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Original Article

Changes in Ferritin and Hemoglobin Levels in Obese Patients before and after Bariatric Surgery: A Cohort Study

Paniz Zare[1], Zahra Sohrabi[2*], Neda Haghighat[3*], Morteza Zare[2], Najme Hejazi[2]

1. Student Research Committee, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
2. Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
3. Laparoscopy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

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**Corresponding authors:*
Zahra Sohrabi, PhD;
Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.
Tel: +98-71-37251002
Email: zahra_2043@yahoo.com
Neda Haghighat, PhD;
Laparoscopy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
Tel: +98-71-32279701
Email: neda.hag@gmail.com
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ABSTRACT

Background: Bariatric surgery has been known as an efficient treatment for morbid obesity during the last few decades. Considering the high prevalence of anemia in obese patients and the changes in the iron status of the body after bariatric surgery, the purpose of this study was to assess the pattern of changes in the ferritin and hemoglobin (Hb) levels in obese patients before and after bariatric surgery.

Methods: The current retrospective cohort study was done on 241 obese patients of both genders undergoing bariatric surgery between 2018 and 2021. Preoperatively, 3, 6, and 12 months post-bariatric surgery, data considering body mass index (BMI), mean corpuscular volume (MCV), Platelet (PLT), Hb, ferritin, and hematocrit (Hct) was extracted from the National Obesity Surgery database.

Results: Before the surgery, the Hb, ferritin, and Hct levels in female and male groups were significantly different ($p<0.001$). The mean Hb, ferritin, and Hct levels in female and male participants were significantly different over the time ($p<0.001$, $p=0.002$, $p<0.001$, respectively). The levels of Hb, Hct, PLT, ferritin, and BMI variables decreased over the time in patients after bariatric surgery, and were significantly lower in women than men.

Conclusion: Our findings revealed that anemia caused by micronutrient deficiency was relatively common in patients who underwent bariatric surgery and got worse over the time.

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Introduction

Obesity has been considered a global health problem among adults and children since the 1970s (1-3). Obesity reduces life quality and life expectancy and raises the risk of non-communicable diseases like cardiovascular diseases, special types of cancer, and diabetes. The obesity pandemic may develop a major health problem for society, in addition to the consequences at the individual level (4-7). According to World Health Organization (WHO) reports, unusual or excessive accumulation of fat that can impair health is called obesity and overweight (8). Obesity is classified by body mass index (BMI). BMI>30 kg/m^2 is considered as obesity and BMI>40 or BMI>35 with risk factors are considered as morbid obesity (9). Bariatric surgery is known as an efficient therapy for morbid obesity during the last few decades (10, 11). The mortality rate from bariatric surgery has been generally less than 1% and it has reduced the risk of obesity-associated co-morbidities (12). However, bariatric surgery itself may have short and long-term complications. Short-term complications include wound infection, anastomotic leak, and incisional hernia (10).

Long-term side effects include nutritional deficiencies like vitamin B12, iron, folate, calcium, and vitamin D. Iron deficiency and anemia could possibly have a great impact on life quality of patients, particularly in menstruating women who are a large number of candidates for bariatric surgery (13). Totally, 5.5-21.9% of bariatric surgery candidates suffer from anemia, more than what was reported in the public population (6-7%) (14, 15). Many factors like nutritional deficiencies and irregular cycles contribute to anemia, but inflammation is the most important factor involved in the different stages of iron cycles (16). In fact, inflammatory anemia is a condition in which, despite enough iron in the macrophages, hepcidin prevents iron from returning to the serum (17). On the other hand, micronutrient deficiency may occur due to food intolerance, dietary restriction, and decreased absorption capacity after bariatric surgery. Iron deficiency has been identified as the most important cause of anemia after bariatric surgery (18).

Therefore, considering the high prevalence of anemia in obese patients and the changes in the body's iron status post-bariatric surgery, as well as the necessity of determining the factors related to anemia, identification of the factors related to iron deficiency anemia and preventive strategies and effective treatment options for iron deficiency is very crucial for managing the iron status of patients after bariatric surgery. Hence, the purpose of this study was to assess the pattern of changes in ferritin and hemoglobin levels in obese patients before and after bariatric surgery, especially in both genders, and the prevalence of anemia and iron deficiency in obese patients during a 12-month follow-up before and after the bariatric surgery.

Materials and Methods

A retrospective cohort study was carried out on patients with morbid obesity that underwent bariatric surgery between January 2018 and July 2022 in the Ghadir Mother and Child Hospital in Shiraz, Iran. Morbid obesity is considered as BMI>40 Kg/m^2 or >35 Kg/m^2 with one co-morbidity (9). The protocol of the study was in accordance with the Declaration of Helsinki and was reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.SCHEANUT.REC.1400.036). The medical charts of the bariatric surgery (total of 731) patients were checked out. This consisted of all patients who had a bariatric procedure from January 2018 to September 2021 at the Ghadir Mother and Child Hospital. Of these, 241 of 731 patients had available clinical and biochemical data measures in the National Obesity Surgery database. Therefore, most of the patients did not have adequate data measurements registered in this national electronic medical record, but may have been followed elsewhere.

Adult patients aged 18-65 years, with morbid obesity that underwent Roux-en-Y Gastric Bypass (RYGB) during the study period, and had complete follow-up for at least 12 months, were included. For the patients, after explaining the study process, obtained informed consent was received before the operation for selecting the type of surgery and using their data. Patients with previous bariatric surgery, smoking and drinking alcohol, kidney disorders, inflammatory and infectious diseases, gastrointestinal disorders, suffering from previous severe anemia or a history of severe bleeding or surgery or any cause of blood loss in the last year, use of non-steroidal anti-inflammatory drugs, estrogen, progesterone, immune-suppressive drugs, diuretics, corticosteroids, antibiotics, breastfeeding, menopause, and unwillingness to participate to continue the study were not included.

Anemia was defined as Hb<12 g/dL in women and <13 g/dL in men according to WHO (19). Iron deficiency was defined as ferritin <20 ng/mL. Body mass index (BMI) was classified into 4 groups: the First group as 30≤BMI≤34.9, the second group with 35≤BMI≤39.9, the third group as 40≤BMI≤44.9, and the fourth group with BMI≥45. A multidisciplinary bariatric team including a psychiatrist, internist, nutritionist, sport medicine specialist, and bariatric surgeon evaluated the patients. The patients were shown a schematic illustration of the procedure with emphasis on its potential advantages and side-effects. A detailed history was taken from all patients about food habits, co-morbidities, and previous treatments for morbid obesity. All study participants underwent an assessment including physical examination, biochemical measurements of complete blood count (CBC), fasting blood glucose (FBG), lipid profile, liver function test, thyroid tests, serum albumin (Alb) and total protein, ferritin, zinc, and vitamin A and D. We also recorded patients' weight and height and calculate the BMI. The esophagogastroduodenoscopy (EGD) was done for patients and for those infected with *Helicobacter pylori* (HP), eradication of infection was done and 6 weeks later, the patients were evaluated again by stool examination (antigen checking). In addition, abdominal ultrasonography was performed to check the liver for liver diseases, gallstones, and other pathological abnormalities.

The study variables were mean corpuscular volume (MCV), Platelet (PLT), hemoglobin (Hb), ferritin, and hematocrit (Hct) which had been measured pre-operatively and at 3, 6, and 12 months post-bariatric surgery. These data were extracted from the database. At the hospital, a cell counter was used to measure CBC. Ferritin was measured based on the sandwich enzyme immunoassay using an ELISA device. The measurement of iron was based on the ferrene method. The secondary outcome was weight loss in the first year after bariatric surgery. Weight loss was assessed by % excess BMI loss (EBMIL). %EBMIL was calculated as [(preoperative BMI-BMI on follow-up)/(preoperative BMI−25)]×100.

SPSS software (Version 16, Chicago, IL, USA) was used for statistical analysis of the data. The normality of the data was evaluated using the Kolmogorov Smirnov test. Continuous variables with normal distribution were compared between groups by the independent t-test and the variables with abnormal distribution were compared by the nonparametric Mann-Whitney U test. Data were reported as mean and standard deviation (SD). Repeated measure test was used to compare quantitative variables through the time. Repeated measure ANOVA was used for assessing the interaction between variables and time. *P* values less than 0.05 were considered significant.

Results

The baseline characteristics and biochemical variables of 241 patients included in the current study were displayed in Table 1. The mean age and BMI of the study participants were 38.43±10.626 years and 43.14±5.441 kg/m^2, respectively at baseline. Forty-seven patients (19.4%) were female and 195 were male (80.6%). The mean weight, waist circumference, hip circumference, and BMI were higher than normal (Table 1). Thirteen percent of patients were shown to suffer from iron deficiency before the surgery. During the 12-month follow-up period, the prevalence of iron deficiency demonstrated a preliminary increase and then a decrease over time; while the prevalence of patients with iron deficiency was 16.18% during the 3rd month after the surgery, 17.42% during the 6th month post-operation, and 14.52% during the 12th month post-surgery. Totally, 9.12% of patients reported anemia before the surgery. During the 12-month follow-up period, the prevalence of anemia revealed a preliminary increase that further decreased over time; while the prevalence of patients with anemia was 9.54% during the 3rd and the 6th months after the surgery, and 7.88% during the 12th month post-operation (Figure 1).

Before the surgery, the mean Hb, ferritin, and PLT levels in both genders were significantly different (p<0.001, p<0.001, and p=0.002, respectively). The mean Hb, ferritin, and PLT levels in females and males were significantly different during the time (p<0.001, p=0.002, p<0.001, respectively). During 12 months of follow-up, the interaction between time and gender was not significant (p=0.293, p=0.051, p=0.185, respectively); in other words, the pattern of Hb, ferritin, and PLT changes in male and female groups were the same over time. Also, 12 months post-surgery, the Hb, ferritin, and PLT levels in both genders were significantly different (p<0.001, p<0.001, p=0.021 respectively, Figure 2).

Before the surgery, the mean Hct level in both genders was significantly different (p<0.001). The mean Hct level in female and male participants was significantly different during the time (p<0.001).

Table 1: Baseline characteristics investigated for the study participants.

Variable	Mean	Standard deviation	Median	Interquartile range
Age (years)	38.43	10.62	38.00	16
Height (cm)	162.81	8.96	162	11
Weight (kg)	115.20	18.57	110.73	21
Waist (Cm)	127.54	12.65	126	16
Hip (Cm)	132.87	11.44	132	14
BMI (kg/m^2)	43.14	5.44	42.06	7
Hb (g/dL)	13.51	1.66	13.50	2
Hct (%)	41	4.18	40.70	5
MCV (fL)	81.91	8.90	84	8
PLT (10*3/µL)	282.83	73.84	280	99
Ferritin (ng/mL)	71.06	76.21	42.70	66

BMI: Body Mass Index; Hb: Hemoglobin; Hct: Hematocrit, MCV: Mean Corpuscular Volume; PLT: Platelets

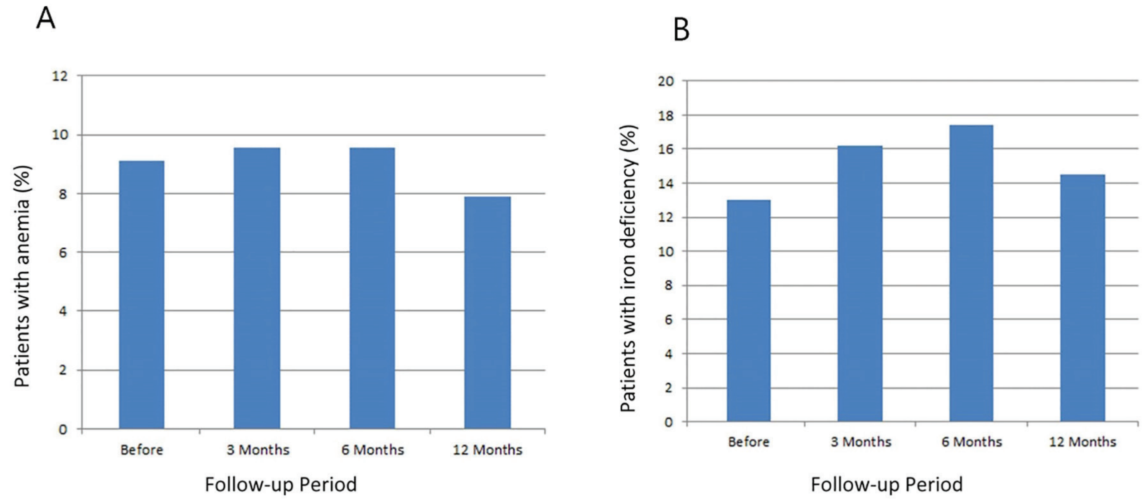

Figure 1: A: Prevalence of anemia before, 3, 6 and 12 months after bariatric surgery. Number of patients evaluated at each time including before: 241; 3 months: 213; 6 months: 201; and 12 months: 132. **B:** Prevalence of iron deficiency before, 3, 6 and 12 months after bariatric surgery. Number of patients evaluated of each time included before: 211; 3 months: 208; 6 months: 196; and12 months: 132.

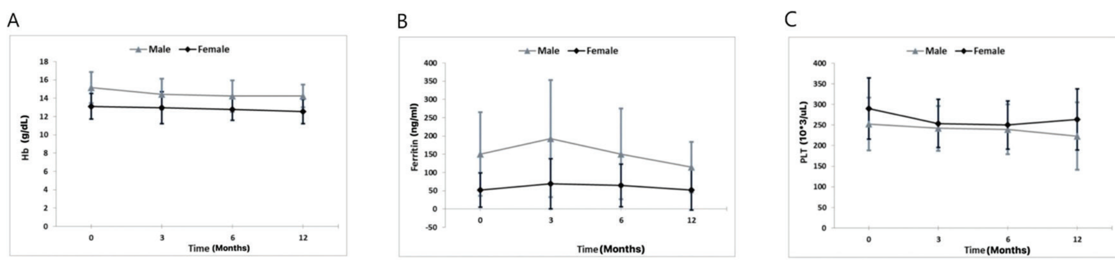

Figure 2: A: Changes in hemoglobin (Hb) level in male and female participants before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was considered as pre-operative measurement). **B:** Alterations in ferritin level in male and female patients before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was defined as pre-operative measurement). **C:** Modifications in Platelet (PLT) level in male and female groups before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was regarded as pre-operative measurement).

Moreover, during 12 months, the interaction between time and gender was significant ($p<0.001$); in other words, the pattern of Hct changes in male and female patients was not the same over time. Also, 12 month post-surgery, Hct level in both genders was significantly different ($p<0.001$, Figure 3A). Before the surgery, the mean MCV level in female and male groups was not significantly different ($p=0.09$). Also, the mean MCV level in females and males was not significantly different during the time ($p=0.204$). During 12 months of follow-up, the interaction between time and gender was not significant ($p=0.674$); in other words, the pattern of MCV changes in male and female participants was the same over time. Also, 12 months post-surgery, MCV level in both genders was not significantly different ($p=0.6$, Figure 3B).

Before the surgery, the mean BMI level in female and male groups was not significantly different ($p=0.073$). However, the mean BMI level in females and males was significantly different during the time ($p<0.001$). During 12 months of follow-up,

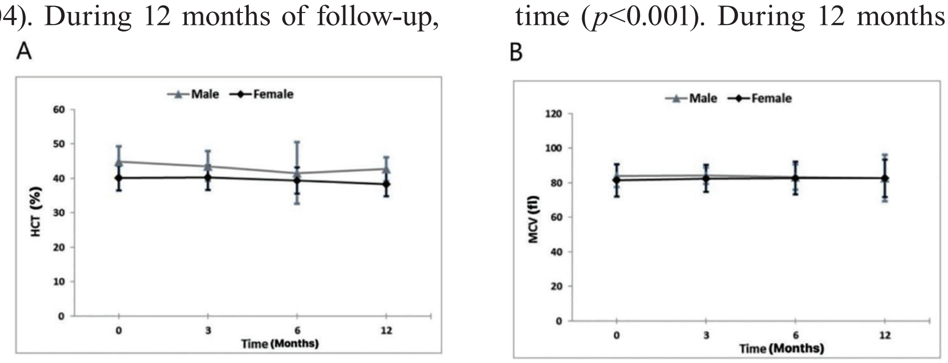

Figure 3: A: Changes in hematocrit (HCT) level in male and female participants before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was considered as pre-operative measurement). **B:** Modifications in mean corpuscular volume (MCV) level in male and female patients before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was regarded as pre-operative measurement).

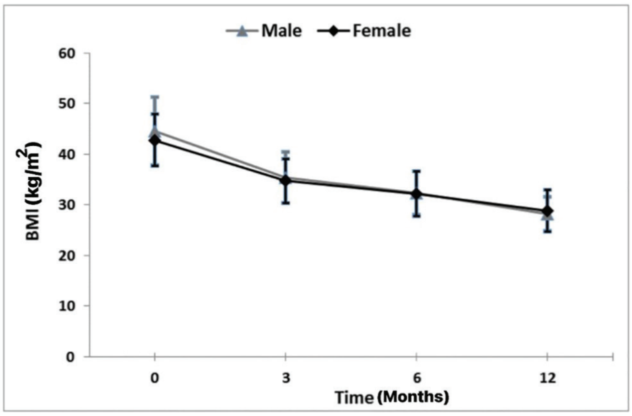

Figure 4: Changes in Body mass index (BMI) level in male and female participants before and after the bariatric surgery (3, 6, 12 months post-operation) (month=0 was considered as pre-operative measurement).

the interaction between time and gender was not significant (p=0.148); in other words, the pattern of BMI changes in male and female patients was the same over time. Also, 12 months post-surgery, BMI level in both genders was not significantly different (p=0.493, Figure 4).

Discussion

Morbid obese patients who underwent bariatric surgery are at high risk of nutrient deficiencies, i.e. vitamins and minerals, after the surgery. Due to the increase in the number of annual bariatric surgeries, it led to an increase in concern about their complications in the medical and public community (20). According to the current study, the levels of Hb, Hct, PLT, ferritin, and BMI decreased over time in patients after bariatric surgery, and anemia caused by micronutrient deficiency was relatively common among patients who underwent bariatric surgery. Many studies are in line with the results of the present study. Dorte Worm *et al.* carried out a study to investigate the changes in hematologic parameters after bariatric surgery and they found that 25.8% of women and almost 22.1% of men were anemic 24 months post-bariatric surgery. The mean Hb and ferritin levels decreased significantly before the surgery and 24 months post-bariatric surgery among both men and women (21). Also in a study by Ting-Chia Weng *et al.*, the risk of anemia increased from 12.2% at baseline to 25.9%, and 24 months after the bariatric surgery based on the decreases in Hb, ferritin, and Hct levels (22). Also, Ferreira *et al.* reported that the effect of time was significant for Hb, ferritin, and Hct and the levels of these indicators decreased before and after the bariatric surgery (23).

However, some studies showed different results. Salgado *et al.* (16) conducted a study to evaluate the risk of anemia and also iron deficiency before and after the bariatric surgery. They reported that no changes were visible in the number of anemic patients during 4 years of study. The reason for this difference could be possibly due to the long follow-up period of their study compared with the current study. In obese patients undergoing bariatric surgery for the sake of weight loss, primary iron deficiency occurred due to the reduced consumption of food sources of iron, reduced gastric acid secretion, and reduced contact of food with the iron-absorbing area in the digestive system. Also, Hb level decreased after surgery due to the blood loss (24) .

In the current study, a significant difference was observed between different genders considering ferritin and Hb indices before and 3, 6, and 12 months post-surgery. It means that lower levels of Hb and ferritin were seen in women compared with men before and 3, 6, and 12 months post-surgery, and these indicators were different between two genders. Many studies agreed with the our findings (25, 26), as they reported iron deficiency as well as low ferritin level after bariatric surgery, to be more common in women than in men. Flancbaum *et al.* reported that low ferritin levels were more common in women, but contrary to the present study, low Hb levels were more common in men than women, and anemia was more common in men (20).

Women of child-bearing age who experienced menstruation had high risk of anemia and also iron deficiency anemia after the bariatric surgery and were also more exposed to post-operative complications such as hospitalization and blood transfusion. Lower pre-operative iron stores in women may partly explain why women were more likely than men to be deficient in iron. Resumption of menstruation after surgery may also contribute to the increased iron deficiency among women (13). In our study, a significant difference was observed between male and female groups in terms of Hct level, at all times before, and 3, 6, and 12 months post-surgery. It means that Hct level was significantly lower in women than in men before and 3, 6, and 12 months after the surgery, and this indicator was different between the two genders. Ramsey *et al.* found that blacks and women had a significantly lower Hct after the bariatric surgery (27). But, Bamehriz *et al.* performed a study to investigate the association between pre and post-operative hematological changes and they reported that the mean Hct level was significantly different in males before and after the surgery (28). The reason for this difference could be possibly due to the larger sample size of their study or the different population compared to the present study.

Moreover, in our study, a significant difference was noticed between male and female groups in terms of PLT level before, and 3, 6, and 12 months post-surgery. It means that PLT level was significantly lower in women than in men before and 3, 6, and 12 months after the surgery, and this indicator was different between the two genders. Bamehriz *et al.* reported a significant difference between the mean of PLT level for females (28). However, Marta *et al.* found a reduction in PLT 6 months after the bariatric surgery in both genders; but the changes were non-significant (29). The reason for this difference could be possibly due to the long follow-up period and larger sample size of their study compared to the present study. Changes in the PLT level could possibly indicate tissue damages caused by the surgery, which activated the exogenous coagulation system and caused an increase in exogenous coagulation factors (30).

Further in this study before the surgery, the mean BMI level in both genders was not significantly different. However, the mean BMI level in females and males was significantly different during the time. The pattern of BMI changes in male and female groups was the same over the time. Also, 12 months after surgery, no significant differences were demonstrated in BMI level between females and males. Marta *et al.* found that the average BMI and waist circumference decreased significantly after the surgery in the female group (29). However, Bamehriz *et al.* reported that there was significant differences in BMI between the pre and post-operative measurements in males (28). The reason for this difference could be possibly due to the larger sample size of their study compared to the present study. Some limitations can also be mentioned for our study. First of all, in this cohort study, no clinical outcome was observed and no causal relationship was defined. Hence, more longitudinal studies can warrant better determination of the exact relationships. However, the complete assessment of the anemia markers in various times can be considered as strength of our study.

Conclusion

To sum up, the levels of Hb, Hct, PLT, ferritin, and BMI variables decreased over time in patients after the bariatric surgery and were significantly lower in female patients compared to the males. Anemia caused by micronutrient deficiency was relatively common in patients who underwent bariatric surgery and got worse during the time. However, further studies seem essential to better elucidate the pattern of changes for hematologic markers pre and post-surgeries among bariatric surgery candidates and to better generalize the results to other populations too.

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Authors' Contribution

PZ: Study idea, Research design, Data collection, and writing and drafting the manuscript. ZS: Research idea, study design, data interpretation, and critical revision of the manuscript. NH: Research idea, study design, data interpretation, and critical revision of the manuscript. NH: Research idea, study design, data interpretation, and critical revision of the manuscript. MZ: Research idea, study design, data analysis and interpretation, and critical revision of the manuscript.

Conflict of Interest

None declared.

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