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Relationship between Obesity and Iron Deficiency

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ABSTRACT

Background: obesity and iron deficiency anemia are major health problems that are increasing in Egypt especially in females.

Aim of work: this study aimed to evaluate the iron status in obese Egyptian females in comparison to normal weight females. **Patients and Methods:** forty four obese adult female patients and 44 normal weight healthy females as control group were included in this study. They were all tested for iron profile and CRP using semi quantitative rapid latex agglutination test. **Results:** the patient group in this study showed a significant lower serum Fe and TSI than the control group, while ferritin was higher in patients than the control group. The comparison between the three groups of obesity showed that the grade III patients had the lowest median value in serum iron and the highest median value in TIBC and ferritin, however no statistical significant differences were detected between the three groups of patients (P>0.05). Our results showed that 70.4%) of patients had positive CRP with positive correlation between CRP and BMI.

Conclusion and Recommendations: obesity is a low inflammatory disease which affects iron profile and increases CRP. Further, study on larger number of cases is recommended to analyze the exact mechanism of iron deficiency anemia in obese female patients.

Keywords: iron deficiency, anemia and obesity.

INTRODUCTION

Iron deficiency remains the most common nutritional deficiency and cause of anemia worldwide. Populations in the developing countries, premenopausal females, pregnant women, children, vegetarians and frequent blood donors are largely affected by iron deficiency due to low dietary intake, inadequate bioavailable iron, increased iron demand required for growth and development, iron losses and changes in blood volume [(1)]. WHO recognized obesity as disease, which is prevalent in both developing and developed countries. Overweight and obesity are now so common and thereby replacing the more traditional public health concerns (under nutrition and infectious diseases) as some of most significant contributors to ill health [(2)].

Obese individuals who develop ID have an increased health burden. Initially presenting with iron depletion, ID can progress to iron-deficient erythropoiesis, eventually leading to iron deficiency anemia (IDA) [(3)]. The mechanism explaining the relationship between iron status and obesity remains unclear; this may be due to lower iron intakes and/or increased iron requirements in overweight individuals. In addition, the chronic inflammation and increased leptin production characteristic of obesity increase hepcidin secretion from the liver, which, along with hepcidin produced by adipose tissue, could reduce dietary iron absorption [(1)].This study aimed to evaluate the iron status in obese Egyptian females in comparison with normal weight females.

PATIENTS and RESULTS

This study was conducted on 44 obese adult female patients attending the outpatient clinics in the National Nutrition Institute (NNI). Diagnosis of obesity was based on anthropometric measurements (weight, height and accordingly the BMI). Participants were classified as **grade I** obesity (if BMI =30.0 kg/m^2 to 34.9 kg/m^2), **grade II** obesity (if BMI =35.0 kg/m^2 to 39.9 kg/m^2) and grade III obesity (if BMI $\geq$ 40.0 kg/m^2) [(4)]. Patients were excluded if they were on iron therapy or consuming dietary supplements or vitamins containing iron, received non-steroidal anti-inflammatory drugs 48h prior to blood sampling, had a history of blood donation or transfusion, and had chronic or hematologic diseases or during the menstrual and post-natal period.

All patients were subjected to:

1- Weight measurement using a digital weighting scale with light clothing on and without shoes.
2- Height measurement via standing on a fixed stadiometer
3- BMI is calculated by taking a person's weight in kilograms divided by square of person's height in meter (kg/m²).The normal range is 18.5-24.9,while overweight is 25-29.9 and obese is 30 and above [(4)]. Complete blood count (CBC) using automated blood counter, (Diagon D-CELL-60) with

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examination of leishman-stained peripheral blood smears.

4- Measurement of C-reactive protein (CRP) using semi quantitative rapid latex agglutination test kit (Omega Diagnostics, Scotland, United Kingdom).
5- Measurement of serum iron and unsaturated iron binding capacity (UIBC) using auto-analyzer (BT 1500), (Biotecnica Instruments S.P.A,ViaLicenza 18,00156 Rome (Italy).
6- Measurement of serum ferritin using kit, Enzyme-linked Immunosorbent Assay (ELISA),(ChemuxBioScience,USA).

Sample collection and storage:

For each case, (6ml) of venous blood were withdrawn by sterile venipuncture and divided as 3ml in EDTA tube for CBC analysis and 3ml in serum separator tube. The serum was divided for measuring serum iron, UIBC, ferritin and CRP.

The serum was stored in Eppendorf at (-20) until analysis.Then thawed at room temperature at time of analysis.

Iron profile measurement:

Serum iron and UIBC was measured by using diagnostic reagent for quantitative *in vitro* determination of iron and UIBC in human serum on photometric systems.The expected normal serum iron value 50-170 µg/dl. TIBC was calculated from this Formula:

TIBC (µg/dl) = UIBC (µg/dl) + Iron (µg/dl).

The expected normal value for TIBC: 274-497 µg/dl.

Serum ferritin was measured spectrophotometrically at an absorbance of 450 nm.The expected normal value was 13-150 ng/ml.

C-Reactive protein:

Was done by using rapid latex agglutination test for the qualitative screening and semi-quantitative determination of serum CRP.The expected normal CRP value: <6.

The study was approved by the Ethics Board of Ain Shams University.

Statistical Methods

The data were coded and entered using the statistical package SPSS version 15. The data were summarized using descriptive statistics: mean, standard deviation and median values for quantitative variables and number and percentage for qualitative values. Statistical differences between the groups were tested using Chi Square test for qualitative variables, independent sample t test and ANOVA (analysis of variance) with post Hoc Bonferroni test for quantitative normally distributed variables, while nonparametric Mann Whitney test and Kruskal-Wallis test were used for quantitative variables which aren't normally distributed. Correlations were done to test for linear relations between variables. P value less than or equal to 0.05 were considered statistically significant, while P value less than or equal to 0.01 were considered highly significant.

RESULTS

This was a case control study that was conducted on 88 adult female; 44 adult obese female patients their age ranged from 18-53 years with mean age of (31.55±9.83) years and BMI mean (38.81± 4.79) kg/m² and 44 normal weight healthy controls their age ranged from 18-50 years with mean age of (25.41±7.40) years and BMI mean (21.58 ± 2.19) kg/m². CRP was measured in all patients. The percent of CRP positive and negative in patients were 70.45%and 29.54% respectively. According to the BMI, patients were classified **to grade I, grade II** and **grade III** obesity with percent 20.4%, 38.6% and 40.9% respectively.

Comparative studies:

On comparing the anthropometric measurement between patients groups and the control group, highly statistical significant differences were revealed between both groups as regards weight and BMI (P<0.001) (**Table 1**).

The comparative studies between patients group and the control group regarding CBC parameters showed that Hb, MCV and MCH were significantly lower in patients group than the control group (P<0.001), but RDW was significantly higher in patient group than the control group (P<0.001) (**Figure 1).** Also WBCs values were significantly higher in patients group than the control group (P=0.022).The platelets count was significantly higher in patients group than the control group (P=0.012) (Table 1). As regards iron profile results, the patients group showed a significant lower Fe and TSI than control group (P<0.001).Ferritin was higher in patients group than the control group, but it was not statistically significant(P=0.446).TIBC revealed no statistical significant differences between patient and control groups (P=0.885) (Table 2) (**Figure2).** The comparison between the three groups of obesity revealed no statistical significant differences between the groups as regards all CBC parameters (P>0.05). Regarding iron profile the comparison between the three groups of obesity showed that the **grade III** patients had the lowest median value in serum iron than **grade I** and **II**, they also showed the highest median value in TIBC and ferritin than **grade II**

and I, however these results revealed no statistical significant differences between the three groups of patients (P>0.05). Also the comparison showed that the median of CRP **in grade III** patients was higher than **grade II** and **I** with no statistical significant difference (P=0.111).

Table 1: comparison between the patients group and the control group regarding anthropometric measurements and CBC parameters.

Parameters		Patient group n = 44	Control group n = 44	Test of sig.(t)	P value
Weight (kg)	Mean ± SD	94.30 ± 12.04	53.09 ± 7.19	18.56	0.001
	Range	66.0 – 120.0	31.50 – 66.50		
Height (cm)	Mean ± SD	156.59 ± 5.97	155.32 ± 22.13	0.36	0.715
	Range	144.0 – 171.0	150.2 ± 169.0		
BMI (kg/m^2)	Mean ± SD	38.81 ± 4.79	21.58 ± 2.19	21.69	< 0.001
	Range	30.0 – 49.18	18.0 – 25.0		
WBC (x 10^9/L)	Mean ± SD	6.99 ± 1.77	6.08 ± 1.86	2.33	0.022
	Range	4.20 – 11.10	3.20 – 10.0		
RBC (million/µl)	Mean ± SD	4.46 ± 0.40	4.30 ± 0.37	1.84	0.069
	Range	3.61 – 5.42	3.44 – 5.42		
Hb (g/dl)	Mean ± SD	11.63 ± 1.03	12.59 ± 0.57	-5.42	< 0.001
	Range	8.70 – 13.70	12.0 – 14.0		
MCV (fl)	Mean ± SD	79.26 ± 5.84	83.83 ± 4.37	-4.14	< 0.001
	Range	61.40 – 91.20	74.50 – 93.60		
MCH (pg)	Mean ± SD	26.20 ± 2.38	28.66 ± 2.39	-4.83	< 0.001
	Range	19.30 – 30.70	24.40 – 33.60		
RDW (%)	Mean ± SD	15.88 ± 0.88	14.85 ± 0.39	7.02	< 0.001
	Range	14.30 – 19.00	14.10 – 15.60		
Platelets (x 10^9/L)	Mean ± SD	278.59 ± 58.34	246.73 ± 58.56	2.55	0.012
	Range	160.0 – 417.0	150.0 – 400.0		

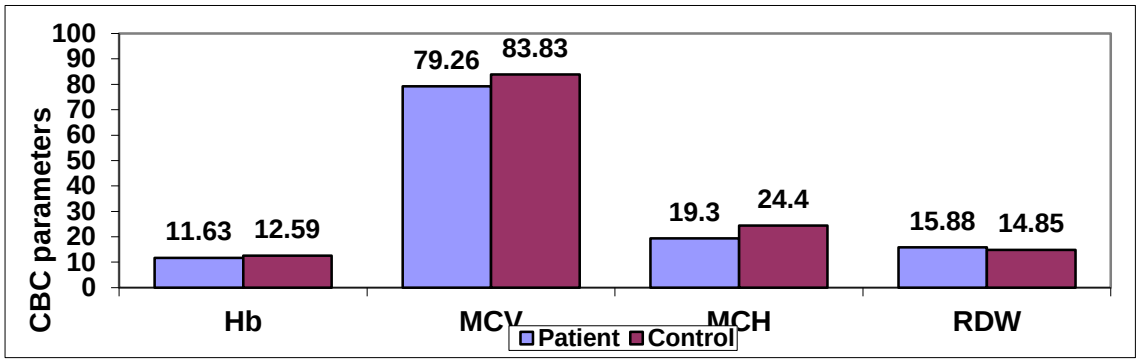
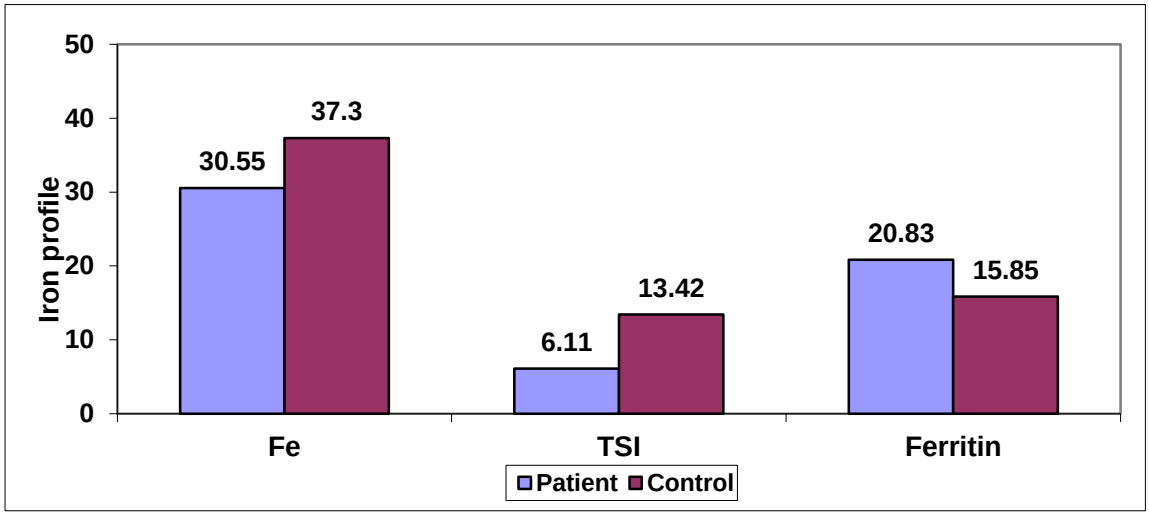


Figure 1: comparison between patients group and the control group regarding CBC parameter

Table 2: comparison between the patients group and the control group regarding iron profile.

Iron profile		Patient group N = 44	Control group N = 44	Test of sig.	P value
Fe (µ/dl)	Median	30.55	57.3	-6.897	< 0.001
	25th – 75th	14.42 – 44.37	53.15 – 62.03		
TIBC (µ/dl)	Median	403.95	430.80	-0.184	0.885
	25th – 75th	383.8 – 500.1	386.85 – 520.62		
TSI (%)	Median	6.11	13.42	-0.491	< 0.001
	25th – 75th	3.06 – 11.77	11.02 – 15.91		
Ferritin (ng/ml)	Median	20.83	15.85	0.766	0.446
	25th – 75th	5.64 – 37.55	14.65 – 19.65		

Figure 2: comparison between the patients group and the control group regarding iron profile



Correlation studies

The age was directly correlated with BMI (P=0.03). BMI showed a positive correlation with WBC, RBC, Hb, TIBC and ferritin and a negative correlation with platelets, Fe and TSI but with no significant difference (p>0.05).CRP was positively correlated with BMI but with no significant difference (P=>0.05).

DISCUSSION

Egypt Health Issues Survey (EHIS) showed that 26% of women in the reproductive age (15-59 years old) were considered overweight and 50% were considered obese.

Prevalence of overweight and obesity reached an alarming rate, the obesity increased directly with age, from a level of 15% among women age 15-19 to 76% or more among women in the 45-59 age groups. Urban women were more likely to be obese than rural women, and the percentage classified as obese ranged from 36% in rural Upper Egypt to 56% in the urban Lower Egypt

Results of the current study showed a highly significant relation between obesity and age with mean age 31.5 years. This was in agreement with **Cepeda- Lopez *et al.*[6]** who stated that the mean age of obese women was 34.9 in their study. Similarly **NNI [7]** stated that prevalence of obesity increases with age with higher prevalence among women at 20-30 years to reach the peak at 50 years.

This study showed low Hb values in obese patients with mean 11.63 in contrast to results of **Cepeda- Lopez *et al.*[6]** and **Yanoff *et al.*[8]** who reported normal Hb values with mean 13.7 and 13.5 respectively within obese patients in their studies.

Our study showed that obese women had low serum iron and TSI than the control one. On the other hand, serum ferritin, TIBC and CRP was higher in obese patient than the control. This agreed with **Yanoff *et al.*[8]** who reported that increases BMI affected the iron status of obese patient by showing low serum iron and TSI values and high ferritin and CRP values in obese patients than the normal weight subjects.

In this study, there was a negative correlation between BMI and both serum iron level and TSI with no significant difference. This results agreed with those of **Lecube *et al.*[9]** that showed a negative correlation between BMI and both serum iron level and TSI. A positive correlation between BMI and ferritin was detected which was in accordance with **Yanoff *et al.*[8]** who reported that ferritin in obese females was positively correlated with BMI, but had a non-significant relation with it. In contrast **Lecube *et al.*[9]** reported that there was no difference in serum ferritin between the normal weight and obese patients.

Accordingly, WHO proposed the use of both serum ferritin and transferrin receptor concentration (sTfR) as the best approach for measuring the iron status of population as (sTfR) is less affected by the acute phase response and is therefore considered to be more useful clinical marker to access iron status in individuals with chronic illness and inflammation [1]. CRP is an acute-phase protein that serves as an early marker of inflammation or infection; it is considered a non-specific "marker" for disease. Regarding the relation between BMI and CRP, our results demonstrated that 70.4% had positive CRP with positive correlation with BMI, this means that the percent of obese females with positive CRP

increased by increase in BMI. This difference was not significant. This can be explained by the usage of latex CRP in our study which was no specific. Interestingly [10] stated that in humans, high sensitive CRP (hs-CRP) is the main acute phase protein and it is also a sensitive marker of systemic inflammation.

Another studies had linked obesity with the presence of a low-grade systemic inflammation in their subjects[11,12]. In addition, others had shown that the CRP concentration decreases significantly after massive weight reduction[1,6]. This decrease indicated that fat mass plays an important role in the production of CRP. Also this agreed with **Gartner *et al.*** [11] who stated that inflammation was strongly linked with adiposity and increased dramatically with BMI with prevalence (20.1%, 37.6%, and 68.4% in normal, overweight, and obese women respectively; $P < 0.0001$).

Our study revealed that about 75.67% of low serum iron obese females had positive CRP versus 42.8% of normal serum iron females with positive CRP. This agreed with **Tussing-Humphreys *et al.***[1] who stated that the greater adiposity was associated with lower fractional iron absorption in humans, independent of iron status. Also this relation was in harmony with **Cepeda- Lopez *et al.***[6] who stated that CRP concentrations were higher in obese women and children and were positively associated with BMI and negatively associated with iron status.

The diagnosis of ID related to the inflammatory process in obese women may be missed if clinicians relay primarily on the falsely normal ferritin concentration, which are likely increased by chronic inflammation rather than by iron over load. The precise mechanisms of the obesity related, inflammation induced effect on serum iron remain to be elucidated.

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