The relationship between BMI and iron status in iron-deficient adolescent Iranian girls

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Abstract

Objective: Many Iranian adolescent girls are Fe-deficient, but it is unclear whether Fe deficiency is associated with other nutritional risk indicators. The present study aimed to investigate the association between Fe deficiency and weight status (measured as BMI) among a representative sample of adolescent girls.

Design: A cross-sectional study. Fe-deficient high-school girls (with or without anaemia) were selected by systematic random sampling among all students in grades 1 to 4 from high schools for girls. Blood samples were collected and analysed for Hb, haematocrit, serum ferritin, Fe and total Fe binding capacity. Weight and height were measured. BMI was calculated and compared with age- and gender-specific BMI reference values.

Setting: South Iran.

Subjects: A total of 431 adolescent girls aged 13–20 years.

Results: Some 15·3% of the participants were at risk for overweight and 9·5% of them were overweight. An inverse association was found between serum ferritin and BMI (r = −0·38, B = −0·21, P < 0·001). Anaemia was more prevalent among overweight Fe-deficient adolescents than among those Fe-deficient and at risk for overweight or normal weight (34·1% v. 28·8% v. 27·8%, respectively; P < 0·001). Conclusions: An inverse association was found between BMI and serum ferritin. Overweight adolescents demonstrated an increased prevalence of Fe-deficiency anaemia. It seems that both abnormalities of weight and Fe status should simultaneously be targeted in overweight female adolescents.

Adolescence is a time of rapid growth and development, and nutrition plays an important role in during this life cycle stage. Healthy eating habits formed during childhood can persist into adulthood and can prevent premature onset of a number of morbidities(1). Nutritional surveys have shown that the highest prevalence of nutritional deficiency occurs during adolescence, with deficiencies of Ca, Fe, riboflavin, thiamin and vitamins A and C being the most common reported. Nutritional deficiencies and poor eating habits established during adolescence can have long-term consequences, including delayed sexual maturation, short adult stature, osteoporosis, dyslipidaemias and obesity(2). Iran experienced a rapid ‘nutrition transition’ during the 1990s. The implantation of Western lifestyles, especially the intake of energy-dense food with undesirable composition, increased consumption of animal fats and sugars and reduced consumption of dietary fibre, along with a lack of sufficient physical activity, has resulted in an increasing prevalence of overweight and obesity in Iranian children and adolescents(3). Existing evidence shows that these changes in the nutritional status of Iranian children and adolescents are similar to those that have occurred in other nations with faster-growing economies(4,5).

Interestingly, despite their excessive energy intake compared with expenditure, obese children and adolescents may be at risk of several micronutrient deficiencies, including Fe deficiency, as they tend to consume imbalanced meals with low nutrient density. In a US study, low-nutrient-density foods contributed more than 30% of daily energy intake, and micronutrient intake was inversely related to the intake of low-nutrient-density foods(6). Other work found that obesity was associated with poor dietary Ca intake in both adults and children(7).

A few small studies have noted a possible association between Fe deficiency and obesity. Two epidemiological studies published in the early 1960s noted an association between overweight status among children and adolescents and Fe deficiency(8,9). A more recent cross-sectional study found that overweight children and adolescents
exhibited lower Fe levels; of those with Fe-deficiency anaemia, more than 50% had BMI >97th percentile\(^{(10)}\).

Fe deficiency results in increased sympathetic activity, as evidenced by increased plasma and urinary catecholamine concentrations\(^{(11,12)}\), increased turnover rates of noradrenaline in sympathetically innervated tissues and decreased tissue noradrenaline content\(^{(13,14)}\). One study\(^{(15)}\) has confirmed findings on Fe deficiency, where increased sympathetic nervous system activity\(^{(11,12)}\) was coupled with overt hypothyroidism\(^{(16)}\). Thyroid hormones have been indicated to have at least a permissive role in adaptive thermogenesis by influencing several aspects of energy metabolism, such as substrate cycling, ion cycling and mitochondrial proton leaks\(^{(17)}\). Whether a deficit in resting energy expenditure plays a role in the development of weight gain leading to obesity is matter of debate\(^{(18)}\).

Therefore, in order to evaluate a possible association between BMI and Fe status among Fe-deficient Iranian adolescent girls, we conducted a cross-sectional study using representative data from high-school adolescent girls in southern Iran, where Fe deficiency is quite prevalent\(^{(19)}\).

**Materials and methods**

**Participants**

A cross-sectional study was carried out in the city of Lar and its suburbs in southern Iran (altitude: 800 m above sea level), an area with a high prevalence of Fe deficiency. The study was conducted among female students studying in eight high schools. In total, 1,431 Fe-deficient students (with or without anaemia) were selected using systematic random sampling from among 2038 students in grades 1 to 4. Inclusion criteria were: (i) the absence of any systemic disease, except Fe deficiency (with or without anaemia), defined as Hb <12 g/dl, serum ferritin <12 \(\mu\)g/l and transferrin saturation <16%; (ii) serum albumin within the normal range (3.5 to 5.5 mg/l); (iii) age within the range of 13 to 20 years; and (iv) no vitamin or mineral supplements taken regularly during the past year. Data were collected by trained interviewers.

**Anthropometric measurements**

Anthropometric assessment included measurements of weight, height, waist and hip circumferences. All anthropometric measurements were obtained by a trained person and supervised by the investigator. Body weight was measured to the nearest 0.1 kg using a Seca 713 scale while participants were minimally clothed. Height was measured without shoes to the nearest 0.2 cm using a wall-mounted tape. Subsequently BMI was calculated by dividing weight by the square of height (kg/m\(^2\)). Waist circumference was measured midway between the lower hip margin and the iliac crest. Hip circumference was measured at the largest circumference (with undergarments)\(^{(20)}\). Waist-hip ratio (WHR) was calculated as the ratio of waist to hip circumferences. BMI-for-age was classified according to the US National Institutes of Health (NIH) data for age and gender\(^{(21)}\). Those with a BMI-for-age \(\geq\)85th percentile but <95th percentile were classified as at risk of overweight. BMI-for-age \(\geq\)95th percentile was used to define overweight and identify those children and adolescents with a significant likelihood of persistence of obesity into adulthood. Those students with BMI-for-age <5th percentile, and >5th percentile but <85th percentile, were defined as underweight and normal weight, respectively.

**Biochemical analyses**

A fasting venous blood sample (10 ml) was drawn from each participant. Blood was collected in two tubes and analysed for Hb, haematocrit, serum albumin, serum Fe, total Fe binding capacity (TIBC) and serum ferritin. Fe deficiency was defined as serum ferritin concentration <12 \(\mu\)g/dl and transferrin saturation <16%; anaemia was defined as Hb level <12 g/dl according to the WHO cut-off point\(^{(22)}\). Hb was measured using the cyanomethaemoglobin method\(^{(23)}\). Serum Fe, TIBC and albumin were measured by a colorimetric method\(^{(24)}\) (lots no. 11-514, 12-515 and 10-502, respectively; Zist Chimbie Company, Tehran, Iran). The within-run and between-run assay CV (%) for serum ferritin, Fe and Hb were 2.63 and 4.12, 2.3 and 3.8, 3.1 and 4.9, respectively. Transferrin saturation was calculated as serum Fe divided by TIBC multiplied by 100. Serum ferritin was determined by RIA\(^{(25)}\) using commercially available kits (Diagnostic Systems Laboratories, Inc., Webster, TX, USA).

**Statistical analysis**

Data processing and statistical analyses were done using the SPSS for Windows statistical software package (SPSS Inc., Chicago, Il, USA, 2001). Normally distributed data are expressed as means and standard deviations, and differences between group means were tested using one-way ANOVA with Tukey’s post hoc test when ANOVA was significant. A simple linear regression model was used to test for possible association and multiple linear regression analysis using stepwise methods was performed to determine the most significant predictors of change in serum ferritin concentration. A \(P\) value \(\leq0.05\) was considered statistically significant.

**Ethics**

The study protocol was reviewed and approved by the Human Ethics Committee of the Research Council, Tehran University of Medical Sciences, Tehran, Iran. Participants’ parents and/or guardians were asked to read and sign an informed consent document.

**Results**

Overall, 431 students constituted our sample population. Age and BMI of the studied students ranged from 13 to
20 years and 14±80 to 31±24 kg/m², respectively. According to the criteria of the Centers for Disease Control and Prevention (26), the haematological indices of Fe status showed that all participants were Fe-deficient (Table 1). In order to compare anthropometric characteristics at different BMI values, we categorized all participants into four groups. As Table 2 shows, according to NIH BMI cutoffs, 7±6% of the adolescent girls were underweight and 24±8% were overweight and at risk of overweight. Overweight and obesity were more prevalent among older than younger adolescents. A similar trend was observed for WHR.

Haematological parameters in different categories of BMI are shown in Table 3. Mean transferrin saturation and serum ferritin concentrations in the overweight adolescents (13±1 (SD 0±3)% and 7±8 (SD 0±7) μg/l, respectively) were significantly lower (P<0±001) than in the adolescents at risk for overweight (13±9 (SD 0±6)% and 10±3 (SD 0±6) μg/l, respectively), and also significantly (P<0±001) lower than in the normal weight adolescents (14±5 (SD 0±8)% and 11±5 (SD 0±3) μg/l, respectively). The highest prevalence of Fe-deficiency anaemia in our sample was observed in overweight adolescents.

Further analysis into the changes in serum ferritin concentration in these participants was carried out using multiple regression analysis in which the independent variables were age, weight, height, BMI and WHR. It was found that only BMI contributed significantly to serum ferritin concentration (r=-0±38, β=-0±21, P<0±001; Fig. 1), i.e. adolescents with higher BMI had lower Fe stores.

### Discussion

Adolescence is characterized by a growth spurt and the acquisition of adult phenotypes and biological rhythms. During this period, Fe requirements increase dramatically in both boys and girls as a result of the expansion in total blood volume, the increase in lean body mass and the onset of menses in young females. The consequences of Fe deficiency are more serious for women. However, anaemia is only one manifestation of Fe deficiency; it can also impair physical endurance, immune response, temperature regulation, energy metabolism and cognitive performance (27).

As shown by national statistics on anaemia in Iran, the prevalence of Fe deficiency among females aged 15 to 49 years is almost 39±% (28). In the present study, 21±% of the

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>Range (SD)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>15±8 (1±4)</td>
<td>13±20</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64±3 (8±1)</td>
<td>53±5-78±0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155±5 (3±5)</td>
<td>139±177</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0±68 (0±90)</td>
<td>0±64-0±93</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>39±6 (6±1)</td>
<td>10±5-14±1</td>
</tr>
<tr>
<td>Serum ferritin (μg/l)</td>
<td>9±3 (1±3)</td>
<td>6±7-11±8</td>
</tr>
<tr>
<td>Serum Fe (μg/dL)</td>
<td>56±6 (1±8)</td>
<td>31±5-39±3</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>13±8 (0±9)</td>
<td>14±4-15±6</td>
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### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Underweight (n 33, 7±6%)</th>
<th>Normal weight (n 291, 67±5%)</th>
<th>At risk for overweight (n 66, 15±3%)</th>
<th>Overweight (n 41, 9±5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>15±4 (2±3)</td>
<td>16±1 (3±8)</td>
<td>16±8 (1±8)</td>
<td>17±1 (1±3)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>40±5 (2±9)</td>
<td>55±8 (3±6)</td>
<td>67±9 (2±1)</td>
<td>74±8 (1±1)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151±1 (4±0)</td>
<td>156±0 (4±3)</td>
<td>158±0 (3±6)</td>
<td>155±0 (2±3)</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0±67 (0±13)</td>
<td>0±69 (0±10)</td>
<td>0±79 (0±16)</td>
<td>0±88 (0±13)</td>
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### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Underweight (n 33)</th>
<th>Normal weight (n 291)</th>
<th>At risk for overweight (n 66)</th>
<th>Overweight (n 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>12±9 (0±4)</td>
<td>13±1 (1±1)</td>
<td>12±6 (0±7)</td>
<td>12±5 (0±5)</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>39±3</td>
<td>39±4</td>
<td>38±2</td>
<td>37±2</td>
</tr>
<tr>
<td>Serum ferritin (μg/l)</td>
<td>11±1 (0±7)</td>
<td>11±5 (0±3)</td>
<td>10±3 (0±6)</td>
<td>7±8 (0±7)</td>
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<tr>
<td>Serum Fe (μg/dL)</td>
<td>37±9 (1±3)</td>
<td>37±6 (1±8)</td>
<td>36±1 (2±6)</td>
<td>35±4 (3±1)</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>14±8 (0±3)</td>
<td>14±3 (0±8)</td>
<td>13±9 (0±6)</td>
<td>13±1 (0±3)</td>
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### Notes

a,b,c Mean values were significantly different (P<0±001) from those of the normal weight group, the at risk for overweight group and the underweight group, respectively.
adolescent female students were Fe-deficient, with or without anaemia. Although malabsorption and bleeding are regarded as two main causes of Fe deficiency, the overwhelming cause is dietary in origin.

The present study explored the hypothesis that serum ferritin concentrations might be lower among the obese as reported previously\(^{(10)}\). The prevalence of overweight or at risk for overweight among the Fe-deficient participants was almost the same as recent national rates\(^{(29)}\). However, Fe-deficiency anaemia was more prevalent among the overweight participants compared with the participants of normal weight or at risk for overweight. In the present study, 27.8% of adolescents in the normal weight group had low Hb levels. According to BMI classification, parallel with the increase in BMI, the rate and intensity of Fe-deficiency anaemia increased. On the other hand, regression analysis showed that there was a negative correlation between Fe stores and BMI, i.e. adolescents with higher BMI had lower Fe stores.

Iran has experienced a rapid nutrition transition in the last two decades, with a decrease in physical activity and increased energy and fat intakes. Increased obesity prevalence might therefore be expected\(^{(30)}\). So, the consistent and strong negative association between BMI and decreased serum ferritin concentrations may pre-sage a future increase in adult anaemia, if the prevalence of obesity keeps increasing.

Diverse hypotheses may explain this phenomenon. The urbanization that has taken place in recent decades has obliged children and adolescents to limit the time they spend outside. As urban violence has increased, they have learned to spend their leisure time on sedentary activities such as television watching, electronic games and computers. The combination of these factors coincided with the ever greater availability of wide variety of foods with high energy content and low Fe density to result in an epidemic increase in obesity and Fe deficiency in children and adolescents. Many children in Western societies now live on carbohydrate-rich, nutritionally imbalanced or inadequate food. This, together with increased fat intake, has led to increasing prevalence of obesity among children, and an epidemic of chronic Fe deficiency, particularly in many inner-city areas\(^{(31)}\). It is possible that Fe requirements are increased in obese adolescents because of their increased growth and body surface area\(^{(10)}\). In addition, animal studies have shown that Fe deficiency may reduce fatty acid metabolism through a reduction in carnitine levels\(^{(32)}\). This phenomenon can serve as another explanation for the increased prevalence of overweight and obesity in our Fe-deficient adolescents.

Many studies have shown that Fe deficiency is associated with decreased physical endurance and maximal exercise capacity\(^{(33)}\). Moreover, Fe deficiency in young women has been shown to impair adaptation to aerobic exercise\(^{(34)}\). Therefore, we can assume that poor exercise capacity of Fe-deficient adolescents can be a promoting factor for obesity. Kelishadi et al. showed that the rate of acceptable regular exercise and physical activity was not sufficient in adolescents in Iran, and trend analysis of regular exercise by adolescents did not show any improvement\(^{(35)}\).

In summary, during the past decades, great efforts have been made to decrease the prevalence of Fe-deficiency anaemia among female schoolchildren. But the intervention motivation and quality varies between regions and schools. This could be one of the explanations why Fe deficiency seems to be still a big nutritional problem in this area, especially among adolescents. On the other hand, our findings show that in parallel with the increase in body weight, the rate of Fe-deficiency anaemia increases. Causes may be poor quality of diet, increased Fe needs, poor exercise capacity related to Fe deficiency and poor access to sidewalks, parks and playground. Thus, public health interventions to improve the consumption of Fe-rich foods should be recommended in this setting. Fe fortification of suitable food vehicles, such as salt and bread, has been of value in geographical areas where Fe deficiency is a problem.

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