Obesity, Metabolic Syndrome, and Insulin Resistance in Urban High School Students of Minority Race/Ethnicity

Michael Turchiano, BA; Victoria Sweat, MA; Arthur Fierman, MD; Antonio Convit, MD

Objectives: To determine the point prevalences of metabolic syndrome (MetS) and its components among healthy weight, overweight, and obese inner-city public high school students, to compare the prevalences of MetS when using 2 different definitions (one with the impaired fasting glucose [IFG] level and the other with a homeostasis model assessment of insulin resistance [HOMA-IR] of 3.99 or higher to define the glucose regulation component), and to compare the degree to which HOMA-IR and fasting glucose level are associated with the other MetS components.

Design: Cross-sectional analysis.

Setting: Two New York City public high schools, from April 2008 through August 2011.

Participants: Convenience sample of 1185 high school youth, comprising predominantly Hispanic and African American students from low-income households, participating in The Banishing Obesity and Diabetes in Youth Project, a medical screening and education program.

Main Outcome Measures: Prevalences of the following individual MetS components: IFG threshold, HOMA-IR, hypertension, central adiposity, hypertriglyceridemia, and low high-density lipoprotein cholesterol. Rates of MetS\textsubscript{IFG} and MetS\textsubscript{HOMA-IR} were also assessed.

Results: MetS\textsubscript{IFG} and MetS\textsubscript{HOMA-IR} point prevalences were both 0.3% in the healthy weight group; they were 2.6% and 5.9%, respectively, in the overweight group and were 22.9% and 35.1%, respectively, in the obese group ($P<.05$ for both). An IFG threshold of 100 mg/dL or higher was found in 1.0% of participants, whereas a HOMA-IR of 3.99 or higher was found in 19.5% of participants.

Conclusions: An elevated HOMA-IR is much more sensitive than an IFG threshold in identifying adolescents with metabolic dysregulation. Using a HOMA-IR threshold of 3.99 identifies more youth with MetS than using an IFG threshold of 100 mg/dL. In addition to increasing the sensitivity of MetS detection, HOMA-IR has a much higher association with the other MetS components than the IFG threshold and may better reflect a unified underlying pathologic process useful to identify youth at risk for disease.

glucose levels often remain normal owing to compensatory hyperinsulinemia and adequate pancreatic beta-cell reserve.\textsuperscript{5,16,17} As a result, elevated fasting insulin levels are more common than IFG levels in adolescent populations.\textsuperscript{2,18} Some researchers have used oral or intravenous glucose tolerance tests to identify impaired glucose tolerance and to define MetS.\textsuperscript{19,20} These dynamic assessments of insulin function are too invasive or time-consuming to be used in large population studies or in a clinical setting. Therefore, the homeostasis model assessment of insulin resistance (HOMA-IR), an estimate of insulin resistance incorporating paired fasting insulin level and glucose level, has been suggested as an alternative to the use of an isolated fasting glucose level.\textsuperscript{21} HOMA-IR has been validated against clamps and against intravenous glucose tolerance tests in healthy weight youth and in overweight youth.\textsuperscript{2,22,24}

Given the long-term health consequences of metabolic abnormalities in childhood, our study had the following objectives: (1) to determine the point prevalences of MetS and its components among healthy weight, overweight, and obese inner-city public high school students; (2) to compare the prevalences of MetS using 2 different definitions (one using the IFG level and the other the HOMA-IR to define the glucose regulation component); and (3) to compare the degree to which HOMA-IR and fasting glucose level are associated with the other MetS components.

### METHODS

#### PARTICIPANTS AND PROCEDURE

The study was approved by the institutional review boards of the New York University School of Medicine, the New York City Department of Education, the New York City Department of Health and Mental Hygiene, and the Nathan Kline Institute for Psychiatric Research. Data for this project are representative of a convenience sample obtained from The Banishing Obesity and Diabetes in Youth Project, a school-based medical screening and education program that is part of New York University Langone Medical Center’s Community Service Plan, which is described in detail elsewhere.\textsuperscript{23} Students in grades 9 through 12 were recruited from 2 New York City public high school campuses from April 2008 through August 2011, comprising predominantly Hispanic and African American students from low-income households (82% were eligible for or enrolled in the free lunch program, for which low family income is a prerequisite). We measured the height and weight of all the students in each participating school. Body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) percentile adjusted for age and sex was calculated using the BMI Percentile Calculator for Child and Teen on the Centers for Disease Control and Prevention’s Anthromometry Procedures Manual.\textsuperscript{27}

#### BLOOD PRESSURE MEASUREMENTS

Blood pressure was measured using an electronic vital signs monitor (SureSigns VS1; Philips) and a cuff appropriate for the participant’s arm diameter. The first blood pressure measurement was obtained after the participant had been seated for 5 minutes, with a second reading taken within 10 minutes of the first. The lower of the 2 readings was used in data analyses. Blood pressure percentiles were calculated using commercially available software (EZ Blood Pressure Calculator; EZ BMI Software)\textsuperscript{26} using normative data from the US National Heart, Lung, and Blood Institute’s Task Force Report on High Blood Pressure in Children and Adolescents from 2004 for the participants up to age 18 years. Adult criteria were used for those older than 18 years. Three hundred fifty-nine participants who were evaluated before we had properly implemented these blood pressure procedures had unreliable blood pressure measurements and were excluded from the analyses.

#### BLOOD CHEMISTRY MEASUREMENTS

Using blood samples collected in fluorinated tubes, the fasting blood glucose level was measured using a glucose oxidase method (VITROS 930 AT; Johnson & Johnson), and insulin was assayed using chemiluminescence (Advia Centaur; Bayer Corporation). Total cholesterol, HDL-C, and triglyceride levels were analyzed using chemistry slides (VITROS DT; Johnson & Johnson). The glycated hemoglobin level was mea-
DEFINITION OF MetS

We used 2 definitions of MetS. In the first definition of MetS, published by Cook et al10 and used in other studies,3,12 the IFG level is the component measuring glucoregulatory control.33 MetS based on this definition is referred to as MetS-IFG. An adolescent was considered to have MetS-IFG when 3 or more of the following 5 criteria were met: (1) central adiposity (waist circumference at the 90th percentile or higher for age and sex),3 (2) hypertriglyceridemia (triglycerides level ≥1.70 mmol/L [to convert HDL-C to millimoles per liter, multiply by 0.0259]), (3) low HDL-C level (HDL-C <1.04 mmol/L [to convert HDL-C to millimoles per liter, multiply by 0.0259]), (4) elevated blood pressure (for children ≤18 years, systolic or diastolic blood pressure exceeding the 90th percentile adjusted for age and sex), and (5) IFG level (fasting glucose level ≥1.00 mmol/L).

In the second definition of MetS, we constructed an alternate criterion; MetS based on this definition is referred to as MetS-HOMA, substituting the IFG level with an elevated HOMA-IR. As has been previously described in adolescent populations,16 we used a HOMA-IR of 3.99 or higher as the cut point for abnormal glucose regulation instead of a fasting blood glucose level of 100 mg/dL or higher.

Table 1. Characteristics of 1185 Students With Complete Medical and Anthropomorphic Data by Body Mass Index Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Healthy Weight (n = 356)</th>
<th>Overweight (n = 387)</th>
<th>Obese (n = 442)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female sex, %</strong></td>
<td>57.3a</td>
<td>61.5a</td>
<td>46.4</td>
</tr>
<tr>
<td><strong>Race/ethnicity, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>74.7</td>
<td>74.2</td>
<td>74.7</td>
</tr>
<tr>
<td>Non-Hispanic African American</td>
<td>18.5</td>
<td>17.8</td>
<td>17.4</td>
</tr>
<tr>
<td>Other</td>
<td>6.7</td>
<td>8.0</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Age, mean (SD), y</strong></td>
<td>16.9 (1.2)a,b</td>
<td>16.7 (1.3)</td>
<td>16.6 (1.2)</td>
</tr>
<tr>
<td><strong>Body mass index, mean (SD)c,d</strong></td>
<td>21.9 (2.2)</td>
<td>26.6 (1.5)</td>
<td>33.8 (4.6)</td>
</tr>
<tr>
<td><strong>Waist circumference, mean (SD), cm</strong></td>
<td>75.2 (8.4)</td>
<td>85.7 (6.6)</td>
<td>102.3 (11.7)</td>
</tr>
<tr>
<td><strong>Blood pressure, mean (SD), mm Hg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>114.4 (9.3)a</td>
<td>115.8 (9.9)a</td>
<td>121.8 (11.5)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>64.0 (7.7)</td>
<td>69.4 (9.3)</td>
<td>73.0 (10.4)</td>
</tr>
<tr>
<td><strong>Fasting plasma glucose level, mean (SD), mg/dL</strong></td>
<td>79.2 (7.0)a</td>
<td>79.4 (6.6)a</td>
<td>81.4 (7.6)</td>
</tr>
<tr>
<td>Fasting insulin level, mean (SD), µIU/mL</td>
<td>10.0 (5.7)</td>
<td>12.0 (6.7)</td>
<td>18.6 (9.3)</td>
</tr>
<tr>
<td><strong>Homeostasis model assessment of insulin resistance, mean (SD)c</strong></td>
<td>2.0 (1.3)</td>
<td>2.3 (1.4)</td>
<td>3.8 (2.0)</td>
</tr>
<tr>
<td>Glycated hemoglobin level, mean (SD), %</td>
<td>5.43 (0.21)c</td>
<td>5.35 (0.33)</td>
<td>5.40 (0.36)</td>
</tr>
<tr>
<td><strong>Cholesterol level, mean (SD), mg/dL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-density lipoproteinc</td>
<td>85.4 (22.0)</td>
<td>92.0 (24.6)</td>
<td>98.0 (24.9)</td>
</tr>
<tr>
<td>High-density lipoproteinc</td>
<td>52.5 (11.1)</td>
<td>48.4 (10.9)</td>
<td>43.4 (9.1)</td>
</tr>
<tr>
<td>Triglycerides level, mean (SD), mg/dL</td>
<td>66.2 (24.9)a</td>
<td>73.4 (45.7)a</td>
<td>90.6 (64.3)</td>
</tr>
<tr>
<td><strong>C-reactive protein level, mean (SD), mg/Lc</strong></td>
<td>0.9 (1.4)</td>
<td>1.4 (2.1)</td>
<td>3.1 (3.2)</td>
</tr>
</tbody>
</table>

SI conversion factors: To convert glucose level to millimoles per liter, multiply by 0.0555; insulin level to picomoles per liter, multiply by 6.945; glycated hemoglobin level to proportion of total hemoglobin, multiply by 0.01; cholesterol level to millimoles per liter, multiply by 0.0259; triglycerides level to millimoles per liter, multiply by 0.0113; and C-reactive protein level to nanomoles per liter, multiply by 9.524.

a Significant difference from the obese group.
b Significant difference from the overweight group.
c Significant difference among all body mass index groups.
d Calculated as weight in kilograms divided by height in meters squared.

STATISTICAL ANALYSIS

Differences in anthropomorphic and metabolic variables were compared across BMI percentile groups using 1-way analysis of variance with the Tukey honestly significant difference test. Prevalence of MetS was compared using a paired-sample t test, where appropriate. Categorical variables were compared using the Cochran-Armitage test for trend. Linear regression analyses were used to establish how well BMI, blood pressure, waist circumference, and HDL-C, triglycerides, and CRP levels could predict HOMA-IR or IFG thresholds. We used the raw data (adjusted for age, sex, and race/ethnicity) rather than the percentiles because some participants were older than 18 years. For these analyses, the independent variables were BMI, waist circumference, systolic and diastolic blood pressure, and HDL-C, triglycerides, and CRP levels. The dependent variables were HOMA-IR or fasting glucose level. Except for investigations using the Cochran-Armitage test for trend, all analyses were performed using a commercially available statistical software program (SPSS version 19; SPSS, Inc). Statistical significance was set at α = .05.

RESULTS

DEMOGRAPHIC AND BLOOD CHEMISTRY DATA

After the exclusions, 1185 participants were included in the study sample. Their ages ranged from 14 to 19 years inclusive, with a mean (SD) age of 16.7 (1.2) years. In total, 54.6% were female, and 74.5% were Hispanic or Latino, 17.9% were non-Hispanic black, and 7.6% were of other race/ethnicity (white or Asian). The participants’ characteristics are summarized in Table 1. There
were significantly fewer girls in the obese group than in the healthy weight group or the overweight group ($P < .001$ for both). Race/ethnicity did not vary by weight group. As expected, waist circumference, diastolic blood pressure, and fasting insulin, HOMA-IR, low-density lipoprotein cholesterol, HDL-C, and CRP levels differed significantly across all BMI categories ($P < .05$ for all). The participants in the obese group had higher systolic blood pressures, higher fasting glucose levels, and higher triglycerides levels than the participants in the healthy weight or overweight groups. The participants in the overweight group had lower glycated hemoglobin values than the participants in the healthy weight or obese groups.

Furthermore, we contrasted 106 participants having a BMI at the 99th percentile or higher with the remaining 336 participants in the obese group having a BMI at the 95th percentile but less than the 99th percentile. Those with a BMI at the 99th percentile or higher had significantly higher blood pressure, waist circumference, and CRP, HOMA-IR, triglycerides, and fasting insulin levels, as well as significantly lower HDL-C levels relative to the remainder of the participants in the obese group. No significant difference in fasting glucose levels was observed between these 2 subsets of the obese group (data not shown).

### COMPARISON OF MetS RATES USING THE 2 DEFINITIONS

As summarized in Table 2, 9.5% of the participants in our sample met the criteria for MetS using an IFG level of 100 mg/dL or higher, and 15.1% met the criteria using a HOMA-IR of 3.99 or higher. MetS$_{HOMA-IR}$ consistently identified more participants with MetS than MetS$_{IFG}$. One girl in the healthy weight group met the criteria for MetS$_{IFG}$ and for MetS$_{HOMA}$. Regardless of the definition used, boys tended to have higher rates of MetS than girls, and MetS point prevalence increased with BMI.

### POINT PREVALENCE OF MetS COMPONENTS

As summarized in Table 3, a trend toward higher prevalence of all MetS components was observed with increasing BMI percentile. In the healthy weight group, a low HDL-C level was the most common abnormality observed. Central adiposity was the most commonly observed abnormality in the obese group. Impaired fasting glucose levels were present much less frequently than insulin resistance. In total, 4.5% of healthy weight participants, 12.4% of overweight participants, and 37.8% of obese participants had a HOMA-IR of 3.99 or higher ($P < .001$). Overall, only 1.0% of students had an IFG level, and 19.5% of students had a HOMA-IR of 3.99 or higher. Although no clinically relevant differences were observed in the percentages of participants with IFG levels across the 3 weight categories (0.6% of the healthy weight group, 0.3% of the overweight group, and 2.0% of the obese group), these small differences reached statistical significance in the trend analyses ($P = .03$) because of the large sample size.

### ABILITY OF METABOLIC AND ANTHROPOMORPHIC VARIABLES TO PREDICT HOMA-IR AND IFG LEVEL

Using linear regression analysis and adjusting for age, sex, and race/ethnicity ($R^2 = 0.020$), all the other MetS components and the CRP level were significant predictors of
HOMA-IR, and all but HDL-C level (P = .06 for trend) were predictors of IFG level. However, as shown in Table 4, the total variance (adjusted $R^2$) explained by all the other variables was consistently higher (range, 2-fold to 5-fold larger) in the predictions of HOMA-IR than of IFG level.

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>HOMA-IR</th>
<th>IFG Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$ Coefficient</td>
<td>Adjusted $R^2$</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.488</td>
<td>0.256</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>0.301</td>
<td>0.099</td>
</tr>
<tr>
<td>Systolic</td>
<td>0.199</td>
<td>0.056</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.498</td>
<td>0.263</td>
</tr>
<tr>
<td>Triglycerides level</td>
<td>0.336</td>
<td>0.128</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol level</td>
<td>0.223</td>
<td>0.064</td>
</tr>
<tr>
<td>C-reactive protein level</td>
<td>0.326</td>
<td>0.122</td>
</tr>
</tbody>
</table>

*a* All analyses were adjusted for age, sex, and race/ethnicity (adjusted $R^2 = 0.020$). $P$ values indicate significant difference in metabolic syndrome component prevalence according to weight category.

In a sample of predominantly Hispanic and African American inner-city high school students, we demonstrate that obesity is linked to a host of metabolic abnormalities. As noted by other investigators, we found that increasing BMI not only was related to a larger waist circumference but also was associated with blood pressure elevation, abnormalities in the lipid profile, a higher fasting insulin level, and a higher CRP level. While the MetS components and CRP level were significant predictors of IFG level, they systematically accounted for 2-fold to 5-fold higher variance in the predictions of HOMA-IR relative to the IFG threshold has been described by others. For example, in their analysis of data from individuals aged 12 to 19 years who were included in the National Health and Nutrition Examination Survey from 1999 to 2002, Cook et al found that 8.6%, 15.4%, and 16.5% of normal, overweight, and obese children, respectively, had a fasting blood glucose level exceeding 100 mg/dL. Meanwhile, using data from the same surveys, Lee and colleagues reported that roughly 9%, 20%, and 60% of normal, overweight, and obese children had a HOMA-IR of 3.99 or higher. Using similar data, Li and co-workers found that 13.1% of the population in a nationally representative sample of individuals aged 12 to 19 years had a fasting glucose level exceeding 100 mg/dL, while 37.1% had hyperinsulinemia (fasting insulin level, >13.8 µIU/mL [to convert insulin level to picomoles per liter, multiply by 6.945]). Although our data are consistent with nationally representative findings in demonstrating that an elevated HOMA-IR and hyperinsulinemia are more common than IFG levels among adolescents, our point prevalence of the IFG threshold is lower than that in similar school-based or nationally representative investigations. For the measurement of glucose levels, samples were collected in tubes containing sodium fluoride (10.0 mg)–potassium oxalate (8.0 mg) to prevent red blood cells from metabolizing glucose and artificially reducing glucose levels before measurement. Nevertheless, given the approximate 3-hour delay in our study between the blood sample being drawn and the assay being performed, it is possible that our low prevalence of hyperglycemia is the result of a systematic underestimation of glucose values due to our measurement procedure.

While the MetS components and CRP level were significantly associated with fasting blood glucose level and with HOMA-IR, they systematically accounted for 2-fold to 5-fold higher variance in the predictions of HOMA-IR than of IFG level (Table 4). This is likely owing to the causal role that has been attributed to insulin resistance and to hyperinsulinemia in the development and progression of hypertension and the dyslipidemic components of MetS. Our work is in agreement with that by Sharma and colleagues, who suggested that the incorporation of HOMA-IR into a pediatric MetS definition cre-
and inflammation in the pediatric population. Given that levels, also poses serious health risks and has been implicated by age in normal and overweight adolescents and showed high variability in obese adolescents. Moreover, insulin resistance also varies by sex and race/ethnicity, therefore, future work should determine appropriate age, sex, and race/ethnicity cutoffs for estimates of insulin resistance.

While IFG level is a significant risk factor for a host of diseases, it represents an abnormality further along in the progression of obesity to type 2 diabetes mellitus and likely reflects concurrent insulin resistance and beta-cell insufficiency, which occurs after insulin resistance has already been established. Reduced insulin sensitivity, resulting in compensatory fasting hyperinsulinemia, even in the presence of normal fasting glucose levels, also poses serious health risks and has been implicated in the development of precursors to cardiovascular disease, type 2 diabetes mellitus, hypertension, dyslipidemia, hepatic steatosis, polycystic ovary syndrome, and inflammation in the pediatric population. Given that a primary objective of the MetS construct is to identify children and youth at risk for diabetes and cardiovascular disease as early as possible, the use of a MetS definition that includes HOMA-IR provides greater opportunity for interventions that are intended to halt or reverse the progression of MetS to more advanced disease.

Accepted for Publication: May 1, 2012.
Published Online: September 24, 2012. doi:10.1001/archpediatrics.2012.1263

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Conflict of Interest Disclosure: None reported.

Funding/Support: This study was supported by grant T32DK007328-31 from the National Institutes of Health (Mr Turchiano), the New York University Langone Medical Center (Dr Convit), the Assurant Foundation (Dr Convit), and the Nathan Kline Institute (Dr Convit).

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