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Effect of Anemia on the Treatment of Obesity

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Abstract: The present study was carried out to investigate the effect of iron supplement (IS) and high iron diet (HID) on obese anemic women. The study included 120 obese anemic women (MBI ≥ 30) aged 30 to 50 years followed in obesity and slim clinic in Cairo, Egypt for 12 weeks. Their diet was modified to provide 1250–1350 kcal. The patients were divided into 3 groups (n=40) as follows:Group1 was taken a normal diet program;Group2 was taken iron supplement (IS) (Ferro Sanol Duodenal® capsule 50 mg) with normal diet program and Group3 was taken a high iron diet program (HID). The results showed significantly decreased of weight in IS group (74.43kg) compared with group 1 (80.01 kg) and HID group (79.47 kg). Similar findings were found in BMI. Waist circumference (WC) of IS group decreased significantly (95.02cm) compared with group1 (103.35 cm). Also the WC of group 3 (HID) decreased significantly (99.75cm). Hemoglobin (Hb) level increased significantly in IS group (13.98g/dl) compared with group1 (10.78g/dl) and HID group (11.54g/dl). The results of red blood cells RBCs indicated significantly increased in IS group (4.81mm^3) compared with group 1 (3.14mm^3) and HID group (3.58mm^3). In conclusion the results of this study show association of overweight and obesity with iron deficiency. This study suggests that the treatment of anemia is important for the treatment of overweight and obesity.

Key words: Iron deficiency, Anemia, Obesity, Hepcidin

Introduction

Obesity is a disease defined by an excess accumulation of body fat to the extent that health is adversely affected **(WHO, 2000)**. Within only a few decades, obesity has become a global public health concern

(Ogden *et al.,* 2006). The obesity epidemic is not limited to certain societies. The prevalence of obesity is increasing in all regions of the world **(WHO, 2000)**. In 2005, an estimated 400 million adults worldwide were obese **(WHO, 2006).**The recent annual report from the International Association for the Study of Obesity documented approximately 1.5 billion of adults that are overweight, of whom around 525 million are clinically obese **(Abu-Farha*et al.,* 2013)**.

By 2010 an estimated one in seven children in the Americas and one in ten in the Eastern Mediterranean and European regions are predicted to be obese **(Wang and Lobstein,2006)**. In very recent report about the association between socioeconomic status (SES) and overweight or obesity in Cairo, **Mowafi*et al.,* (2014),** analyzed the data which were taken from the 2007 Cairo Urban Inequity Study which collected information on 3993 individuals from 50 neighborhoods in the Cairo Governorate. Five different measures of SES were utilized–education, household expenditures, household assets, subjective wealth, and father's education. No significant associations were found between most measures of SES and overweight/obesity in this population. Overweight and obesity are prevalent across the SES spectrum.The global epidemic of obesity will continue to worsen. The public health implications of the obesity epidemic are staggering; obesity is associated with increased mortality from cardiovascular disease, diabetes, kidney disease, and some cancers **(Flegal*et al.,* 2007).**

Anemia has been associated with obesity and increased BMI **(Bentley and Griffiths, 2003; Nead et al. 2004; Batista *et al.,* 2008)**. According to WHO 1.3–2.15 billion people are anemic all over the world and more than 90% are living in the developing countries. Apart from developing countries, Middle East and North African countries also share the health problem of anemia **(Sultan, 2007 and Hanafi*et al.,* 2013).**

The first reports of a potential connection between iron status and obesity appeared over 40 years ago, when **Wenzel *et al.,* (1962),** unexpectedly found a significantly lower mean serum iron concentration in obese compared with non-obese adolescents. Very few studies pursued the reported connection between iron status and obesity until recently, when a series of investigations described an increased prevalence of iron deficiency in overweight and obese populations. The first of these, a cross-sectional study published in 2003, described a greater prevalence of iron deficiency, as indicated by serum iron levels <8 mmol/L, in overweight and obese children and adolescents **Pinhas-Hamiel*et al.,* (2003)**.

Menzie*et al.,* (2008), found significantly lower levels of serum iron and transferrin saturation (the ratio of serum iron to total iron binding capacity) in obese as compared to non-obese adult volunteers, and fat mass was shown to be a significant negative predictor of serum iron concentration. Collectively, these reports suggest that excess adiposity may negatively affect iron status.If overweight and obese individuals are at greater risk for reduced iron absorption and iron deficiency, what is the mechanistic link between body fat and iron homeostasis? A number of hypotheses have been proposed, including increased plasma volume in the obese, the consumption of energy-dense, nutrient-poor foods **(Pinhas-Hamiel*et al.*, 2003),** and chronic inflammation in response to excess adiposity **(Yanoff*et al.*, 2007)**. Few of these hypotheses have been explored in detail.Unfortunately, no available study link between obesity and iron status in Egypt. The present study aimed mainly to determine iron status of obese women and its effect on obesity treatment.

Subjects and Methods

Subjects

The present study was done on a group of female patients between 30 and 50 years old suffering from anemia and obesity (BMI higher than 30 kg/m^2). They were selected among those attending the obesity and slim out patient's clinic, Cairo, Egypt and were agreeing to involve in this study. 120 obese anemic women of the total 150 cases had continued in the program regularly until the end. The patients were randomized either to a control group, Iron supplement (IS), and High Iron diet (HID) all with a caloric content of 1250-1350 kcal. No information was given to change the level of physical activity of the participants.

Iron supplement

Ferro Sanol Duodenal® capsule each capsules contains the (equivalent to 50 mg Fe2+) in form of ferrous2-glycine-sulphate complex. Patients were taken one capsule a day of Ferro Sanol Duodenal(50 mg).

Design of the study:

The patients were randomized into 3 groups 40 patients in each group as following:

Group1: control was taken a normal diet program.
Group2: was taken iron supplement (IS) **(Ferro Sanol Duodenal® capsule 50 mg)** with normal diet program.
Group3: was taken a high iron diet program (HID).

Nutritional education brochures about obesity and anemia were given to each patient. The Anthropometric measurement Weight, height, body mass index, Waist Circumference and Hip Circumference and Waist to Hip Ratio (WHR) were recorded for each case weekly. Fasting blood samples were obtained from each patient. The blood samples were divided into two parts; the 1st part was collected into heparinized tubeto measure Automated Complete blood count (CBC). The 2nd part was centrifuged at 3500 rpm for 15 min to obtain serum to measure lipid profile. Serum total cholesterol level was assayed by the method of **Naito, (1984)**. The serum level of triglyceride was determined by **Fossati and Prencipe, (1982).**Serum HDL-c was determined according to **Grove, (1979).**The low density lipoprotein (LDL) and very low density lipoprotein (VLDL) was calculated using the formula of **Friedewald*et al.,*** (**1972)**.Free T4 (Thyroxine)according to**Beck-Peccoz*et al.*,(1984**).Thyroid Stimulating Hormone (TSH) according to the method of**Uotila*et al.*,(1981**).

Results

The results of weight of obese anemic women showed decreased significantly of group 2 (IS) to be 74.43±10.91 kg compared with group 1 which was 80.01±11.87 kg; while the mean value of weight of group 3 (HID) showed not significant compared with group1. Similar findings were found in BMI. The results of waist circumference (WC) of obese anemic women showed decreased significantly in group2 after the study to be 95.02±6.86 cm compared with group1 which was 103.35±6.81cm. Also the WC of group 3 (HID) was decreased significantly to be 99.75±8.13cm compared with group1. With regarding of hip circumference (HC), the mean value of HC of group 2 (IS) showed decreased significantly after the study compared with HC of group 1 (control); whereas the mean value of HC of group 3 (HID) showed not significant with control group. The results indicated that the mean value of WHR of group 2 (IS) at the end of the study showed decreased significantly compared with group1; while the mean value of WHR of group 3 (HID) showed non-significant difference compared with group1(**Table 1**).

The results of serum total cholesterol indicated that decreased level of group1 to be 144.70±26.67 mg/dl. However, the level of serum total cholesterol of group 2 (IS) was decreased significantly to 147.20±25.98 mg/dl; while the level of serum cholesterol of group 3 (HID) increased to be 168.03±19.26mg/dl. Similar findings were recorded in the level of serum triglyceride (TC) that indicates lower levels in group 1 (not treated) and group 2 (IS). But the level of triglyceride of group 3 was significantly higher compared with groups 1 and 2. The level of serum high density lipoprotein HDL recorded significantly higher in patient of group 2 (IS) compared with control group; whereas the level of HDL in group 3 (HID) was decreased significantly compared with group 1 (control). The result of serum low density lipoprotein (LDL) showed decreased significantly in group 2 (IS) compared with group 1 (not treated). However significant higher in serum LDL level was recorded in group 3 (HID)**.** Very low density lipoprotein (VLDL) level showed decreased level in group 2 (IS); while the level of VLDL of group 3 was significantly higher compared with groups 1 (**Table 2**).

The level of serum thyroid stimulating hormone (TSH) showed slightly increased in groups 1 and 2 compared with the levels of at the beginning of the study; while group 3 (HID) showed slightly decreased compared with group 1 and 2**.** The results of serum T4 level of group 1 (control) was decreased to be 1.36±0.30 µlU/mL; while the results showed slightly increased in groups 2 and 3(**Table 3**).

The results of hemoglobin indicated that significant improvement in hemoglobin (Hb) level in group 2 (IS) from 10.55±1.72 g/dl to be 13.98±2.76 g/dl compared with group 1(control). However the level of hemoglobin of group 3 increased slightly to 11.54±1.88 g/dl compared with group1. The results of red blood cells RBCs indicated significantly increased in group 2 (IS) to be 4.81±0.50mm^3 compared with group 1 which showed slightly decreased to be 3.14±0.42 mm^3; also the level of RBCs of group3 was increased to be 3.58±0.25mm^3 after the study.The results of hematocrit of group 2 (IS) showed significantly increased after of the study to be 49.13±2.19%compared with group 1 which was 40.37±2.94% to be 40.95±3.23%; while the level of hematocrit of group 3 (HID) increased after of the study to be 42.55±4.03% (**Table 4**).

With regarding to the results of MCH, the results showed significant improvement in group 2 (IS) to be 28.62±1.48g/dL compared with group 1 (not treated) 28.10±1.88 g/dL; also the result of group 3 (HID) showed increased to be 29.77±1.47g/dL. The result of MCV of group 2 (IS) showed increased significantly compared with group 1. However the results of group 3 (HID) showed increased from to be 81.75±4.75 fL at the end of the study. The result of platelets of group 2 (IS) showed significantly increased at the end of study to be 285.50±58.14 mm^3 compared with group 1 which increased to be 266.67±55.24; also the platelets of group 3 (HID) was increased to be 268.10±46.21 mm^3(**Table 4**).

Table (1): Effect of effect of iron supplement (IS) and high iron diet (HID) on anthropometric measurements of obese anemic women

	Group 1 (not treated)		**Group2 (Iron Supplement)**		**Group3 (high iron diet)**	
	Before	**After**	**Before**	**After**	**Before**	**After**
Weight (kg)	85.81± 10.61[a]	80.01± 11.87[a]	88.50± 11.11[a]	74.43± 10.91[b]	87.92± 13.53[a]	79.47± 10.36[a]
BMI (kg/m^2)	33.16± 3.14[a]	31.03± 3.42[a]	33.65± 4.06[a]	28.29± 3.51[b]	33.45± 4.30[a]	30.38± 3.79[a]
WC (cm)	108.00± 7.91[ab]	103.35± 6.81[a]	109.97± 8.43[a]	95.02± 6.86[c]	104.80± 9.65[b]	99.75± 8.13[b]
HC (cm)	109.29± 7.59[a]	105.90± 6.81[a]	108.20± 5.90[a]	100.55± 5.39[b]	106.45± 6.01[a]	103.20± 5.06[ab]
WHR	0.988± 0.052[a]	0.975± 0.048[a]	0.952± 0.054[a]	0.921± 0.052[b]	0.984± 0.080[a]	0.966± 0.061[a]

*Values are means ± SD

** The mean difference is significant at the 0.05 level.

Table (2): Effect of iron supplement (IS) and high iron diet (HID) on serum total cholesterol (TC), triglyceride (TG), HDL-C, LDL-C and VLDL of obese anemic women.

	Group 1 (not treated)		**Group2 (Iron Drug S)**		**Group3 (Iron Natural S)**	
	Before	**After**	**Before**	**After**	**Before**	**After**
TC (mg/dl)	152.35± 34.21[b]	144.70± 26.67[b]	168.27± 30.70[a]	147.20± 25.98[b]	164.32± 23.20[ab]	168.03± 19.26[a]
TG (mg/dl)	128.62± 31.07[b]	121.60± 24.97[b]	144.57± 26.55[a]	125.82± 21.63[b]	138.05± 26.38[ab]	147.55± 24.18[a]
HDL (mg/dl)	54.40± 10.09[b]	56.60± 9.31[b]	46.54± 10.66[c]	63.86± 19.91[a]	59.95± 9.20[a]	51.25± 7.51[c]
LDL (mg/dl)	72.23± 31.99[b]	63.76± 22.96[b]	92.82± 32.22[a]	58.18± 28.13[c]	76.77± 24.30[b]	87.27± 15.74[a]
VLDL (mg/dl)	25.72± 6.21[b]	24.34± 4.93[b]	28.91± 6.16[a]	25.16± 4.35[b]	27.61± 5.10[ab]	29.51± 5.21[a]

*Values are means ± SD

**The mean difference is significant at the 0.05 level.

Table (3): Effect of iron supplement (IS) and high iron diet (HID) on serum thyroid stimulating hormone (TSH) and free thyroxine (T4) of obese anemic women.

	Group 1 (not treated)		**Group2 (Iron Drug S)**		**Group3 (Iron Natural S)**	
	Before	After	Before	After	Before	After
TSH (ng/dL)	2.38± 0.89[c]	2.39± 0.90[b]	2.77± 0.70[b]	2.79± 0.73[a]	3.10± 0.56[a]	3.04± 0.54[a]
T4 (µlU/mL)	1.38± 0.32[a]	1.36± 0.30[ab]	1.46± 0.42 [a]	1.47± 0.41[a]	1.23± 0.19[b]	1.27± 0.17[b]

*Values are means ± SD
** The mean difference is significant at the 0.05 level.

Table (4): Effect of iron supplement (IS) and high iron diet (HID) on complete blood count (CBC) ofobese anemic women.

	Group 1 (not treated)		**Group2 (IS)**		**Group3 (HID)**	
	Before	After	Before	After	Before	After
Hemoglobin (g/dL)	10.36± 0.87[ab]	10.78± 1.52[c]	10.55± 1.72[a]	13.98± 2.76[a]	10.20± 0.98[b]	11.54± 1.88[b]
RBCs (mm^3)	3.21± 0.49[a]	3.14± 0.42[b]	3.02± 0.34[b]	4.81± 0.50[a]	3.13± 0.16[ab]	3.58± 0.25[b]
Hematocrit %	40.37± 2.94[a]	40.95± 3.23[b]	37.45± 2.56[b]	49.13± 2.19[a]	38.65± 2.25[b]	42.55± 4.03[b]
MCH(g/dL)	28.95± 2.04[a]	28.10± 1.88[b]	28.62± 1.48[a]	30.32± 2.69[a]	28.50± 1.52[a]	29.77± 1.47[a]
MCV (fL)	81.55± 4.16a	82.04± 4.27b	80.12± 5.13a	87.60± 9.94a	77.35± 5.21b	81.75± 4.75b
Platelets (mm^3)	261.92± 56.68a	266.67± 55.24b	263.47± 59.43a	285.50± 58.14a	257.05± 45.98a	268.10± 46.21b

*Values are means ± SD

** The mean difference is significant at the 0.05 level.

Discussion

Obesity and iron deficiency (ID) are 2 of the most common nutritional disorders worldwide **(Del-Giudice et al, 2009)**. ID, in developed countries, is the most common nutritional deficiency and has been linked to obesity in adults and children **(Amato*et al.*, 2010).** The association between iron status and obesity is one that should be explored further, as obesity and ID are diseases that continue to evolve globally, and both have significant public health implications **(McClung and Karl, 2009)**. The global incidence of obesity has increased dramatically over the past 50 years. Currently more than 1 billion people are thought to have a body mass index (BMI) of more than 30 kg/m2, and the number is expected to increase dramatically over the next 30 years **(Chung*et al.*, 2007).**

The global obesity epidemic reflects rapidly changing environments as societies develop, cultures integrate, food habits globalize, and urbanization and its corollary urban lifestyle replaces more active rural living. These shifts are often captured by the term nutrition transition, which refers to the interplay of economic, demographic, environmental and cultural changes in a society that are associated with shifting patterns of nutritional intake **(Mowafi*et al.*, 2014).** Urban Egyptian women are disproportionately affected and have a higher prevalence of overweight/ obesity compared with most other developing nations. Egypt's observed overweight/obesity prevalence was (69.9%) far exceeded that which was expected (~35.0%) given **(Mendez *et al.*, 2005).**

Iron plays a vital role in hemoglobin production and erythrocyte maturation. Two of the most common causes of anemia, IDA and the anemia of chronic inflammation, result from abnormalities in iron homeostasis **(Ausk and Ioannou, 2008**). Iron homeostasis in the body is controlled by a very complex mechanism, the main components of which are erythropoietic activity, hypoxia, iron stores, and inflammation **(Choudhry, 2010).**

However, iron may also function in the maintenance of body weight and composition, as a number of studies have suggested an association between iron status and obesity. The first such study, published in 1962 by Wenzel ***et al.,*** demonstrated significantly lower serum iron concentrations in obese adolescents in comparison to normal controls **(Wenzel *et al.*, 1962)**.

Menzie*et al.*, (2008), found significantly lower levels of serum iron and transferrin saturation in obese people when compared to non-obese adult volunteers. They reported that the obese and the non-obese subjects did not differ in total daily iron consumption but that fat mass was a significant negative predictor of serum iron level.

There is an expanding body of literature demonstrating that obesity has an important role in modifying iron homeostasis. The association between excess weight, iron status, and iron absorption has been elegantly assessed in women and children from transition countries **(Zimmermann et al 2008)**. Confirming previous studies, poorer iron status was notably more common in heavier participants. Independent of iron status, both BMI and inflammation (as measured by C-reactive protein) were negatively correlated with absorption of isotopically labeled iron from fortified foods. In addition, those with greater adiposity were unable to improve their iron status by dietary means compared to lean controls. Although hepcidin was not measured, it was suggested by the authors that inflammation-induced hepcidin was likely causing a decrease in dietary iron absorption by diminishing the expression of Fpn located on the basolateral membrane of intestinal enterocytes thus impairing dietary repletion efforts.

Several studies have investigated the effect of diet-induced weight loss on iron status in both adults and children; however, results are conflicting. In adults, diet-induced weight loss was associated with maintenance or improvement in serum iron, TSAT, and hemoglobin **(Weinsier*et al.*, 1983 and RodrÎguez*et al.*, 2007)**.

However, **Beard *et al.*, (1997),** reported a significant decrease in TSAT after just 1 week of adherence to a very low- energy diet. Similarly, **Kretsch*et al.*, (1998)** reported a significant decrease in hemoglobin, hematocrit, and red blood cell count after a 15-week energy-restricted diet in a group of women with obesity.

Our study found that the mean of serum iron levels significantly lower among obese women; similar findings was recorded by**Pinhas-Hamiel*et al.*, (2003)** whoreported that Iron-deficiency is common in overweight and obese children. A significantly greater proportion of obese than normal-weight children have iron-deficiency anemia.Also **Chambers *et al.*, (2006)** found a significant inverse association between central and total fat mass with serum iron concentrations in Hispanic women. Similar findings recorded by **Ausk and Ioannou, (2008)** who found that overweight and obesity were associated with changes in serum iron.

Results of this study shows significant of the mean value of weight which correlated with BMI of obese anemic women before and after treatment with daily dose of iron supplement 50mg and high iron diet. After three months of treatment with iron supplement the mean value of weight and BMI decreased significantly compared with control group and high iron diet group as shown in table **(1).** The results of our study indicated that the treatment with iron supplement of obese anemic women affects the waist and hip circumference, which decreased significantly compared with not treated patients and patients who taken high iron diet this effect reflect on waist to hip ratio.Our results found that thyroid hormones FT4 and TSH were in normal range in most cases that indicated that no intervention with the weight loss results **(Table3)**.

Our results indicated significant improvement in hemoglobin, red blood cells hematocrit, MCV and MCH status in obese anemic women who treated with iron supplement (IS) compared with those who dependant of high iron diet only **(Table4)**. The improvement of hemoglobin, RBCs and Hematocrit in patient who treated with (IS) is related to the dose of ferrous bisglycinate 50mg/daily. The same results recorded by **Nils *et al.*, (2014),** who indicated that ferrous bisglycinate in a low dose of 25 mg iron/day appears to be adequate to prevent IDA in more than 95% of Danpish women during pregnancy and postpartum. Also **Aycicek A. (2015),** reported that ferrous sulfate and ferrous fumarate plus zinc and vitamin C were well tolerated and were highly effective in correcting IDA in children

Enhancing in iron status in the case of a patient who intake high iron diet is related to nutrition education, diet modification (high Iron in the diet, intake foods rich in vitamin C after meals); The relationship between iron intake and iron status is complicated by variations in the efficiency of iron absorption, but a systematic review of randomised clinical trials show a positive time-dependent association between iron intake from supplemental iron and serum ferritin **(Casgrain*et al.*, 2012).**

Khoshnevisan*et al.*, (2013), found that during three months of nutrition education and diet modification, groups were significantly correlated to serum ferritin alteration. Frequency of fruit juice intake (rich in vitamin C) after meals (at least five times a week) can significantly increase serum ferritin within three months.

Our study showed association of overweight and obesity with iron deficiency. Our study suggests that the treatment of anemia is important for the treatment of overweight and obesity.

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