMI, WC, and fat mass. In another study conducted by Laudisio et al.,[17] a significant but weak inverse correlation was found between serum iron levels and BMI and WC. Our study revealed that while there was no significant difference in BMI between the groups with and without ID, similar to the mentioned studies, WC and DAI were found to be significantly higher in the ID group. Considering the critical role iron ion plays in adipose tissue homeostasis, these results may also indicate that the use of BMI alone is not sufficient to evaluate the morpho-functional properties of adipose tissue and thus the risk of metabolic diseases.

In the present study, as indicated in the studies by Stoffel et al.[18] and Olefsky et al.,[19] transferrin saturation, ferritin, and serum iron levels were found to be lower in women with increased waist circumference. In the mentioned studies, it was stated that one of the possible pathways of this effect may be systemic low-level inflammation caused by central obesity.

It is known that the iron ion plays a role in many metabolic biological processes and is in a complex interaction with lipid, glucose metabolism, insulin resistance, and obesity.[14] In the present study, no difference was observed between the two groups in terms of lipid parameters, including HDL, LDL, and triglyceride levels, as in a study conducted by Wolide et al.[20] Nonetheless, HDL levels in the ID group were considerably higher than those in the normal group in the research published by Sawada et al.[21] and Ellidag et al.[22] Ferritin levels were positively correlated with TG and LDL levels, according to Ellidag et al.[22] study.

Due to its retrospective design, the inability to evaluate HOMA-IR-like insulin resistance parameters, body composition by bioimpedance analysis, and the relatively small number of patients can be considered among the limitations of the study.

Conclusion

We think that this study contributes valuable information to the current understanding of the interaction between serum iron parameters and DAI, a metabolic risk marker. The results of our study emphasize the close relationship between iron deficiency and increased waist circumference, which are very common and constitute global health problems, and underline the importance of the interaction of these two entities in clinical evaluation. However, the contradictory nature of the literature highlights the complexity of this relationship, highlighting the need for larger, well-designed prospective studies to provide a more detailed understanding of the role of serum iron parameters, especially among individuals with high waist circumference and DAI.

Ethical Approval

This study was conducted in accordance with the ethical principles outlined in Declaration of Helsinki and approved by Gaziosmanpaşa Education and Research Hospital Ethics Committee with the date 25.10.2023 and number 100.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: O.E:, A.S., S.Y.; Design: O.E:, A.S..; Supervision: OE; Fundings: O.E.; Materials: O.E.; Data: O.E., S.Y., A.S.; Analysis: O.E., S.Y.; Literature search: O.E., S.Y., A.S.; Writing: O.E.; Critical revision: O.E., A.S.

Conflict of Interest

None declared.

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Kadınlarda Demir Düzeyi ile Disfonksiyonel Adipoz İndeks Arasındaki İlişki

Amaç: Serum demir düzeyleri ile yağ dokusu ve metabolik parametreler arasındaki karmaşık bağlantı birçok klinik çalışmanın konusudur. Bu doğrultuda çalışmamızda serum demir durumu ile disfonksiyonel adipoz indeks (DAİ) arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Tek merkezli retrospektif çalışmamıza hasta grubu olarak demir eksikliği olan 32 kadın, kontrol grubu olarak ise demir eksikliği olmayan 45 kadın dahil edildi. Bireylerin demografik verileri, laboratuvar testleri, boy, kilo ve bel çevresi (BÇ) ölçümleri hastanemiz kayıtlarından elde edildi. DAİ şu formülle hesaplandı: [BÇ/[24.02+[2.37* vücut kitle indeksi]]*[trigliserid (mmol/L)/1,32]*[1.43/yüksek yoğunluklu lipoprotein (mmol/L)].

Bulgular: Hemoglobin değerleri ve ferritin, total demir bağlama kapasitesi, transferrin satürasyonu gibi demir parametreleri açısından iki grup arasında istatistiksel olarak anlamlı fark bulduk ($p<0.001$). Gruplar arasında bel çevresi açısından istatistiksel olarak anlamlı fark bulunurken ($p<0.001$), diğer DAİ bileşenleri açısından farklılık yoktu. Ayrıca DAİ ile serum demiri, ferritin düzeyleri ve transferrin satürasyonu arasında da güçlü bir negatif korelasyon tespit ettik (sırasıyla, $r=-0.321$, $p=0.004$; $r=-0.416$, $p<0.001$; $r=0.359$, $p=0.001$).

Sonuç: Bu çalışma, serum demir parametreleri ile bir metabolik risk belirteci olarak DAI arasındaki etkileşime ilişkin mevcut literatüre katkı sağlamayı amaçlamaktadır. Çalışmamızın sonuçları, toplumda yaygın olarak görülen ve küresel sağlık sorunu oluşturan demir eksikliği ile özellikle bel çevresi artışı arasındaki yakın ilişkiye dikkati çekip klinik değerlendirmede bu iki antitenin etkileşimlerinin önemini vurgulamaktadır. Bununla birlikte, mevcut literatürün çelişkili sonuçları bu ilişkinin karmaşıklığını vurgulamakta ve özellikle yüksek bel çevresi ve DAI seviyelerine sahip bireyler arasında serum demir parametrelerinin rolünün daha ayrıntılı bir şekilde anlaşılmasını sağlamak için daha büyük, iyi tasarlanmış prospektif çalışmalara ihtiyaç duyulduğuna işaret etmektedir.

Anahtar Sözcükler: Anemi; bel çevresi; demir; demir eksikliği; disfonksiyonel adipoz indeks; ferritin.