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A Higher Rate of Iron Deficiency in Obese Pregnant Sudanese Women

Wisal Abbas[1], Ishag Adam[2*], Duria A. Rayis[2], Nada G. Hassan[2], Mohamed F. Lutfi[1]

[1]Faculty of Medicine, Alneelain University, Khartoum, Sudan; [2]Faculty of Medicine, University of Khartoum, P.O. Box 102, 11111, Khartoum, Sudan

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***Correspondence:** Ishag Adam. Faculty of Medicine, University of Khartoum, P.O. Box 102, 11111, Khartoum, Sudan. Tel +249912168988. Fax +249183771211. E-mail: ishagadam@hotmail.com

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Abstract

AIM: To assess the association between obesity and iron deficiency (ID).

MATERIAL AND METHODS: Pregnant women were recruited from Saad Abualila Hospital, Khartoum, Sudan, during January–April 2015. Medical history (age, parity, gestational age) was gathered using questionnaire. Weight and height were measured, and body mass index (BMI) was calculated. Women were sub-grouped based on BMI into underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥ 30 kg/m^2). Serum ferritin and red blood indices were measured in all studied women.

RESULTS: Two (0.5%), 126 (29.8%), 224 (53.0%) and 71 (16.8%) out of the 423 women were underweight, normal weight, overweight and obese, respectively. Anemia (Hb <11 g/dl), ID (ferritin <15µg/l) and iron deficiency anemia (IDA) were prevalent in 57.7%, 21.3% and 12.1%, respectively. Compared with the women with normal BMI, significantly fewer obese women were anemic [25 (35.2%) vs. 108 (85.7%), P < 0.001] and significantly higher number of obese women [25 (35.2) vs. 22 (17.5, P = 0.015] had iron deficiency. Linear regression analysis demonstrated a significant negative association between serum ferritin and BMI (– 0.010 µg/, P= 0.006).

CONCLUSION: It is evident from the current findings that prevalence of anaemia and ID showed different trends about BMI of pregnant women.

Introduction

There is an increased rate of overweight and obesity among pregnant women [1]. The prevalence of overweight and obesity among Sudanese pregnant women at term are as high as 35.6% and 19.4%, respectively [2]. To our best of knowledge, Sudanese pregnant women have relatively higher body mass index (BMI) compared with other African countries especially in the Sub-Saharan region [2,3]. This creates a real challenge to obstetric practice because of the negative effects of obesity on the mother as well as the fetus [4]. The fetus of obese pregnant women is at higher risk of stillbirth, macrosomia, neural tube defects and other congenital anomalies [4–6]. Alternatively, gestational diabetes mellitus, preeclampsia, premature labour and caesarian delivery are more likely in obese compared with lean pregnant women [5,6].

Recent researches also revealed an intimate relation between high BMI and iron deficiency (ID) [7–9], adding more potential complications to obese pregnant women like iron deficiency anaemia (IDA) [9–14]. The negative impact of BMI on iron homoeostasis was established in many studies targeting obese children [15,16] and adolescents [16,17]. In adults, studies exploring the link between high BMI and ID showed variable results, where significant associations were demonstrated in some reports [8,13] but not others [14,18]. Comparable studies among obese pregnant women are limited and mostly based on small sample size [19]. Likewise, studies assessing the impact of obesity on iron status during pregnancy did not consider the potential effect of the expected ID on erythropoiesis [10].

In this study, we assessed the association between high BMI and ID in pregnant Sudanese women. Also, the prevalence of IDA was evaluated in different BMI categories to judge the impact of ID on

erythropoiesis. The findings of the present study are expected to give more insight about iron homoeostasis in obese pregnant women and to help health care providers in planning the proper intervention during antenatal visits.

Material and Methods

A cross-sectional study was conducted at Saad Abualila Maternity Hospital (Khartoum, Sudan) during the period January–April 2015. This is a tertiary hospital governed by the Faculty of Medicine, University of Khartoum. After signing an informed consent, eligible women were enrolled in the study. Inclusion criteria were: women with singleton pregnancy, at their early pregnancy (< 14 weeks of gestation), and willingness to participate in the study. Women with diabetes mellitus, thyroid disease, hypertension or any other chronic disease were excluded from the study. Obstetrics and medical history (age, parity, and gestational age) were gathered by a trained medical officer. Weight and height were measured, and BMI was calculated and expressed as weight in kilogrammes divided by the square of height in meters. The complete maternal hemogram with blood cell count was measured for all women, using an automated haematology analyser (Sysmex KX-21, Japan). Based on BMI, women were categorized into four groups: underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥ 30 kg/m^2). This classification follows the world health organisation, which addresses obesity during pregnancy as well as the general population [20]

Five ml of venous blood were taken from each participant, allowed to clot, centrifuged, and stored at −20°C until analysed. Serum ferritin was measured using radioimmunoassay gamma counter (Riostad, Germany) and kits provided by Beijing Isotope Nuclear Electronic Co., Beijing, China.

A total sample size of 430 participants was calculated using the previous incidence of obesity (19.4%) and incidence of IDA (29.4%) among pregnant women in Sudan [2], [21]. A formula was used to calculate the rate of iron deficiency in the obese and normal weight women, that would provide 80% power to detect a 5% difference at α = 0.05, with an assumption that complete data might not be available for 10% of participants**.**

Statistics

SPSS for Windows (version 20.0) was used for data analyses. Studied variables were described with means (M), standard deviations (SD), median and interquartile. Proportions of the studied groups were expressed in percentages (%). The difference of the continuous variables was compared between BMI groups using ANOVA when normally distributed (age, parity, gestational age, haemoglobin). Kruskal –Willis test was used for abnormally disturbed variables (serum ferritin). Linear regression analyses were performed, where BMI was the dependent variable and age, parity, gestational age, haemoglobin, and serum ferritin were the independent variables. P < 0.05 was considered statistically significant.

Ethics

The study received ethical clearance from the Research Board at the Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Khartoum, Sudan.

Results

General characteristics of the 423 enrolled women are shown in Table 1. Around two fifths (176, 41.6%) of the women were primiparae. The mean (SD) of the age, parity and gestational age was 26.1 (6.2) years, 1.7 (2.2) and 10.7 (3.1) weeks, respectively.

Table 1: General characteristics of Sudanese women in the current study in their early pregnancy

Variable *The mean (SD) of*	N = 423
Age, years	26.8 (6.2)
Parity	1.7 (2.2)
Gestational age, weeks	10.7(3.1)
Body mass index kg/m^2	26.6(3.7)
Haemoglobin, gm/dl	10.5(0.8)

Two (0.5%), 126 (29.8%), 224 (53.0%) and 71 (16.8%) out of the 423 women were underweight, normal weight, overweight, and obese, respectively.

Anaemia (Hb <11 g/dl) and iron deficiency (ferritin <15µg/l) were prevalent in 57.7% and 21.3% of the study sample, respectively. Of the total sample, 12.1% had iron-deficiency anaemia.

Although, there was no significant difference in the hemoglobin level and the other haematological parameters e.g. haematocrit (HCT), mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) between women with normal BMI, underweight, overweight and obese, the median (interquartile) of serum ferritin level was significantly lower in obese compared with women with normal BMI, Table 2.

Compared with the women with normal BMI, significantly fewer obese women were anemic (25

[35.2%] vs. 108 [85.7%], P < 0.001) and significantly higher number of obese women (25 [35.2] vs. 22 [17.5], P = 0.015) had iron deficiency. There was no significant difference in the rate of iron deficiency anaemia (IDA) between women in the different BMI groups, Table 2.

Table 2: Comparison of socio-demographic, medical and obstetric characteristics between BMI groups among early-pregnancy Sudanese women

Variables	Underweight N (2)	Normal N (126)	Overweight N (244)	Obese N (71)	P
		The mean (SD)			
Age, years	19.5 (6.3)	24.9 (6.5)	26.7 (6.1)	26.4 (5.4)	0.021
Parity	1.0 (1.4)	1.7 (2.6)	1.9 (2.1)	1.6 (1.9)	0.724
Gestational age, weeks	10.0 (2.8)	10.6 (3.0)	10.7 (3.2)	11.0 (3.1)	0.798
Inter-pregnancy interval	-	20.4 (12.3)	11.4 (17.8)	17.7 (26.2)	0.007
Hemoglobin, gm/dl	11.1 (1.2)	10.4 (0.8)	10.5 (0.8)	10.5 (0.8)	0.628
		Median and interquartile			
Hematocrit,%	31.0 (30.0)	35.0 (32.1–37.5)	35.0 (32.2–37.1)	34.9 (32.2–37.1)	0.503
MCV, fl	82.9 (78.7)	83.3 (79.9–87.0)	83.6 (79.5–86.9)	82.3 (79.2–87.5)	0.990
MCH, pg	28.0 (25.7)	28.4 (26.6–30.1)	28.3 (26.3–30.0)	28.3 (26.2–30.0)	0.858
MCHC, g/dl	33.7 (32.7)	34.1 (33.0–35.0)	34.0 (33.0–34.8)	33.8 (33.0–34.9)	0.721
Ferritin, µg/l	89.5 (36.0–89.5)	39.0 (21.0–78.0)	28.6 (15.9–53.6)	24.0 (12.3–58.0)	0.010
		Number (%) of			
Education ≤ secondary level	2 (100)	91 (72.2)	153 (68.3)	40 (56.3)	0.076
Anemia	1 (50.0)	108 (85.7)	108 (48.2)	25 (35.2)	< 0.001
Iron deficiency	0 (0)	22 (17.5)	43 (19.2)	25 (35.2)	0.015
Iron deficiency anemia	0 (0)	19 (15.1)	24 (10.7)	8 (11.3)	0.619

Linear regression analysis demonstrated a significant negative association between serum ferritin and BMI (– 0.010 µg/, P = 0.006), Table 3.

Table 3: Linear regression analyses of the factors and body mass index in Khartoum, Sudan

Variables	Coefficient	Standard error	P
Age	0.099	0.033	0.003
Parity	– 0.167	0.090	0.063
Gestational age	0.068	0.057	0.230
Hemoglobin	0.098	0.217	0.650
Serum ferritin	– 0.010	0.004	0.006

Discussion

It is evident from the current findings that prevalence of anaemia and ID showed different trends in relation to BMI of pregnant women. According to the present results, anaemia is less common in overweight and obese pregnant women in spite of predominance of ID among these categories. Interestingly, the higher prevalence of ID among overweight and obese pregnant women does not induce a significant reduction of HCT, MCV, MCH and MCHC in these groups.

The association between high BMI and ID was documented in several previous reports [7, 9, 16, 22, 23], but not others [14, 18]. An inverse relationship between iron level and BMI was repeatedly demonstrated among children and adolescents [7, 16, 22, 23]; however, comparable studies in adults showed non-reproducible results [14, 18, 24].

In 321 children and adolescents, ID was noted in 38.8%, 12.1% and 4.4% of the studied obese, overweight and normal-weight subjects, respectively. In comparison, the percentages of IDA were 6.7%, 35% and 58.3% in the respective groups [7]. Similar findings were reproduced in at least three separate Iranian [16], Chinese [23] and Mexican [25] studies. Also, the cross-sectional data obtained from National Health and Nutrition Examination Survey III (1988-1994) confirms a twice risk of ID in high compared with low BMI children [22].

In adults, ID was documented among other micronutrient deficiencies in morbidly obese patients before bariatric surgery [8, 24]. A meta-analysis study evaluating iron status among overweight/obese subjects demonstrated an intimate relationship between ID and obesity, though haemoglobin level was higher in obese compared to normal weight adults [13]. The association analysis of the same study showed significant differences between studies investigating subjects under 18 years of age (Odds ratio = 1.78) and subjects 18 of age and older (Odds ratio = 0.92). This finding was further supported by Ogata *et al.,* who failed to demonstrate significant differences in iron concentration between obese and normal weight adult subjects [18]. In a separate study, decreased serum iron level was validated in overweight women, but not men [14].

High prevalence of ID among overweight/obese children and adolescents was attributed to insufficient iron intake, increased physical growth and blood volume in these age groups [7, 12, 25]. Alternatively, studies exploring iron homoeostasis in obese women [11] and children [26] also demonstrated impaired iron absorption and consequently poor response to iron fortification. There are repeated evidence that impaired absorption of iron from the gastrointestinal tract (GIT) is secondary to increased expression of hepcidin [15, 17], which is a major inhibitor of iron absorption from GIT in humans [27]. Hepcidin was proved to correlate positively with leptin in iron deficient obese children, even after adjustment for possible confounders like BMI [15]. This suggests that enhanced hepcidin production, and consequently disturbed iron metabolism, is probably secondary to associated high leptin levels in obese subjects. Another hypothesis attributes high hepcidin levels to the mild inflammation associated with obesity [28].

The normal trend for hepcidin levels is to decrease progressively from the first to the third trimester [29]; however, the reverse was proved in obese pregnant women [10]. On the other hand, iron transfer across the placenta is enhanced during pregnancy even if maternal iron stores are depleted [30]. Studies on animal models [30] as well as humans [31] confirmed increased iron transfer across the placenta in ID states, probably secondary to enhanced expression of placental transferrin receptor 1 (pTFR1). This suggests that iron metabolism during

gestation is biased toward keeping an adequate iron supply to the fetus, even if mother iron stores were depleted. Based on the above narrative, the conjunction of increased hepcidin levels and pTFR1 expression is a likely explanation for ID in the obese pregnant women we studied. However, this hypothesis remains for further investigation by the researchers in the field.

Interestingly, the higher prevalence of ID among overweight and obese pregnant women we studied does not induce a significant reduction of HCT, MCV, MCH and MCHC in these groups. It was hypothesised that low grades of iron depletion might be asymptomatic [32] but progress gradually to iron-deficient erythropoiesis [33], and eventually IDA [33, 34]. Lack of significant reduction in red blood cells indices among obese pregnant we studied may be indicative of lower grades of ID in this group.

Noteworthy, hepcidin and pTFR1 levels were not estimated in the present report, which constituted potential study limitations. Evaluation of these parameters in future researches can help in a better understanding of the pathophysiology of ID among obese pregnant women.

The current findings obviously demonstrate paradoxical variations in the prevalence of anaemia and ID in obese pregnant women. Anaemia is infrequent in overweight and obese pregnant women in spite of their high risk of ID. The higher prevalence of ID among overweight/obese pregnant women we studied did not induce a significant reduction in red blood cells indices, suggesting lower grades of ID in these groups.

In conclusion, further studies that also evaluate hepcidin and pTFR1 levels are desirable for a better understanding of the pathophysiology of ID among obese pregnant women.

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