Is Childhood Obesity Associated with Iron Deficiency Anemia?

Original Article

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Abstract:

Background: The prevalence of obesity is increasing and many countries are struggling with its high rate and serious complications. As a result of distinct diet in obese children, they may be susceptible to nutritional deficiencies in particular, iron deficiency. This study aimed to examine the relationship between obesity and iron indices.

Methods: In this cross-sectional study, 206 elementary school students were selected by stratified random sampling. Anthropometric parameters (waist circumference and body mass index) were measured and fasting venous blood was collected to test serum iron, ferritin, transferrin saturation and complete blood count. To recognize the association between obesity and anemia, data were entered to SPSS and Lisrel software and analyzed using appropriate related test.

Results: It was revealed that waist circumference was negatively associated with levels of serum iron and transferrin saturation ($p<0.05$). In contrast, the highest waist circumference was positively and significantly related to higher levels of TIBC ($p<0.05$) compared to normal-weight children. Generally, it was concluded that waist circumference was significantly related to total iron binding capacity and serum iron levels ($p<0.05$). Similar negative significant associations were observed among children with an increase in body mass index and transferring saturation. Central and general obese children were more likely to have iron deficiency with and without anemia.

Conclusion: This study suggests that the higher levels of total and central obesity should be taken into account when assessing the children’s body iron status and should be treated before providing dietary recommendations to correct anemia.

Key Words: Iron Deficiency, Anemia, Obesity, Overweight, Children.

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Introduction:

Obesity is a growing global health problem; the prevalence of this condition has increased dramatically in recent years [1, 2]. Generally, it can be claimed that, 16-31% of children are suffering from obesity nowadays [2, 3]. One of the major causes of obesity is the rapid changes in lifestyles and dietary patterns, namely, from traditional to new diets, a drastic shift which heralded large amounts of fat, sugar and oil [4-6]. Incorrect eating habits along with a sedentary lifestyle can lead to overweight and obesity among children and adolescents [5, 7]. The results of the studies conducted in Iran fully illustrate the prevalence of 7-16% of this problem among children, which is almost three times higher than the last three decades [8, 9]. Obese children are not only susceptible to complications such as hypertension, dyslipidemia and type 2 diabetes but also exposed to a variety of micronutrient deficiencies due to poor diet caused by the consumption of foods high in calorie but low in nutrients [10,11].

Furthermore, overweight and obesity, as low-grade inflammatory diseases, can lead to transformation of iron metabolism, tissue iron overload, mobility decline and subsequently reduce the breakdown of myoglobin and a decrease in serum iron for hematopoiesis [12-15]. Iron deficiency anemia is the most prevalent nutrition problem in the world [2, 16] that may increase not only the risk of behavioral disorders and learning problems but also the cognitive delays among children [2, 17].

This issue has been at the helm of health problems therefore, many countries applied iron deficiency anemia screening program for students (especially for girls) to their school curriculum. According to the classification of World Health Organization (WHO), the prevalence of iron deficiency anemia is in the medium level [18]. It is estimated that approximately 18-38% of children under 5 years are suffering from iron deficiency anemia [19].

Some studies showed that obese people are almost two times more likely to be diagnosed with iron deficiency and iron deficiency anemia is significantly higher among obese than normal weight people. Studies also introduced the most common age of this problem as 12-16 years old [20-22]. In addition, obese girls usually grow faster, thus they reach to puberty at an earlier age than the rest of the girls. Therefore, the possibility of saving iron is reduced [23].

However, the hypothesis was also presented about the relationship of iron deficiency and anemia, with overweight and obesity. This study examined the relationship between overweight and obesity indicators with serum iron indices, with the objective to identify and screen high-risk groups using careful planning for this problem an achievable possibility.

Methods:

Sample Collection

This cross-sectional study was conducted on elementary children who were selected using stratified random sampling in 2011 in Babol, Mazandaran, Iran. The population under study included 9-11 year-old children in rural and urban areas of Babol. From 250 children who took part in this study, only 44 students were excluded due to the unavailability of their blood samples and the rest, 206 students, were as test subjects. The exclusion criteria were: (i) any disorder, such as liver disease, cardiac disease, chronic GI disease, heart disease, chronic hematologic disorders except iron deficiency (with or without anemia), (ii) vitamin or mineral supplements taken regularly during the previous year.

Anthropometric Assessment

Information about weight, height, and waist circumference (WC) was recorded by a trained research team and school health teacher under standard protocol using zero calibrated instruments. The anthropometric assessment included weight, height, and WC. Weight was measured with the use of digital scale (Omron BF-511 model) with a precision of 0.1 kg and height was measured with the use of SECA height gauge with an accuracy of 0.5 cm in a standing position without shoes and keeping the shoulders in a relaxed position. WC was measured using a non-elastic tape with an accuracy of 0.1cm at the midpoint of the lower end of the rib cage and top of the iliac crest in a standing position. Body Mass Index (BMI) was calculated weight (kg)/(height (m)) ^{2}. BMI was considered as a criterion to assess total obesity and WC to assess central or abdominal obesity. The assessment of obesity with BMI index using the CDC2000 reference percentile was divided into four categories 5^{th}, 50^{th} , 85^{th} and 95^{th}, namely; underweight, normal, overweight and obese respectively [24]. According to CDC 2000, for WC 95^{th} percentile was considered as a cut-off point for central or abdominal obesity [24].

Iron Status Indicators Measurement

The blood samples were collected and hematological variables were measured by trained technician in Rouhani Hospital and interpreted by specialist. About 5 cc of fasting blood were taken to evaluate the serum iron, ferritin, total iron binding capacity (TIBC), and about 2cc citrated fasting blood sample were evaluated for complete blood count (CBC) which were analyzed according to standard protocols. Photometric method was used to measure the serum iron level with a standard detection kit (Pars Azmoon) while ferritin level was measured by ELISA method using Eleccsys kits with electrochemilisance device. Iron Deficiency (ID) and Iron Deficiency Anemia (IDA) were defined according to WHO criteria [25]. ID was defined as Transferrin Saturation (TS) lower than 16% and IDA was defined as TS lower than 16% and hemoglobin (Hb) concentration lower than 120 g/l or 12 mg/dl for children.

Dietary Iron Intake

Iron intake data were obtained by trained nutritionists using a 24-h recall questionnaire for two days; one weekday and one weekend day. The

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interview was conducted in the presence of children's mothers. The diet records were coded and entered into Nutritionist IV diet analysis software. Iron intake was calculated from the food quantities intake.

Statistical Analysis

The data were imported to SPSS-18 software and for all data normal distribution was tested in histogram and Kolmogorov-Smirnov. Independent sample t-test, one way ANOVA, and Linear Structural Relations method (LISREL) 8.80 were applied to assess the association of BMI and WC with hematological indicators. Binary logistic regression analysis was conducted and adjusted OR with 95% CI was computed. P-values<0.05 and t-value>1.96 were considered as the level of threshold for statistical significance. The project protocol was approved by the Ethics Committee of Babol University of Medical Sciences and all subjects' parents signed an informed consent form.

Results:

Out of 206 participants, 98 (47.6%) and 108 (52.4%) persons were boys and girls, respectively. Totally, children consumed 8.08±40.27 mg/1000 kcal/day dietary iron. The daily dietary iron intake was higher in boys (8.09±44.81 mg/1000kcal/day) than girls (7.20±35.64 mg/1000kcal/day), but this difference was not significant. Furthermore, no significant differences of dietary iron intake were found with BMI and WC. Based on the location, 42.5% of pupils live in urban areas and 57.2% in rural areas. According to the CDC2000, the study population included 17.5% overweight and 21.8% obese (Table 1). The prevalence of obesity was higher in girls than boys (24.1% vs. 19.4%). Furthermore, the mean of WC in boys was higher than that in girls (68.2±14.2 vs. 67.9±13.3). No significant differences were found between boys and girls with respect to anthropometric and biochemical characteristics (Table 1). However, it was shown that low serum iron levels were significantly higher in boys than girls (28.3% vs. 2.4%, p<0.001). The prevalence of ID and IDA was 30.7% and 11.7%, respectively that the prevalence of ID and IDA was higher among girls than boys (34.0% vs. 27.3% in ID; p = 0.4 and 14.2% vs. 9.1% in IDA; p=0.3).

In the model made by LISREL, χ^2/df ratio was less than 3 and root mean square error of approximation (RMSEA) as a best indicator to assess goodness-of-fit test was less than 0.08. In addition, other indicators include normed fit index (NFI)=0.91, root mean square residual (RMR)=0.06, normed-fit index (NFI)=0.91, non-normed fit index (NNFI)=0.93, comparative-fit index (CFI)=0.95, adjusted goodness-of-fit index (AGFI)=0.91, incremental-fit index (IFI)=0.95, and relative fit index (RFI)=0.88 showed that the fit of this model was strongly acceptable.

Generally, it was learned that TIBC level would enhance with the increase of BMI (beta=0.212, t=2.896); moreover, results depicted that serum iron level and TS had inverse associations with BMI (beta=-0.236, t=-3.239; beta=-0.261, t=-3.605, respectively) while RBC had a positive association (beta=0.161, t=2.179), yet BMI showed no significant relationship with hemoglobin and serum iron. As Figure 1 (A) displays, serum iron (beta=-0.189, t=-2.544) and TS (beta=-0.222, t=-3.012) were negatively related to waist circumference; in other words, they were higher among the thin and normal weight than in the centrally overweight and obese ones. As a consequence, in pupils TIBC showed positive relationship with WC (beta=0.219, t=2.975) (Figure 1 A, B).

Moreover, the prevalence of ID was higher in overweight boys (53.8%) and girls (60.0%) compared to their obese (50.0% and 31.8%) and normal weight (27.6% and 35.9) peers (P=0.05 in boys and P=0.25 in girls). Similarly, the prevalence of IDA was higher in overweight boys and girls than in obese or normal weight boys and girls (P= 0.03 in boys and p=0.02 in girls). The prevalence of ID and IDA was significantly higher in the highest tertile (50.0% and 25.0%, respectively) than in the lowest tertile (14.7% and 2.9% respectively; p=0.02) of WC in boys. Furthermore, girls in the highest tertile of WC exhibited higher prevalence of both ID and IDA (45.2% and 25.8%, respectively) than girls in the lowest tertile (35.5% and 9.7%, respectively) but it was not significant (P>0.05). The logistic regression analysis showed that overweight and obese boys were 3.48 (95% CI, 1.29-9.34) times more likely to be iron deficient than normal weight and it was significant even after adjustment for iron intake (Table 2). Furthermore, in boys the middle tertile of WC was 5.8 (95% CI:1.59-21.11) times more likely to be iron deficient in comparison with boys in the lowest tertile. Overweight and obese girls and boys were 2.69 (95% CI: 1.09-8.43) and 5.90 (95% CI: 1.32-26.30) times more likely to have iron deficiency anemia than normal weight. Additionally, boys in the middle tertile of WC were 11.2 (95%CI: 1.17-106.9) times more likely to have iron deficiency anemia than lowest tertile (Table 2).

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Table 1. Descriptive characteristics of the study population

Characteristics	Girls	Boys	Total
weight status(kg/m^2)			
Underweight (%)	24 (22.2)	17 (17.3)	41 (19.9)
Normal (%)	40 (37.0)	44 (44.9)	84 (40.8)
Overweight (%)	18 (16.7)	18 (18.4)	36 (17.5)
Obese (%)	26 (24.1)	19 (19.4)	45 (21.8)
WC (cm)(mean ±SD)	67.9±13.3	68.2±14.2	68.1±13.7
Biochemical indices (mean ±SD)			
RBC (million/µ l)	5.1±3.6	4.7±0.5	4.92±2.6
Hemoglobin (g/dl)	12.5±0.9	12.4±1.1	12.4±1.0
Hematocrit (%)	37.7±2.2	36.9±3.8	37.3±3.1
MCV(fl)	79.9±4.9	78.1±9.2	79.04±7.3
MCH(pg/cell)	26.5±2.3	26.3±3.0	26.4±2.6
MCHC	33.2±1.4	34.3±9.5	33.7±6.6
Iron (µg/dl)	69.2±31.4	74.8±29.6	71.8±30.6
Ferritin (µg/dl)	50.8±29.5	57.4±47.2	53.9±38.9
TIBC (µg/dl)	351.6±35.9	352.3±45.8	351.9±40.7
TS (%)	21.7±9.6	20.1±10.2	20.8±9.8

WC: Waist Circumference; Mean Cell Volume (MCV); Mean Corpuscular Hemoglobin (MCH); Mean Corpuscular Hemoglobin Concentration (MCHC); TIBC: Total Iron Binding Capacity TS: Transferrin Saturation; All differences were not significant p>0.05.

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Table 2. Risk for iron deficiency with and without anemia among children with different BMI and waist circumference.

	Girls (n=108)				Boys (n=98)			
	Crude		Model 1§		Crude		Model 1§	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
ID								
BMI groups								
Normal	1.00		1.00		1.00		1.00	
Overweight and obesity	1.48	0.63-3.45	1.50	0.64-3.52	3.48	1.29-9.34*	3.49	1.28-9.49*
Waist circumference tertiles								
Lowest tertile	1.00		1.00		1.00		1.00	
Middle tertile	1.49	0.54-4.15	1.51	0.54-2.25	5.8	1.59-21.11*	5.70	1.53-21.2*
Highest tertile	1.72	0.62-4.72	1.75	0.63-4.83	2.0	0.61-6.55	1.96	0.57-6.65
IDA								
BMI groups								
Normal-weight	1.00		1.00		1.00		1.00	
Overweight and obesity	2.83	1.18-8.78*	2.69	1.09-8.43*	5.89	1.34-25.9*	5.90	1.32-26.30*
Waist circumference tertiles								
Lowest tertile	1.00				1.00		1.00	
Middle tertile	3.24	0.77-13.66	3.10	0.73-13.18	11.0	1.18-102.5	11.2	1.17-106.9*
Highest tertile	2.60	0.69-9.47	2.43	0.64-9.21	4.16	0.17-24.2	4.25	0.70-25.8

ID: Iron Deficiency; IDA: Iron Deficiency Anemia; Adjusted for Iron intake; p-value<0.05 was considered significant.

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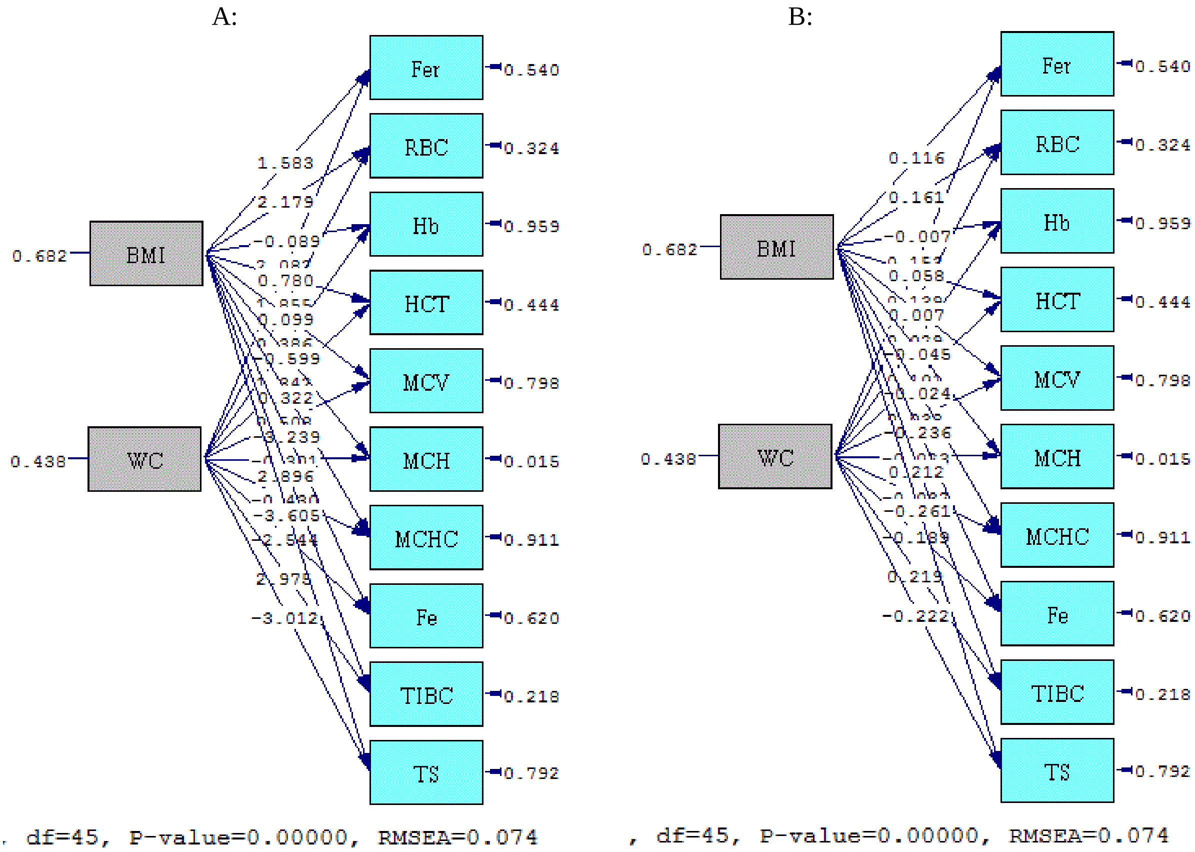

BMI: Body Mass Index; WC: Waist circumference; Fer: ferritin; RBC: Red Blood Cell; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean Cell Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; Fe: serum Iron; TIBC: Total Iron Binding Capacity; TS: Transferrin Saturation.

Figure 1. Relationship of BMI and waist circumference with Hematological factors: Beta coefficient [A] and T-value [B].

Discussion:

The present study examined the association of total and central obesity with biochemical indices of iron status in a representative sample of children in Babol. This study also illustrates that there is a statistically significant negative correlation between BMI and serum iron levels that is consistent with the study of Chambers et al.'s in which they have reported lower iron levels in obese individuals [21].

In a study conducted in the United States on 2 - 16 years old children, the prevalence of iron deficiency in overweight or at risk of overweight was two times higher than normal weight children [22]. In contrast, Keikhaei et al.'s (2012) in their study did not find a clear difference in serum iron levels with different levels of BMI among boys and girls [20].

On the other hand, some other studies concluded that the significant relationship between obesity and iron deficiency can be attributed to a combination of nutritional and functional parameters as well as genetic influence, lack of physical activity, and an increase in hepcidin concentration, reduce in iron intake, increase in needs for iron and disorder in iron absorption in obese subjects and break less myoglobin and subsequently a decrease in the release of iron in the blood, poor diet and less iron-rich foods [22,26,15].

In the current study, significant negative correlation was observed between TS and obesity. A similar result was found among 5-12-year–old Mexican obese children with lower TS percentage (r = -0.07, p = 0.07) than the normal-weight group and the same result was found by Moschonis et al.'s 2011 [27, 28]. In contrast to other studies that have reported an association between serum ferritin levels and BMI [29, 30], the current study has not found any significant association of ferritin in children with different levels of BMI. Based on our findings, the children showed significant increase in ferritin and TIBC along with an increase in WC from normal to central obesity. In particular, pupils with the highest visceral fat mass had significantly lower TS than their peers with the lowest visceral fat mass. This

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was also true with serum iron. Similar to our study, the study on 9-11-year-old children showed that TS in central obese boys was significantly lower compared to subjects with normal WC [27].

Obesity can lead to an increase in ferritin levels as an acute phase reactant due to the chronic inflammation in the body. The increase in hepcidin production in response to inflammation caused by obesity may be responsible for the increased ferritin level and serum iron reduction [31].

It is hypothesized that with an increase in serum ferritin level, when the body iron stores are high, the hepcidin secretion will increase, and may cause a reduction in intestinal absorption of iron with an unknown mechanism; whereas when the body iron stores are low, the hepcidin production will decrease to enhance intestinal iron absorption [32]. However, it is necessary to confirm the relationship to investigate the etiologic mechanisms in future studies.

In our study, the prevalence of ID and IDA was 30.7% and 11.7% respectively and this prevalence was higher among girls than boys; however, the differences were not significant. These results were much higher than the research in south of Iran [20] that showed 4.6% and 6.0% of adolescents were iron deficient with and without anemia, respectively. But our results were in agreement with a study in the western part of Iran (23.7% ID and 12.2% IDA) among the older age group [33]. In addition, in our study obese boys were more likely to have iron deficiency and also the probability of IDA was higher in male pupils with central and overall obesity but it was not significant among girls even after adjustment for iron intake. In contrast to our study, a study by Moschonis et al.'s showed higher probability of IDA and ID among obese boys and girls. The result of our study was in consistent with other studies [25, 34-35, 15]. Greek study indicated that the reason of iron deficiency among adolescents was the lower intake of iron compared with non-obese peers [36] while our study did not show any significant differences between central/general obesity and iron intake. Besides, other studies concluded that the reason of this problem related to the increased hepcidin level that leads to the decrease of iron absorption even after oral iron therapy [35, 15]. Furthermore, general and central obesity stimulates the inflammatory cytokines that were associated with suppression of serum iron level [34, 37]. Ferritin as a protein can increase during inflammation [38] therefore, the results are in consistent with our study, higher levels of serum ferritin among overweight and obese children were observed [27, 34].

The existing study has certain strengths and limitations. With regard to its strengths, despite various publications on the relevance of this topic, to the best of our knowledge based on the available literature, only a few studies have examined the relationship between total and central obesity and iron status among children in Iran particularly in the north of Iran. Additionally, this study relates to the fact that detailed data on blood and anthropometry were collected and such studies can explore a more accurate association between obesity and anemia in children and highlight the further discussion of dietary recommendations on iron intake. The current study is cross-sectional study and because of this it has its own limitation related to the method which cannot determine the causality.

The results of this study highlight the high prevalence of iron deficiency and also illustrate that the obese children have lower levels of serum iron and transferrin saturation than non-obese children. These associations can have important public health implications and these findings can be justified by chronic inflammation caused by obesity. Since central obesity has contradictory effects on serum ferritin, it is one of the most important criteria for iron deficiency. Therefore, total and central obesity should be taken into consideration when assessing children's body iron status and should be treated before providing dietary recommendations to correct anemia. It is suggested to conduct subsequent case-control studies and studies with a larger sample size and a wider age range should be done.

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