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Overweight Children and Adolescents: A Risk Group for Iron Deficiency

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ABSTRACT. ***Background.*** **The prevalence of obesity has increased at an epidemic rate, and obesity has become one of the most common health concerns in the United States. A few small studies have noted a possible association between iron deficiency and obesity.**

Objective. **To investigate the association between weight status, as measured by body mass index (BMI), and iron deficiency in a nationally representative sample of children and adolescents.**

Design. **National Health and Nutrition Examination Survey III (1988–1994) provides cross-sectional data on children 2 to 16 years of age. Recorded measures of iron status included transferrin saturation, free erythrocyte protoporphyrin levels, and serum ferritin levels. Children were considered iron-deficient if any 2 of these values were abnormal for age and gender. With the use of age- and gender-specific BMI percentiles, at risk for overweight was defined as a BMI of ≥85th percentile and <95th percentile, and overweight was defined as a BMI of ≥95th percentile. The prevalence of iron deficiency was compared across weight groups. Logistic regression was used to estimate the association between iron status and overweight, controlling for age, gender, ethnicity, poverty status, and parental education level.**

Results. **In this sample of 9698 children, 13.7% were at risk for overweight and 10.2% were overweight. Iron deficiency was most prevalent among 12- to 16-year-old subjects (4.7%), followed by 2- to 5-year-old subjects (2.3%) and then 6- to 11-year-old subjects (1.8%). Overweight 2- to 5-year-old subjects (6.2%) and overweight 12- to 16-year-old subjects (9.1%) demonstrated the highest prevalences of iron deficiency. Overall, the prevalence of iron deficiency increased as BMI increased from normal weight to at risk for overweight to overweight (2.1%, 5.3%, and 5.5%, respectively), and iron deficiency was particularly common among adolescents (3.5%, 7.2%, and 9.1%, respectively). In a multivariate regression analysis, children who were at risk for overweight and children who were overweight were approximately twice as likely to be iron-deficient (odds ratio: 2.0; 95% confidence interval: 1.2–3.5; and odds ratio: 2.3; 95% confidence interval: 1.4–3.9; respectively) as were those who were not overweight.**

Conclusions. **In this national sample, overweight children demonstrated an increased prevalence of iron deficiency. Given the increasing numbers of overweight children and the known morbidities of iron deficiency, these findings suggest that guidelines for screening for iron deficiency may need to be modified to include children with elevated BMI.** ***Pediatrics*** **2004;114:104–108;** ***overweight, iron deficiency, nutritional deficiency.***

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ABBREVIATIONS. NHANES, National Health and Nutrition Examination Survey; BMI, body mass index.

The prevalence of overweight among children and adolescents has been increasing at an alarming rate.[1,2] More than 1 of 7 children is overweight.[1] Data from the most recent National Health and Nutrition Examination Survey (NHANES) revealed a 3-fold increase in overweight prevalence in the past 3 decades, from ~4% to ~15% among children and adolescents 6 to 19 years of age.[3] In addition to the increased prevalence, the degree to which children and adolescents are overweight has changed dramatically. Data from the National Longitudinal Survey of Youth indicated a marked increase in the severity of overweight among children 4 to 12 years of age in the past 20 years.[2]

Iron deficiency remains the most common nutritional deficiency in the world. Iron deficiency has been linked to behavioral and learning problems among children[4–8] and adolescents,[9] increased risks for preterm infants and small infants among pregnant women,[10] and problems with work and exercise capacity among adults.[11,12] Screening for iron deficiency anemia among vulnerable populations, including infants 9 to 12 months of age, high-risk toddlers, and adolescent female subjects, is recommended by the Centers for Disease Control and Prevention[13] and the American Academy of Pediatrics.[14] However, according to the most recent NHANES data (1999–2000), the percentage of children with iron deficiency remains 2 to 5 percentage points above the 2010 national health objectives.[15] Identifying other groups at risk for iron deficiency could facilitate meeting 1 of the national health objectives for 2010, ie, reducing iron deficiency rates.

A few small studies have noted a possible association between iron deficiency and obesity. Two epidemiologic studies published in the early 1960s noted an association between overweight status among children and adolescents and iron deficiency.[16,17] A recently published cross-sectional study found that overweight children and adolescents exhibited lower iron levels; of those with iron deficiency anemia, >50% had a >97th percentile body mass index (BMI).[18] The objective of this study was to investigate the association between weight status (measured as BMI) and iron deficiency among a nationally representative sample of children and adolescents.

METHODS

Sample

NHANES III was a large, national, cross-sectional survey conducted by the Centers for Disease Control and Prevention, National Center for Health Statistics, between 1988 and 1994.[19] The survey used a stratified, multistage, probability design, with 2 phases of equal length and sample size, and included a representative sample of the noninstitutionalized US population ≥2 months of age. Approximately 40 000 people were selected and asked to complete an extensive interview and an examination in a large mobile examination center. Non-Hispanic blacks and Mexican Americans were oversampled, to ensure weighted reliable estimates for those groups.

We limited our analyses to children and adolescents 2 to 16 years of age ($n = 9698$) for whom there were data on the biochemical indicators of iron status and measurements for BMI calculations. Individuals who were pregnant were excluded from the analyses. Institutional review board approval was not required because NHANES III is a public-access national database from which all identifying individual information has been removed.

Variables

Variables included standard demographic features, poverty status, and head of household education level. Race/ethnicity was based on caregiver proxy or self-report and was categorized as non-Hispanic white, non-Hispanic black, Mexican American, or other. Poverty status was categorized as at or above the poverty level or below the poverty level on the basis of reported family income and the US Poverty Threshold, which is determined annually by the US Census Bureau. The head of household education level was based on the self-reported highest grade of school completed and was categorized as less than high school education, high school education, or greater than high school education. Body weight and height (stature was measured for children ≥2 years of age) were measured by using standardized equipment and procedures.[20] BMI was calculated as weight in kilograms divided by squared height in meters. Standard measurement assays were used for the biochemical measures of iron status and have been reported elsewhere.[21,22]

Definitions of Weight Status

Weight status was defined by using age- and gender-specific BMI percentiles from the 2000 revised Centers for Disease Control and Prevention/National Center for Health Statistics growth charts for the United States.[23] The age- and gender-specific BMI growth charts provide a statistical definition of weight status for children 2 to 20 years of age. With the use of current recommendations, at risk for overweight was defined as a BMI at the 85th through 94th percentile and overweight was defined as a ≥95th percentile BMI.[24,25] Normal weight was defined for all children and adolescents with a <85th percentile BMI on the BMI growth chart.

Definitions of Iron Deficiency and Anemia

The definitions of iron deficiency and anemia were based on criteria used by Looker et al[26] in their article describing the prevalence of iron deficiency in the United States, using the same NHANES III data set. Three laboratory measures of iron status, ie, transferrin saturation, free erythrocyte protoporphyrin levels, and serum ferritin levels, were used to define iron deficiency. A child was considered iron-deficient if 2 of 3 values were abnormal for age and gender. Hemoglobin cutoff points used to define anemia were based on the 5th percentiles for the reference groups.[26] Children were determined to have iron deficiency without anemia if they met the criteria for iron deficiency and had a hemoglobin level above the established cutoff point.

Analyses

With Student's t test for means and χ^2 tests for proportions, the prevalences of normal iron status and iron deficiency were compared for the weight status groups (normal weight, at risk for overweight, and overweight). Separate analyses were performed to evaluate the prevalences of normal iron status, iron deficiency with anemia, and iron deficiency without anemia for children in each weight status group. Logistic regression was used to estimate the independent association between iron status and overweight. Because NHANES III was based on a complex sampling design, all analyses included appropriate sample weights, to account for the unequal probabilities of selection, oversampling, and nonresponse in producing national estimates. SUDAAN software was used to estimate associated variances and to obtain weighted frequencies, means, and SEs.[27]

RESULTS

The sample consisted of 9698 children and adolescents, 2 through 16 years of age. Table 1 presents the

TABLE 1. Population Demographic Features With Respect to Iron Status

	n	Iron-Deficient With Anemia, %	Iron-Deficient Without Anemia, %	Iron-Deficient Total, %
Age				
2–5 y	4553	0.6	1.7	2.3
6–11 y	3309	0.2	1.6	1.8
12–16 y	2088	0.9	3.8	4.7
Gender				
Male	4892	0.3	1.3	1.6
Female	5058	0.8	3.5	4.3
Race/ethnicity				
White	2690	0.2	1.6	1.8
Black	3289	1.2	1.6	2.8
Mexican American	3489	1.2	5.1	6.3
Other	482	1.0	5.7	6.7
Poverty status				
Below poverty	3718	1.0	4.0	5.0
Above poverty	5395	0.3	1.7	2.0
Caretaker education				
<12th grade	3965	0.7	3.1	3.8
12th grade	3165	0.7	2.2	2.9
>12th grade	2699	0.3	2.0	2.3
BMI				
Normal weight	7285	0.4	1.7	2.1
At risk for overweight	1286	0.7	4.6	5.3
Overweight	1127	1.1	4.4	5.5

prevalence of iron deficiency according to the demographic characteristics of the population. Iron deficiency was most prevalent among 12- to 16-year-old subjects (4.7%), followed by 2- to 5-year-old subjects (2.3%) and then 6- to 11-year-old subjects (1.8%). The prevalence of iron deficiency, with or without anemia, followed a similar trend. The groups with the highest prevalences of iron deficiency included Mexican Americans (6.3%), children and adolescents in families living below the poverty line (5.0%), and at risk for overweight (5.3%) and overweight (5.5%) children and adolescents. We chose to perform all subsequent analyses using the total iron-deficient measure to define iron status, to include any child or adolescent with iron deficiency, regardless of the presence or absence of anemia.

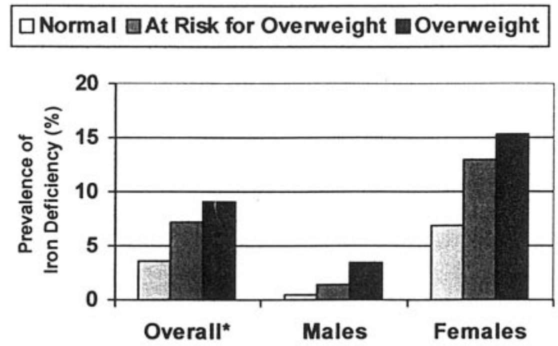
In this population of children and adolescents, 13.7% of subjects were at risk for overweight and 10.2% were overweight. Table 2 presents the prevalence of iron deficiency according to weight status. Results are shown for children and adolescents who were of normal weight, at risk for overweight, or overweight. Overweight 2- to 5-year-old subjects (6.2%) and overweight 12- to 16-year-old subjects (9.1%) demonstrated the highest prevalence of iron deficiency. Overall, the prevalence of iron deficiency increased as BMI increased from normal to at risk for overweight to overweight (2.1%, 5.3%, and 5.5%, respectively; $P = .002$). The at risk for overweight group and the overweight group were both significantly more iron-deficient than the normal-weight group ($P < .05$ and $P < .01$, respectively). Adolescents demonstrated the highest occurrence of iron deficiency, which similarly increased as weight status increased (3.5%, 7.2%, and 9.1%, respectively; $P = .04$). Overweight adolescents were found to be significantly more iron-deficient than their normal-weight peers ($P < .05$). Additional analysis of the adolescent group revealed that most of the increased prevalence of iron deficiency was attributable to female subjects (Fig 1). Almost 13% of the at risk for overweight female subjects and >15% of the overweight female subjects in this age group had iron deficiency. Although neither group was significantly different from normal-weight adolescent female subjects, comparison of the overweight adolescent female subjects with the normal-weight adolescent female subjects trended toward significance ($P = .07$).

A multivariate regression analysis was performed to evaluate the independent association of weight status and iron deficiency (Table 3). Age, gender, race/ethnicity, poverty status, and caretaker education were included in the analysis. Children and adolescents who were at risk for overweight or were overweight had a significantly increased risk of iron deficiency. Specifically, children and adolescents with a BMI in the at risk for overweight range had an odds ratio of 2.0 (95% confidence interval: 1.2–3.5) for having iron deficiency, and overweight children and adolescents had an odds ratio of 2.3 (95% confidence interval: 1.4–3.9).

TABLE 2. Prevalence of Iron Deficiency According to Weight Status for Each Age Group and Overall

BMI	Iron Deficiency, %			
	2–5 y	6–11 y	12–16 y	Overall
Normal weight	1.8	1.2	3.5	2.1
At risk for overweight	3.7	4.4	7.2	5.3*
Overweight	6.2	2.4	9.1*	5.5†

* $P < .05$, compared with the normal-weight group, by χ^2 analysis.
† $P < .01$, compared with the normal-weight group, by χ^2 analysis.



*p<0.05 for overweight group compared with the normal weight group by χ^2 analysis.

Fig. 1. Prevalence of iron deficiency in 12- to 16-year-olds.

TABLE 3. Logistic Regression Predicting Iron Deficiency

	Odds Ratio	95% Confidence Interval	*P* Value
Age			
2–5 y	1.2	0.7–2.2	.4
6–11 y	1.0		
12–16 y	2.6	1.4–4.6	.002
Gender			
Female	2.6	1.7–3.9	<.0001
Male	1.0		
Race/ethnicity			
White	1.0		
Black	1.3	0.7–2.2	.3
Mexican American	3.5	2.2–5.8	<.0001
Other	3.8	2.0–7.1	<.0001
Poverty status			
Below poverty	2.0	0.9–4.2	.06
Above poverty	1.0		
Caretaker education			
<12th grade	0.7	0.3–1.5	.4
12th grade	1.0	0.5–2.0	.9
>12th grade	1.0		
BMI percentile			
<85%	1.0		
≥85% to <95%	2.0	1.2–3.5	.01
≥95%	2.3	1.4–3.9	.002

DISCUSSION

Using data on a large, nationally representative sample of children and adolescents, we found that iron deficiency was more prevalent among subjects with higher BMI values. Children and adolescents who were at risk for overweight or were overweight were approximately twice as likely to be iron-deficient, compared with children of normal weight. In addition, almost 1 of every 10 overweight adolescents was iron-deficient.

These findings are consistent with the results of a few small studies investigating a similar relationship between iron deficiency and weight status among children and adolescents.[16–18] In the 1960s, 2 relevant studies were published. Wenzel et al[16] examined 162 male subjects and 192 female subjects, 11 to 19 years of age, who were participating in a study involving measurements of serum iron levels to establish standards for iron levels. Among those children, 15.3% of the male subjects and 18.7% of the female subjects were overweight, as defined by the Wetzel grid, which is based on weight and height measurements. Those authors observed a highly significant difference in the mean serum iron levels of overweight versus nonoverweight male and female subjects ($P < .005$ and $P < .001$, respectively).[16] Similarly, Seltzer and Mayer[17] studied 160 male subjects and 162 female subjects, 11 to 21 years of age. A total of 15.6% of male subjects and 19.9% of female subjects were overweight, on the basis of subjective clinical evaluations. The overweight male and female subjects demonstrated significantly lower mean serum iron levels ($P < .01$), higher unsaturated iron-binding capacity levels ($P < .01$), and lower mean percentages of iron-binding protein saturated with iron ($P < .01$), compared with the nonobese group.[17]

In a study investigating whether hemoglobin criteria should be adjusted for weight status, Scheer and Guthrie[28] observed that iron deficiency, but not anemia, was significantly more prevalent among overweight children, although the data to support that assertion were not reported. Recently, Pinhas-Hamiel et al[18] examined the prevalence of iron deficiency among 321 overweight children and adolescents in Israel. Using only serum iron levels to define iron deficiency (serum iron levels of <8 μmol/L [<45 μg/dL]), those authors observed iron deficiency for 4.4% of normal-weight children, 12.1% of children at risk for overweight, and 38.8% of overweight children ($P < .001$).[18] Our data are consistent with the aforementioned findings and validate this association by demonstrating it among a national sample of children with the use of validated measures of both iron deficiency and overweight.

A number of different factors have been proposed to explain the association between iron deficiency and overweight, including genetic influences; physical inactivity, leading to decreased myoglobin breakdown and thus decreased amounts of iron released into the blood; and inadequate diet, with limited intake of iron-rich foods. In addition, overweight female children tend to grow faster and mature at an earlier age, compared with nonoverweight children,[29] making it difficult for the subjects to keep up with iron requirements.

The association between iron deficiency and overweight has been examined in obese mouse models. Kennedy et al[30] studied the effects of obesity on tissue concentrations of iron in male and female mice. Iron concentrations were found to be lower in many of the studied tissues, including liver, spleen, small intestine, bone, and muscle. In addition, significantly lower serum iron levels were observed for the older obese mice. Those authors concluded that alterations in the tissue distribution and metabolism of endogenous micronutrients lead to changes in tissue concentrations of trace metals in congenitally obese mice.[30]

Associated work in the same laboratory supports the idea that iron metabolism differs for obese mice. In a study examining the effect of obesity on iron status, including absorption and retention, the group discovered that obese mice absorbed 2 to 2.5 times more radiolabeled iron than did lean mice, when provided with an iron-sufficient diet. Despite this increased absorption, the concentrations of iron in the liver, small intestine, and bone were significantly lower in the obese mice.[31] Additional basic science research is warranted, to better elucidate the effects of obesity on iron metabolism and storage.

There are some potential limitations to the analyses reported here. First, the small number of overweight children and adolescents with iron deficiency and anemia limited our ability to consider this group separately from the group of iron-deficient children without anemia. Second, a number of factors influence both weight status and iron deficiency, including socioeconomic variables, physical activity or inactivity, nutrition, and physical maturity. Although a number of these variables were included in our analyses, some residual confounding is possible. However, the strength of the association observed and the presence of a dose-response relationship make substantial residual confounding less likely. Finally, because the NHANES survey is cross-sectional, a causal relationship between weight status and iron deficiency could not be determined. As a result, we can assert only that the data indicate an association between weight status and iron deficiency.

Given the increasing numbers of overweight children and adolescents and the known morbidities of iron deficiency, the association between iron deficiency and overweight may have important public health and clinical implications. If these data are confirmed, then guidelines for screening for iron deficiency may need to be modified to include children and adolescents with elevated BMI who otherwise do not meet the current criteria for screening. Prospective studies could help delineate more clearly the basis of this association and could provide insight into how best to approach prevention and treatment of these 2 very important pediatric issues.

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