RESEARCH ARTICLE

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The Impact of Intestinal Motility on Serum Iron Levels in Obese Individuals

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Objective: Recent studies have shown a high prevalence of iron deficiency in obese adults. One of the possible reasons for this may be the slowing of intestinal motility, which may adversely affect iron absorption and transfer in obese individuals. To investigate this, serum iron levels were compared between obese and obese+constipated individuals.

Materials and Methods: The study included 22 obese and 22 obese+constipated individuals aged 20-64 years with a body mass index >30 without any chronic disease. Demographic information of the individuals was determined by face-to-face questionnaire method. Serum iron levels in fasting blood samples taken in the morning from obese and obese+constipated individuals were determined with a commercial ELISA kit.

Results: Serum Fe level was found to be significantly lower in obese+constipated individuals compared to obese individuals (p<0.01).

Conclusions: Serum Fe levels are influenced by intestinal motility, possibly because slowing of intestinal motility results in increased inflammation and oxidation, which have adverse effects on Fe absorption and transport. Nutritional and endocrine disorders, which are among the causes of gastrointestinal constipation, may also have an active role on Fe absorption. Consideration of gastrointestinal system motility in iron deficiency treatments may be useful for more accurate and effective treatment methods.

Key Words: *Iron deficiency, intestinal motility, obesity*

Obez Bireylerde Bağırsak Motilitesinin Serum Demir Seviyesi Üzerine Etkisi

Amaç: Son zamanlarda yapılan araştırmalarda, obez yetişkinlerde demir eksikliği prevelansının yüksek olduğu görülmektedir. Bu durumda olası nedenler arasında obez bireylerde demir emilimini ve transferini olumsuz etkileyebilecek bağırsak hareketliliğinin yavaşlaması olabilir. Bunu araştırmak için obez ve obez+kabız bireyler arasında serum demir seviyeleri karşılaştırıldı.

Gereç ve Yöntem: Çalışmaya 20-64 yaşlarında kronik hastalığı olmayan vücut kütle indeksi>30 olan 22 obez ve 22 obez+kabız bireyler dahil edildi. Bireylerin demografik bilgileri yüz yüze uygulanan anket yöntemi ile belirlenmiştir. Obez ve obez+kabız bireylerden sabah alınan açlık kan örneklerinde serum demir düzeyleri ticari ELİSA kit ile belirlenmiştir.

Bulgular: Serum Fe seviyesi obez+kabız bireylerde obez bireylere göre anlamlı derecede düşük (p<0.01) bulunmuştur.

Sonuç: Serum Fe seviyesi intestinal sistem motilitesinden etkilenmektedir. Muhtemelen motilitenin yavaşlaması artan inflamasyon ve oksidasyon sonucunda Fe emilim ve taşınması üzerinde olumsuz etkilere neden olmaktadır. Beslenme ve gastrointestinal kabızlığın nedenleri arasında olan endokrin bozukluklarının da aynı zamanda Fe emilimi üzerinde etkin rolleri olabillir. Demir eksikliği tedavilerinde gastrointestinal sistem motilitesinin de göz önünde bulundurulması daha doğru ve etkin tedavi yöntemleri için faydalı olabilir.

Anahtar Kelimeler: *Demir eksikliği, intestinal motilite, obezite*

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Introduction

Iron (Fe) is an essential trace element involved in various enzymatic processes and physiological reactions that carry out important functions in the human organism and in all living systems. Its homeostasis is well controlled (1). Anemia (iron deficiency, ID) and siderosis (iron overload, IO) are associated with common diseases that have different clinical symptoms, including obesity and even neurodegenerative disorders (2). ID is recognised as the most common eating disorder worldwide (3). The disorder has a multifactorial nature, and the regulation of hepcidin (hep) plays a key role in inflammatory anemia (4). This results in the impairment of ferroportin in lysosomes, slowed transport of iron into serum, accumulation in macrophages, and reduced iron transfer from enterocytes. The potential mechanism of hypoferremia in obesity is considered to be the inflammatory component of obesity, which leads to excessive production of Hep and lipocalin 2. Overproduction of these proteins is associated with the retention of iron in the cells of the reticuloendothelial system. As a result, iron accumulates in adipose tissue, causing oxidative stress and endocrine dysfunction in adipose tissue, as well as inflammation of the endoplasmic reticulum. Iron-mediated mechanisms of toxicity may contribute to the exacerbation of obesity. Therefore, it is possible to explain the reciprocal effect of impaired iron status and the pathogenesis of obesity (5). Low-grade chronic inflammation is common in obesity, and recent studies have provided insights into the intracellular pathways of obesity-related inflammation. Overnutrition is the root cause of inflammation in cells and tissues involved in metabolism, such as adipocytes and hepatic macrophages, which trigger an inflammatory response.

The association between iron deficiency and obesity is still being investigated, and the pathophysiology of iron deficiency during obesity is not well defined. Recent research has investigated the relationship between obesity and the prevalence of ID in adolescents. The study found that there is not much difference between normal weight and obese individuals (6). One possible reason for this is the slowed intestinal motility in obesity, which may adversely affect iron absorption and transfer. To investigate this, serum iron levels were compared between obese and obese+constipated individuals.

Materials and Methods

Research and Publication Ethics: The study was approved by Inonu University Faculty of Medicine Malatya Clinical Research Ethics Committee (Protocol No: 2022/04, Approval Date: 26/01/2022).

The individuals included in the study were selected from patients who presented with obesity and constipation complaints to the obesity clinic of the Department of Endocrinology at Turgut Ozal Medicine Center of Inonu University. The number of patients in each group (sample size) was determined according to the power analysis based on the values specified. Accordingly, the amount of Type I error (α) was 0.05, the power of the test (1-β) was 0.8, and the effect size was 0.84 (large). Our study included 22 obese individuals and 22 obese individuals with constipation. Obese individuals aged between 24-64 years and with a BMI value ≥30 according to WHO's age and gender-specific references were included in our study. Individuals with chronic diseases such as diabetes and hypertension, those receiving psychiatric treatment, and those with infectious diseases or who use prescription drugs or alcohol were excluded from the study. Informed consent forms were signed by all participants. Blood samples were collected from participants after at least 8 hours of fasting, and the serum was separated by centrifugation and stored at -80 degrees until the day of analysis.

Iron Analysis: Iron analysis were conducted using commercial kit protocols for micromethod analysis of Serum Iron Concentration (Catalogue No: XY-W-B802 Shanghai Coon Koon Biotech Co., Ltd Shangai,China). Results was given as μ mol/dL.

Statistical Analysis: Statistical analysis of the data obtained from the study was performed using SPSS 22.0 software. In the data analysis, firstly, checks and correction procedures were applied to prevent missing and erroneous data and excessive/outlier value problems. Quantitative data were summarised with mean±standard deviation. The suitability of the data for normal distribution was evaluated by Shapiro Wilk test. When the data showed normal distribution, one-way analysis of variance was used to compare the variables between groups. Variances in intergroup comparisons Tukey's HSD test was used because the results were homogeneous. A $p<0.05$ was considered statistically significant.

Results

In this study, serum Fe level was measured. This measurement was performed using a commercial kit. Colour change given by 2,2'-bipyridine of iron converted from form with sodium sülfite reduced serum Fe^{+3} to form Fe^{+2} by measuring the absorbance at 520 nm. The results of the commercial kit were converted from international units (μ mol/dL) to the units traditionally (μg/dL) used. The results are presented in Table 1. according to our study findings indicate a statistically significant decrease in serum Fe levels in the obese+constipated (26.31±14.35) group compared to the obese individuals in the control (46.48±10. 78) group ($p<0.01$). The results were given in (μg/dL).

Tablo 1. Serum Fe value relationship between Obese and Obese+Constipated groups

	Obese	Obese+Constipated	P-Value
BKI	40.08^{a}±5.42	42.71^{a}±4.47	0.064
Fe (μg/dL)	8.32 ^{a}±1. 93	2.92 ^{b}±2. 57	0. 01

The results of mean serum Fe levels in the obese and obese+constipated groups are given as mean ± standard deviation. Differences between groups are indicated by different letters. ($p<0.05$).

Discussion

ID is a common finding in cases of metabolic alterations associated with obesity (7). Several studies have reported a primary underlying pathophysiological mechanism, which is a decreased ability for duodenal iron absorption (8). For instance, Mujica-Coopman et al. (2015) identified a significant decrease in the absorption of isotope-labeled iron in obese women of childbearing age compared to their normal-weight counterparts (9). The study found that approximately 7% of women had iron dediciency anemia, while 9% had iron deficiency. Iron status was normal in 66% of women, with no differences observed across BMI categories. Although obese women had a lower percentage of iron absorption, this did not affect their iron status. Zimmermann et al. reported a similar conclusion, stating that a higher BMI is associated with decreased iron absorption. In the study, approximately 20% of women and 42% of children were found to have an iron deficiency. Iron absorption rates were not affected by iron status (10). Recently, Benotti et al. investigated the disruption of iron metabolism in obese individuals undergoing metabolic surgery (11). The International Diabetes Federation recommends bariatric surgery as a treatment and prevention option for type 2 diabetes in obese individuals (12, 13). The American Diabetes

Association uses the term 'metabolic surgery' to refer to the bariatric approach that aims to prevent and treat Type II Diabetes in obese individuals (14). While the terminology may be misleading, the goal is to address the metabolic syndrome through surgery. This may be due to the low-grade inflammation that characterizes obesity. A meta-analysis conducted by Cheng et al. on iron status in obese populations found that obese individuals have higher concentrations of ferritin than normal-weight individuals (15). The authors of a recent meta-analysis concluded that overweight individuals have lower concentrations of serum iron and decreased transferrin saturation percentages than non-overweight individuals. The meta-analysis also found that overweight subjects have a significantly higher risk of iron deficiency than the controls (16).

The reduction of serum Fe may be partially attributed to the chronic inflammation caused by the progression of obesity through a series of pathological mechanisms. Adipose tissue in obese individuals contains excessive amounts of macrophages and pro-inflammatory cytokine producers, as compared to those with normal weight (17). Furthermore, obesity is linked to an increase in the production of adipokines in fat cells. Adipokines play a crucial role in regulating insulin resistance, inflammation, immunity, and susceptibility to viral infections (18, 19). Dysregulation of adipocytokine production is implicated in the development of obesity-related diseases, including diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia. Adipocytokines and pro-inflammatory cytokines, along with free fatty acids, contribute to the development of these diseases. Concurrently, the liver accumulates lipids, resulting in non-alcoholic fatty liver disease. This further disrupts the iron balance due to increased cytokine production and insulin resistance (20).

In obese patients, a decrease in BMI leads to lower Hepcidin levels, which improves iron absorption and metabolism. After a six-month weight-loss programme, the study observed these results. The intervention led to improved inflammatory markers and iron status, resulting in a decrease in BMI (21). Only weight loss programmes based on a well-balanced and healthy approach improved functional iron status due to increased dietary iron absorption, decreased expression of inflammatory cytokines, and diminished insulin resistance (22).

It should be noted that the treatment of iron deficiency may have an impact on obesity. Aktas et al. found that taking iron supplements to treat iron-deficiency anemia significantly reduced BMI, improved waist circumference, and decreased triglyceride levels after treatment compared to the pre-treatment period (23). However, iron deficiency anemia can worsen obesity as it is associated with greater fatigue, leading to a further decrease in physical activity (24). It is essential to identify and control ID in all individuals with overweight and obesity.

In literature evaluating iron deficiency in obese individuals, only objective evaluations are included. Endocrine disorders, increased inflammation, changes in blood lipid levels, and lifestyle factors have been identified as potential contributors to reduced blood iron levels. The present study found that constipation in obese individuals is also associated with lower serum iron levels. Impaired absorption in individuals with constipation suggests that reductions in intestinal function affect the absorption of iron. Slow intestinal motility increases the change in chemical structures in the absorbable form rather than increasing the absorption process. This would be useful to evaluate constipation together in the iron treatment processes to be applied in obese individuals. Even increasing intestinal motility may reduce the need for external supplements.

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