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Does Fat Distribution Play a Role in Obesity-Associated Iron Deficiency Anemia? An Anthropometry-based Analysis in Young Women

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ABSTRACT

Background and aim: High hepcidin levels in obesity reduce iron absorption, leading to iron deficiency anemia. Visceral fat is metabolically more active than subcutaneous fat. We wanted to assess if hemoglobin (Hb), serum iron, and serum ferritin levels correlated with surrogate markers of visceral fat and subcutaneous fat, i.e., waist circumference (WC) and the sum of three skinfold thicknesses (SFT3), respectively.

Material and methods: Thirty young women aged 17-20 years, BMI => 25.0 kg/m^2, participated in the cross-sectional analytical study. Data collected: Anthropometry- weight and height for Body Mass Index (BMI) calculation, WC, and skinfold thickness at three sites – triceps, abdomen, and suprailiac regions for SFT3; Haematology parameters - Hb, serum ferritin, and serum iron levels. Data analysis: Pearson's Correlation coefficient ($p< 0.05$) was calculated for both WC and SFT3, with S. Iron, S. Ferritin, and Hemoglobin.

Results: Thirty percentage of the participants were anemic (Hb < 12.0 mg/dl). Their Iron stores and serum levels were poor (Serum Ferritin < 15.0 ng/ml and S. Iron < 60.0 µ/dl): 67.0% and 70.0%, respectively. WC and SFT3 correlated negatively with hemoglobin. SFT3 and BMI correlated positively with serum ferritin, but WC correlated negatively. Serum iron levels correlated negatively with WC and BMI but positively with SFT3. However, any positive or negative correlation was not found to be significant.

Conclusions: There was a positive association between obesity with iron deficiency anemia. However, whether visceral or subcutaneous fat is more associated with the same remained inconclusive.

1. Introduction

One of the most widespread global health problems is anaemia, which affects one-third of the world's population and increases mortality rates, morbidity, and neurological impairments.[1] It not only affects an individual's health adversely but also hurts the socio-economic development of a country. Iron Deficiency Anaemia (IDA) is the most common among the various types of anemia.[2] Although it can occur in any gender, females are more susceptible to it. In India, anemia affects almost 88% of pregnant women and 74% of non-pregnant women, and most of its burden is due to iron deficiency anemia.[3] Another major health-related issue in today's world is obesity. With decreased physical activity and increased consumption of fast or instant food, the prevalence of obesity is rising. Obesity is a key health issue that may lead to severe chronic illnesses, cardiovascular disease (CVD), and diabetes. Studies have shown that it negatively impacts women's reproductive health. Even during pregnancy, it has many adverse effects. Studies have shown that there is a relationship between miscarriage and obesity.[4] However, in many parts of the world, obesity is neglected due to a mindset that overweight or obese individuals are eating well, and it is hence not considered a health issue. However, if not controlled in time, an overweight individual turns into an obese individual and may acquire several chronic diseases. Young women are an important contributor to the development of a family as well as the nation. But many women in our country suffer from both these conditions, obesity as well as anemia. India is still a developing nation where a big part of any family's income gets diverted toward healthcare. These adversely affect the individual, the family, and the nation in terms of health conditions, quality of life, and economic stability. Also, the health of women in the reproductive age group reflects on their offspring's health. However, poor awareness and paucity of efforts to contain anemia and obesity compound the problem. Given the rapidly changing social and environmental factors that prevail today, where there is easy access to fast food, decreased or complete absences of physical activities, and adoption of western culture, it, therefore, becomes pertinent that effective measures are taken to contain obesity. Fat is widely distributed in every individual's body – subcutaneous as well as around the

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viscera. Moreover, fat at both these sites has a different endocrine/metabolic influence on the body. Fat can be measured around the abdomen, which represents the visceral fat, or it can be measured in skin folds, which is the subcutaneous fat. Either of the two or both may lead to some of the other metabolic disorders that negatively affect the normal functioning of the human body, including iron metabolism. Past researchers have found an association between obesity and iron deficiency anemia.[5] But there is no conclusive evidence that identifies fat at which of these two locations is more closely associated with anemia. Understanding the relationship between different fat distribution patterns and iron profile patterns in young women will contribute to describing their association and tackling the problems of anemia and obesity at an early stage where they are both amenable to conservative treatment. Against this background, we designed our study: to analyze how visceral and subcutaneous fat distributions correlated with hemoglobin level and iron profile in young women. We aimed to examine the correlation of visceral and subcutaneous fats with iron profile and hemoglobin levels in young overweight/ obese females of age 17-20 years with the following objectives of this study to find the mean levels of hemoglobin, serum iron, and serum ferritin in obese/overweight females of age 17-20 years, 2. Serum iron level, and serum ferritin level with subcutaneous fat marker-the sum of three skinfold thicknesses (SFT3) in young overweight/obese females aged 17-20, and 3 to find the correlation of hemoglobin level. Serum iron level, and serum ferritin level with visceral fat marker-waist circumference (WC) in young overweight/obese females aged 17-20 years to find the correlation between hemoglobin level.

2. Material and methods

Study design and participants

It was a cross-sectional analytical study conducted at Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha, Maharashtra, India, after obtaining approval from the institutional ethics committee, DMIMS(DU)/IEC/2020-21/8867 dated 30.06.2020, and its protocol was published. Written informed consent of all the participants of the study was taken: Female students enrolled in I and II years of medical professional courses aged 17-20 years of the Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha, Maharashtra, India. Thirty subjects were selected by simple random sampling from among those who were obese/ overweight, willing to participate in the study, and fulfilled the inclusion criteria of the study: females aged 17-20 years, with BMI> = 25.0 Kg/m^2, non–pregnant, at least one week had passed from last menstrual cycle at the time of blood sample collection, not suffering from menorrhagia and hypermenorrhoea, taking a healthy diet including sufficient sources of iron in the diet, not taking iron supplements, not suffering from any condition that might affect iron and hemoglobin levels like blood loss from the gastrointestinal tract, renal system, recent blood donation, blood loss from an accident. Bleeding, disease, or condition that might affect iron profile and hemoglobin.

Data collection

The data were collected over two months – August 2021–September 2021.

Anthropometry

Anthropometric measurements were made following the standard procedures, and derived anthropometric indices were calculated using standard equations: Height, Weight, Body Mass Index (BMI), Waist Circumference (WC), and Skin Fold Thickness (SFT). Height was measured (in m) with the help of a stadiometer to the nearest 1 mm. The Participants were asked to remove the shoes and stand against the device.[6, 7] Weight was measured (in kg) by using a simple weighing machine to the nearest 100g. The participants were asked to wear light clothes, remove their shoes, and stand on the machine.[7] Body Mass Index (BMI) was calculated using the equation-Weight (kg)/ Height2 (m^2) and the subjects were identified as obese/ overweight according to the following criteria: severely underweight- BMI less than 16.5 kg/m^2, underweight- BMI less than 18.5 kg/m^2, normal- BMI< or = 18.5 to 24.9 kg/m^2, overweight- BMI < or = 25.0 to 29.9 kg/m^2, and obese- BMI< 30 kg/m^2.[8] Waist circumference (WC) was measured using an inelastic measuring tape to the nearest 1 mm at the level of the umbilicus. It was made sure that the abdomen was not compressed during measurement.[7] Skinfold thickness (SFT) was measured using skinfold callipers to the nearest 1mm at the following three sites on the body- triceps - backside of the middle of the upper arm, abdominal at the level of the umbilicus, and supra-iliac above the upper bone of the hip.[8, 9] Waist Circumference was used as a surrogate marker for visceral adiposity.[10] The sum of the three skinfold thickness measures (SFT3) was used as a surrogate marker for total body subcutaneous fat.[11, 12]

Haematological investigations for iron profile and hemoglobin level

Whole blood Hemoglobin, Serum Ferritin, and S. Iron levels were measured in fasting blood samples.

Data analysis

Mean and standard deviation was calculated for each parameter. Pearson's Correlation coefficient, with a significance level of 5% ($p< 0.05$), was calculated for the visceral fat marker, WC, S. Iron, Serum Ferritin, and Hemoglobin, and likewise for the subcutaneous fat marker, SFT3. The data were recorded and analyzed using Microsoft excel ver. 2016 and Social Science Statistics Calculator online.

3. Results

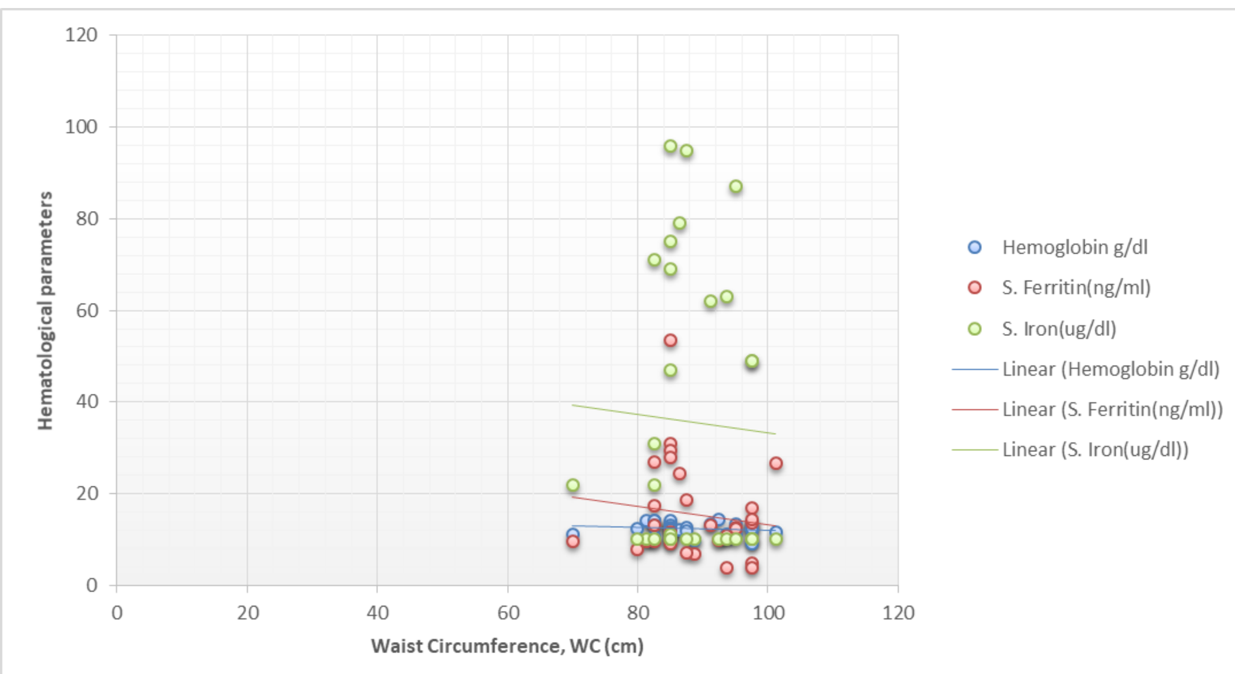
Table 1 shows the mean age, weight, height, BMI, Waist circumference, skinfold thickness in the triceps, abdomen, and suprailiac region, whole blood hemoglobin, serum iron, and serum ferritin levels of the 30 participants of the study and their standard deviations. Hemoglobin level was less than 12.0 mg/dl in 9 (30.0%) participants, S. Ferritin was less than 15.0 ng/ml in (WHO) in 20 (66.7%) participants, and S. Iron was less than 60.0 µ/dl in 21 (70.0%) subjects.

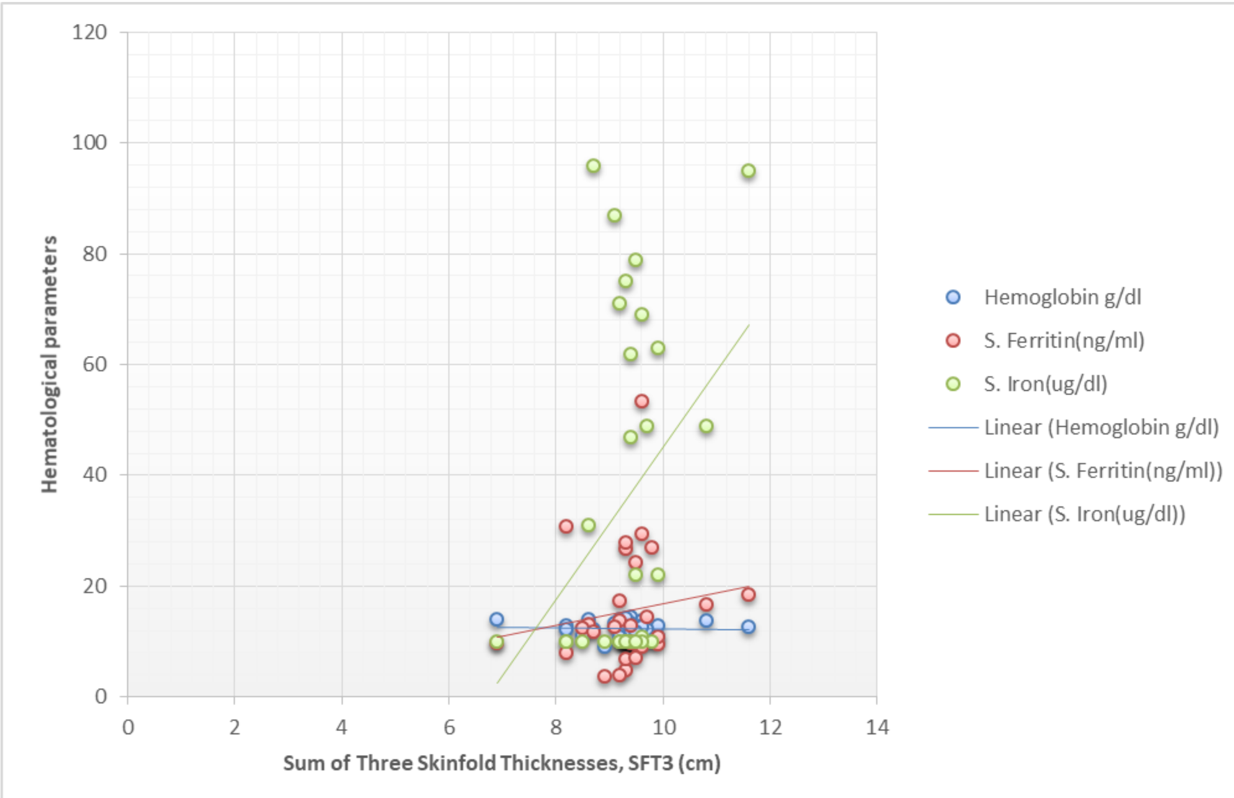
Table 1. Anthropometric and Hematological Parameters of the study subjects.

S. No	Parameter	Mean	S. D
1	Age (years)	20.0	0
2	Height (m)	1.6	0.1

3	Weight (kg)	67.1	6.4
4	BMI (Kg/m^2)	27.3	1.5
5	WC (cm)	88.6	6.9
6	Triceps (cm)	3.1	0.3
7	Abdominal (cm)	3.0	0.2
8	Supra-iliac (cm)	3.1	0.4
9	SFT3 (cm)	9.3	0.8
10	Hemoglobin g/dl	12.4	1.3
11	S. Ferritin (ng/ml)	15.6	10.4
12	S. Iron (µg/dl)	35.6	30.4
S.D. = Standard Deviation, SFT3 = Sum of skinfold thickness at three sites – triceps, abdominal, suprailiac regions.			

Table 2 shows the Pearson's correlation coefficient (r) of Waist circumference, the sum of the three subcutaneous fat thicknesses (SFT3), and BMI with hemoglobin and iron profile. Fig. 1 shows the same on a scatter plot with a trend line.





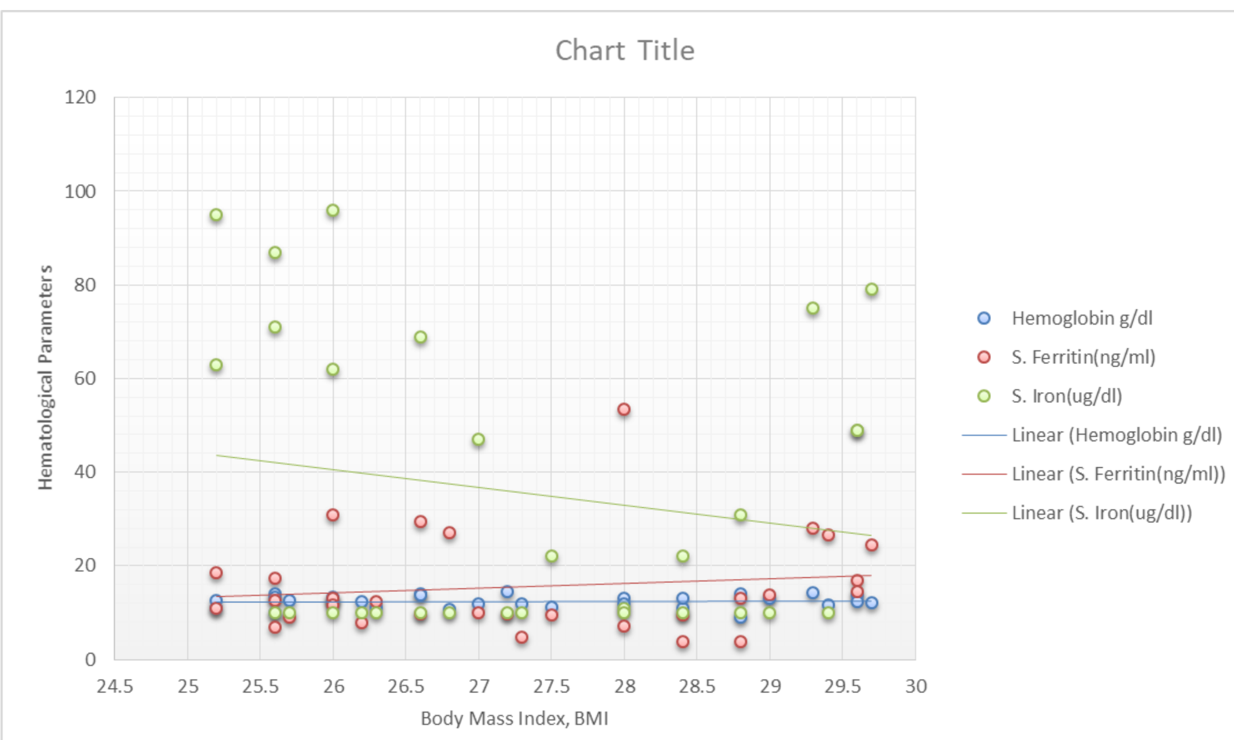


Fig. 1. Correlation of Hemoglobin, Serum Ferritin and S. Iron with Visceral Adiposity (Waist Circumference), Subcutaneous Adiposity (Sum of Three Skinfold Thickness), and BMI.

We observe a weakly negative correlation of both visceral fat and subcutaneous fat with hemoglobin, a weakly negative correlation of visceral fat, with waist circumference as its surrogate marker, with both serum ferritin and serum iron levels, and a weakly positive correlation of subcutaneous fat with both serum ferritin and serum iron levels. With respect to BMI, both Hemoglobin, Serum Ferritin have a weakly positive correlation with it, while S. iron has a negative correlation with it. The correlation, in either case, is not significant at a 5% significance level.

Table 2. Correlation of visceral and subcutaneous fat with hemoglobin and iron profile.

S. No.	Parameter*	Hemoglobin g/dl	Serum Ferritin(ng/ml)	Serum Iron(μg/dl)
1	**Visceral Obesity/ Waist circumference (WC)**			
	r (28)	-0.2	-0.1	-0.1
	p-value	0.4	0.5	0.8
	Significance	No	No	No
2	**Subcutaneous Fat/ Sum of three skinfold thickness measurements (SFT3)**			
	r (28)	-0.1	0.2	0.4
	p-value	0.8	0.4	0.1
	Significance	No	No	No
3	**Body Mass Index (BMI)**			
	r (28)	0.0	0.2	-0.2
	p-value	0.8	0.5	0.3
	Significance	No	No	No
r= Pearson's Correlation coefficient, * At 5% level of significance.				

4. Discussion

Iron is necessary for hemoglobin synthesis, and disrupting its metabolism may result in iron deficiency anemia. Duodenum and upper jejunum are the predominant sites where iron absorption takes place. Ferroportin is a transmembrane protein that participates in the transport of iron out of cells: it is required to absorb iron into the bloodstream from intestinal cells to deliver iron from macrophages to bone marrow. After absorption from duodenal mucosa into the blood, with the help of transferrin, it is transported to the bone marrow to produce red cells by erythropoiesis [13] (Fig. 2).

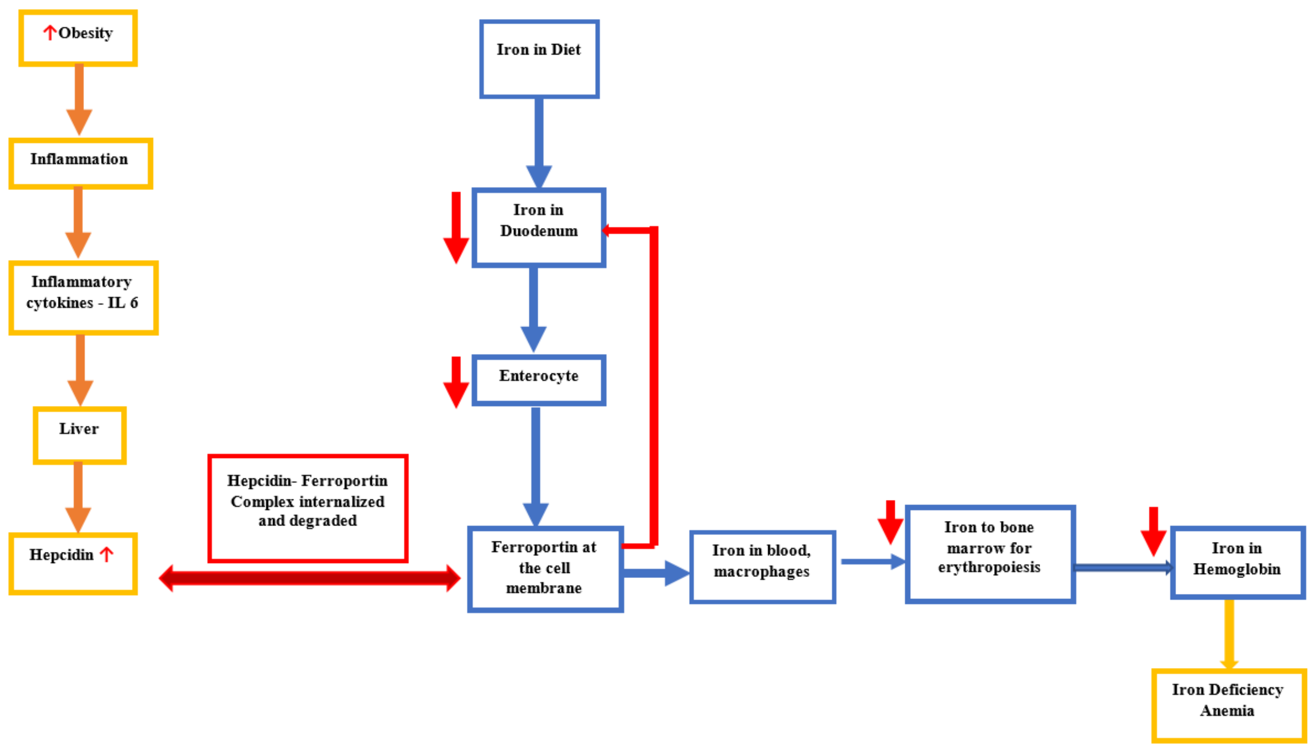


Fig. 2. How obesity may be linked to iron metabolism and anemia: In obesity, high serum hepcidin levels reduce iron availability for erythropoiesis.[13-21]

Hepcidin is a peptide hormone secreted by the liver. It acts as a key regulator in the process of iron metabolism, having a negative regulatory effect on the iron metabolism process.[13] Studies have shown that hepcidin interferes with iron metabolism. Hepcidin combines with ferroportin to form a ferroportin-hepcidin complex which then becomes internalized and degraded. The rise in serum hepcidin levels reduces iron transport out of cells.[14] Therefore, iron absorption becomes vulnerable whenever serum hepcidin levels rise. Studies have shown that with an increase in the hepcidin level, the availability of iron for transport in the bloodstream from other sources, liver as well as macrophages, also suffers adversely, resulting in iron deficiency anemia.[15-18] Studies have found that during obesity, an elevation in the serum hepcidin (S. Hep.) level.[17] Obesity triggers low-grade inflammation, and adipose tissue releases inflammatory cytokines like interleukin 6 (IL 6) and leptin. IL 6 stimulates the synthesis and release of hepcidin from the liver into the blood.[19] Therefore, iron deficiency anemia is observed in obesity.

Association of iron deficiency anemia and pattern of fat distribution in obesity

Body fat is distributed as subcutaneous fat and visceral fat, of which visceral fat is given much attention due to its involvement in various medical conditions.[20] Studies have shown that women with higher central obesity have high S. Hep, resulting in greater impairment of iron metabolism and hence decreased iron absorption.[21] Studies inferred that Interleukin 6, leptin, and necrosing tumor factors are released by visceral adipose tissue. Studies have also shown that IL-6, a cytokine, is responsible for stimulating hepcidin transcription.[19] In our study, we have found that a large proportion of overweight/obese participants (30.0%) are anemic (Hb < 12.0 mg/dl).[22] The majority of iron stores and serum levels are poor (S. Ferritin < 15.0 ng/ml and S. Iron < 60.0 μ/dl): 67.0 % and 70.0 %, respectively.[23, 24] The high proportion of anemic women and the negative correlation of waist circumference as well as skinfold thickness with hemoglobin level in our study are in agreement with the findings of other studies that report a positive correlation between iron deficiency anemia with obesity and with those that implicate obesity as a causative factor of the same.[8, 20] Both markers, waist circumference and skinfold thickness, of the different patterns of obesity, visceral and subcutaneous fat, respectively, correlate negatively with hemoglobin: waist circumference correlates more negatively with hemoglobin than skinfold thickness. A similar finding has been reported by Stoffel NU et al. in their study.[21] While a low serum ferritin level indicates poor iron stores, high serum ferritin does not indicate the opposite. Serum ferritin is an acute-phase reactant whose levels rise in different conditions of inflammation, including obesity.[25] Likewise, in our study, both subcutaneous fat index (sum of skinfold thickness, SFT3) and BMI correlated positively with serum ferritin. However, visceral obesity index waist circumference (WC) correlates negatively with it. Serum iron levels also correlate with the three anthropometric indices of obesity: they correlate negatively with visceral fat and BMI but positively with subcutaneous fat. However, any positive or negative correlation is not found to be significant. Largely, these results indicate a positive association between obesity with anemia. However, it remains inconclusive which type of fat distribution in obesity, visceral or subcutaneous fat, is more loosely associated with iron deficiency anemia. The finding is in agreement with the results of some other studies, which also report a non-significant or inconclusive association of either obesity with iron deficiency anemia or inconclusive the pattern of fat distribution with iron deficiency anemia.[26, 27] Given the contradictory evidence available concerning the association of iron deficiency with anemia with obesity, it is only imperative to look at some other aspects of the association through research conducted worldwide in different populations. Obesity, as we have discussed above, is a pro-inflammatory state with relatively high levels of circulating serum hepcidin that reduces iron absorption as well as its availability to bone marrow for erythropoiesis. Here, poor dietary intake may compound the problem of iron deficiency in obesity. Young people, including overweight/obese individuals, tend to have poor dietary habits, including a calorie-rich diet that may be grossly deficient in essential micronutrients, including iron. Given the above two points, it may be hypothesized here that because of the confounding effect of the poor iron intake itself and that a critical level of adipose tissue, subcutaneous or visceral, may be required to cause significant inflammation to interfere with metabolism, the association of different indices of obesity with those of iron profile and hemoglobin levels remains inconclusive. Another factor that could account for the same may be a limited sample size in our study and the absence of a comparison group. Studies that evaluate dietary habits quantify fat and its distribution and include more parameters to describe iron status and metabolism are required to decipher the relationship between obesity and iron deficiency anemia.

5. Results

There appears to be a positive association between obesity with iron deficiency anemia in our study. However, it remains inconclusive which type of fat distribution, visceral or subcutaneous fat, is more associated with the same. Perhaps, more factors are involved in describing the association than those we included in our study. Studies that include evaluation of dietary habits, quantification of fat and its distribution, and include more parameters to describe the iron status and metabolism are required to decipher the relationship between obesity and iron deficiency anemia. At the same time, we recommend measures to curtail obesity for a healthier population with a reduced burden of morbidity due to obesity's metabolic complications, including iron deficiency anemia.

Conflict of Interest

The authors declared that there is no conflict of interest.

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