# **OBESITY IS A RISK FACTOR FOR IRON DEFICIENCY AND ANEMIA: A CASE CONTROL STUDY**

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#### **ABSTRACT:**

**Background**: Rapid dietary and lifestyle changes produce a double burden of malnutrition. The populations suffer from increasing over consumption of food, but continue to have high rates of micronutrient deficiencies. Adipose tissue of obese persons produces increased amount of pro-inflammatory cytokines contributing to the development of a low-grade systemic inflammation in these persons.

*Aim of the work*: to determine the relation between body mass index (BMI) and hemoglobin (Hg) level, serum iron, total iron binding capacity (TIBC) and C reactive protein (CRP).

**Patient and Methods:** study was carried out on 60 women attending the outpatient clinic of the National Nutrition Institute (Egypt). Participants were divided into two groups; 30 obese women (case group) and 30 normal weight women (control group). Diagnosis of obesity was based on BMI >30 [WHO, 2014]. Anemia was diagnosed according to Hg level, serum iron and TIBC.

**Results:** The mean age of participant women was 32.82 years (SD 6.65) and ranged between 18 and 47 years. The mean Hb level of participant women were 11 gm/dl (SD 1.21) and ranged between 8.7 and 13.8 gm/dl. Hb levels showed no significant difference between obese and normal weight women. Serum iron was higher in normal weight women compared with obese women (P < 0.05). No significant correlation was observed between BMI and Hb levels. BMI had a significant negative correlation with serum iron. BMI has significant positive correlations with TIBC and CRP. Linear regression analysis showed a significant association between Hb levels and waist hip ratio.

**Conclusion:** High BMI affected negatively levels of serum iron and is associated with inflammatory process as indicated by higher levels of CRP. High waist hip ratio is an important risk factor for anemia.

Key words: Obesity, overweight, BMI, anemia, iron deficiency anemia.

#### **INTRODUCTION:**

Obesity is a risk factor for several comorbidities and complications, this includes iron deficiency anemia<sup>[1]</sup>. Anemia is a major global public health issue is caused by hemoglobin deficiency, resulting in a decline in the blood's oxygen-carrying

capacity<sup>[2]</sup>. The high prevalence of obesity in combination with iron deficiency incidence observed suggests an association between obesity and iron status. Obesity may disrupt iron homeostasis, resulting in iron deficiency anemia<sup>[1]</sup>.

The World Health Organization (WHO) reported that anemia affects 1.6 billion people worldwide, which correlate with to 24.8% of the total world population <sup>[3]</sup>. The prevalence of overweight and obesity in Eastern Mediterranean Region ranges from 74% to 86% in adult women<sup>[4]</sup>. According to WHO, Egypt ranks 18<sup>th</sup> with the highest prevalence of obesity worldwide<sup>[5]</sup>.

Disability-adjusted life years (DALYs) attributable to obesity may have reached 4 million in 2020. The economic burden imposed by obesity is around 62 billion Egyptian pounds annually. This value is the cost of treating diseases attributable to obesity in adults<sup>[6]</sup>. Obesity may negatively affect the iron status and cause iron deficiency due to increased serum levels of low-grade chronic inflammation and/or hepcidin<sup>[1]</sup>. Adipose tissue of obese patients produced increased amount of proinflammatory cytokines contributing to the development of a low-grade systemic inflammation in these patients<sup>[7]</sup>. 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<sup>[8]</sup>.

## AIM OF THE STUDY:

The objective of the present study is to determine the relation between body mass index (BMI) and hemoglobin (Hg) level, serum iron, total iron binding capacity (TIBC) and C reactive protein (CRP).

## **PATIENTS & METHOD:**

Type of Study: A case control study.

**Study Setting:** Outpatient clinics of the National Nutrition Institute (NNI).

**Study Period:** From September 2017 till February 2020.

Study Population: The study included obese and normal weight women attending the outpatient clinics of NNI. Diagnosis of obesity was based on anthropometric measurements (weight, height and accordingly the BMI). Participants were classified as normal weight (if BMI = 18 to 24 kg/m2), grade I obesity (if BMI = 30 to 34.9 kg/m2), grade II obesity (if BMI = 35 to 39.9 kg/m<sup>2</sup>) and grade III obesity (if BMI >40.0 kg/m2).

<u>Inclusion Criteria</u>: Newly diagnose adult females with obesity. Their ages ranged between 18 and 47 years.

*Exclusion Criteria:* Women with conditions that could influence body iron store such as clinical evidence of hemorrhage in the preceding six months, iron or folate or vitamin B12 treatment in the previous year, blood donation within the previous six months, Concomitant Infections, chronic diseases, and diabetes mellitus. Also, persons who were on specific regimen were excluded.

**Sampling Method:** Convenient sample was used.

Sample Size: A pilot study was conducted with 30 obese women and 30 normal weight women.

#### **Study Tools:**

I- <u>Interview questionnaires:</u> Socio-bio-Demographic Questionnaire (S-BDQ); El-Gilany 2012 <sup>[9]</sup>.

## II- <u>II- Anthropometric Measures:</u>

- Weight and height were measured and then BMI was calculated for each participant.
- Waist hip ratio.
- Neck circumference.
- **III- Laboratory findings:** Hemoglobin concentration, serum iron, total iron binding capacity, CRP.

**Ethical** consideration: Administrative approval was obtained from the director of the National Nutrition Institute. Approval was obtained from faculty of medicine, Ain Shams University Ethical Committee. Informed consent was taken from all study participants. Privacy and confidentiality of every participant was considered.

## **RESULTS:**

The mean age of participant women was 32.82 years (SD 6.65) and ranged between 18 and 47 years. The age of obese women range between 25 and 47 years, meanwhile the mean age of normal weight women ranged between 18 and 43 years.

Only 17 (28.3%) of participant women had positive family history of anemia.

The mean Hb level of participant women was 11 gm/dl (SD 1.21) and ranged between 8.7 and 13.8 gm/dl.

The mean serum iron level of participant women was 43.58 mg/dl (SD 29.57) and ranged between 0 and 117 mg/dl. TIBC of participant women ranged between 47 and 730mg/dl, meanwhile CRP ranged between 1 and 24.

Table 1 summarizes age, Hb levels, serum iron, TIBC and CRP in both obese and normal weight women.

No significant correlation was observed between BMI and Hb levels. BMI had a significant negative correlation with serum significant iron. BMI has positive correlations with TIBC and CRP. Table 2 summarizes the correlations between BMI and Hb levels, serum iron, TIBC and CRP in obese and normal weight women.

Linear regression analysis showed a significant association between Hb levels and waist hip ratio (Table 3).

Table 1. Comparison between obese women	n (case group) and norr	nal weight women (cor	ntrol group).
Variable	Case Group	Control Group	P value

Variable	Case Group	Control Group	P value
Age Groups			
<24 years old	0 (0)	2 (6.7)	0.106
25-30 years old	10 (33.3)	15 (50)	
>30 years old	20 (66.7)	13 (43.3)	
Anemia in Family Members	12 (40)	5 (16.7)	0.084
Hb levels	11.1 <u>+</u> 1.2	11.5 <u>+</u> 1.2	0.155
Serum iron	38.9 <u>+</u> 29.7	53.3 <u>+</u> 26.5	0.005
TIBC	419.9 <u>+</u> 138.7	348.8 <u>+</u> 89	0.020
CRP	7.8 <u>+</u> 8.2	1 <u>+</u> 0	0.000

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	Correlations with BMI		
Variables	Case Group	Control Group	Both Groups
	(Obese Women)	(Normal Weight Women)	Number: 60
	Number: 30	Number: 30	
Hb levels	R 0.028	R -0.113	R -0.129
	P value 0.882	P value 0.552	P value 0.327
Serum Iron	R -0.285	R -0.050	R -0.386
	P value 0.127	P value 0.791	P value 0.002
TIBC	R 0.270	R -0.090	R 0.349
	P value 0.149	P value 0.637	P value 0.006
CRP	R 0.276		R 0.553
	P value 0.140		P value 0.000

Variable	Standardized	Beta 95% CI	t value	P value
	coefficient Beta			
Age in years	-0.050	-0.061 - 0.042	-0.353	0.726
BMI	-0.091	-0.061 - 0.035	-0.535	0.595
Waist hip Ratio	-0.342	-1.4200.136	-2.430	0.018
Neck circumference	0.141	-0.025 - 0.067	0.905	0.369

Table 3. Lineal regression analysis of Hb levels and age, BMI, waist hip ratio and neck circumference.

# **DISCUSSION:**

The high prevalence of obesity in combination with iron deficiency incidence observed in different age and sex categories suggests an association between obesity and iron status. Obesity may disrupt iron homeostasis, resulting in iron deficiency anemia <sup>[9]</sup>.

Results of the current study showed that obese women were older than normal weight women; about two-third of obese women were older than 30 years old, meanwhile half of normal weight women ranged between 25 and 30 years old. This result agrees with the results of the studies of El-kerdany and collaborators (2017) and Cepeda-Lopez and collaborators (2011) which showed highly significant relations between obesity and age<sup>[10&11]</sup>. Similarly, a study conducted in NNI in 2004 stated that prevalence of obesity increases with age with higher prevalence among women at 20-30 years to reach the peak at 50 years<sup>[12]</sup>.

The mean Hb level of participant women in our study were 11 gm/dl (SD 1.21). This is in accordance with El-kerdany and collaborators (2017) who showed low Hb values in their obese patients with mean 11.63<sup>[10]</sup>, in contrast to the results of Cepeda-Lopez and collaborators (2011) and Yanoff and collaborators (2007) who reported normal Hb values with mean 13.7 and 13.5 respectively within obese patients in their studies <sup>[11&13]</sup>.

The relation between BMI and Hb level showed no significant correlation. This result agreed with Cepeda-Lopez and collaborators (2011) who found no difference in Hb concentrations between obese women and the other BMI groups<sup>[11]</sup>.

In the present study, BMI revealed significant negative correlations with serum levels of iron and a significant positive correlation with TIBC. This is in agreement with the studies of Cepeda-Lopez and collaborators (2011) and Stankowiak-Kulpa (2017)whose results suggested that increasing BMI was associated with lower serum levels of iron and transferrin saturation  $^{[11\&14]}$ . In concordance, Lee (2017) found that there was a significant positive correlation between the subject's BMI and TIBC (r=0.085, p<0.001)<sup>[15]</sup>.

Moreover, El-kerdany and collaborators (2017) showed that obese women had low serum iron than the control one. Similarly, Haidari and collaborators (2018) observed that serum iron levels and Hb concentration had a significant negative correlation with BMI<sup>[16]</sup>.

The finding of this study also agreed with Cepeda-Lopez and collaborators (2011) who indicated that in obese women, the prevalence of iron deficiency was significantly higher than in normal-weight or overweight women <sup>[11]</sup>, in contrast with the results of the study of Lee (2017) who found that BMI was not correlated with serum iron, where serum iron had no significant difference in obesity, overweight, and normal weight <sup>[15]</sup>.

However, according to the study of Ghadiri-Anari and collaborators (2014) in Iranian Population, 32.2% of total sample was normal weight and 37.7% and 30.1% were overweight and obese, respectively. No difference in Hb concentrations, serum iron, TIBC, transferrin saturation index, and ferritin were found between all BMI groups<sup>[17]</sup>.

Regarding the correlation between BMI and CRP, there was a positive correlation highly statistically significant with (P=0.000); this means that positive CRP increased by increase in BMI. These results are in accordance with the study of Lee (2017) which showed that there was a significant positive correlation between obesity and hs-CRP levels<sup>[15]</sup>. This agreed with the study of Gartner and collaborators (2013) which reported that inflammation (42.3%) was strongly linked with adiposity (20.1%, 37.6%, and 68.4% in normal, overweight, and obese women, respectively; P<0.0001<sup>[18]</sup>. In addition, several studies suggested that the CRP concentration decreases significantly after massive weight reduction. This decrease indicates that fat mass plays an important role in the production of CRP.

In fact, the association between adult obesity and low iron stores or anemia has been proved in a meta-analysis conducted in 2012. Although iron deficiency appeared as a typical finding in severe obesity, the systematic review concluded that most of pooled studies demonstrated higher ferritin concentrations in obese subjects compared to normal weight adults. However, serum iron and transferrin saturation decrease as BMI increases. This has mainly been attributed to a growing effect of obesityrelated inflammation with increasing grades of obesity<sup>[19]</sup>.

This is in accordance with Yanoff and collaborators (2007) whose data supported that it is the inflammation of obesity that negatively influences iron homeostasis<sup>[13]</sup>. Similarly, the study of Richardson and collaborators (2009)showed negative associations of hs-CRP with serum iron, transferrin saturation, participants<sup>[20]</sup>. Moreo among obese Moreover, Anty and

collaborators (2008) conducted a follow up study on obese adult women who had bariatric surgery, and found that the postoperative decrease in BMI was associated with decrease in CRP levels, with an associated improvement in markers of iron status. The authors suggested that obesity leads to inflammation, which in turn contributes to abnormal measures of iron homeostasis <sup>[21]</sup>.

Waist hip ratio has been suggested as an additional measure of body fat distribution. The proportion of fat stored on the body around the waist and hip could have the same value of measuring BMI <sup>[22]</sup>. The Linear regression analysis of the present study showed a significant negative association between Hb levels and waist hip ratio which agreed with several previous studies<sup>[23]</sup>. In contrary, the study of Kankanamge and collaborators (2016) could not prove such association<sup>[24]</sup>.

Our results suggest that the chronic inflammation of obesity might disturb the basic iron homeostasis and leads to a low iron profile among obese people, thus the findings emphasize the significance of closely monitoring and treating iron deficiency in people with overweight and obesity. In those patients, routine iron status markers such as Hb, serum iron and TIBC appear to be a sound indicator of iron status with avoiding iron testing during periods of apparent infection. Initial assessment for iron status in patients with overweight and obesity seeking medical nutrition therapy for weight loss might be advantageous in the clinical setting, and also the significant correlation between Hb level and waist hip ratio suggested the significant role of these anthropological indices for the development of anemia. Further controlled studies are needed to prove these suggestions.

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# السمنة كأحد عوامل الخطر المسببة لنقص الحديد

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المقدمه:
تؤدى التغييرات السريعة في النظام الغذائي ونمط الحياة إلى عبء مضاعف من سوء التغذية. يعاني السكان من زيادة
الاستهلاك المفرط للغذاء ، لكن لا يزال لديهم معدلات عالية من نقص المغذيات الدقيقة. الأنسجة الدهنية للأشخاص الذين
يعانون من السمنة المفرطة تنتج كمية متزايدة من السيتوكينات المؤيدة للالتهابات مما يساهم في تطوياالالتهاب لدى هؤلاء
                                                                                                  الأشخاص.
                                          الهدف من الدراسة:لتحديد العلاقة بين مؤشر كتلة الجسم والمكونات التاليه:
                                                                                          •الحديد في الدم
                                                                              •ملاز مةإجمالي تشبع الحديد
                                                                                    •تركيز الهيموجلوبين
                                                                                             البروتين التفاعلي
الطريقة: أجريت الدراسة على ٦٠ سيدة يترددن على العيادة الخارجية للمعهد القومي للتغذية تم تقسيم المشاركين إلى ا
                      مجموعتين. ٣٠ امرأة بدينة (مجموعة الحالات) و ٣٠ امرأة ذات وزن طبيعي (مجموعة التحكم).
استند تشخيص السمنة إلى مؤشر كتلة الجسم> ٣٠ [منظمة الصحة العالمية ، ٢٠١٤]. تم تشخيص فقر الدم وفقاً لمستوى
                                                                                   الهموجلبين والحديد في الدم .
النتائج: كان متوسط عمر النساء المشاركات ٣٢.٨٢ سنة (SD 6.65) وتراوحت بين ١٨ و ٤٧ سنة. كان متوسط مستوى
الهيموجلوبين للنساء المشاركات ١١ جم / ديسيلتر (SD 1.21) وتراوحت بين ٨.٧ و ١٣.٨ جم / ديسيلتر. أظهرت
                            مستويات الهيمو غلوبين عدم وجود فرق معنوي بين النساء البدينات وذوات الوزن الطبيعي.
التوصيات: أثر ارتفاع مؤشر كتلة الجسم سلبًا على مستويات الحديد في الدم ويرتبط بعملية الالتهاب كما يتضح من ارتفاع
                       مستويات بروتين سي التفاعلي. ارتفاع نسبة الخصر إلى الارداف هو عامل خطر مهم لفقر الدم .
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