

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

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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, hypertriglyc-

eridemia, and low high-density lipoprotein cholesterol. Rates of MetS_{IFG} and MetS_{HOMA-IR} were also assessed.

Results: MetS_{IFG} and MetS_{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.

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METABOLIC SYNDROME (MetS) has been clearly defined in adults, but defining MetS in children and adolescents is more challenging owing to normal changes in blood pressure, lipid values, and insulin sensitivity that occur during development and that are influenced by sex and race/ethnicity.¹⁻⁴ Furthermore, a lack of large prospective studies capturing the natural history of childhood MetS and its progression to adult disease adds to the difficulty.⁵ To provide continuity with the adult literature, various age-dependent and sex-dependent adjustments to adult MetS criteria have been made, resulting in several definitions of childhood MetS and leading to wide-ranging variability in the reported prevalence.⁴ Nevertheless, the prevalence of

MetS in adolescence rises with increasing excess weight, tends to be higher among boys, and varies by race/ethnicity.⁶

Some investigators have proposed that insulin resistance is the central factor driving the abnormalities observed in MetS.^{7,8} Insulin resistance and concurrent fasting hyperinsulinemia short of type 2 diabetes mellitus not only are independently associated with MetS markers, including blood pressure elevation, high triglycerides level, and low high-density lipoprotein cholesterol (HDL-C) level,⁹⁻¹² but also have been linked to compromised brachial artery distensibility,¹³ hepatic steatosis,¹⁴ and polycystic ovary disease.¹⁵

Most definitions of MetS use impaired fasting plasma glucose (IFG) level as a marker of insulin resistance. However, in youth with insulin resistance, fasting blood

glucose levels often remain normal owing to compensatory hyperinsulinemia and adequate pancreatic beta-cell reserve.^{5,16,17} As a result, elevated fasting insulin levels are more common than IFG levels in adolescent populations.¹⁸ Some researchers have used oral or intravenous glucose tolerance tests to identify impaired glucose tolerance and to define MetS.^{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.²¹ HOMA-IR has been validated against clamps and against intravenous glucose tolerance tests in healthy weight youth and in overweight youth.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.²⁵ 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 website.²⁶ Students with a BMI at less than the 85th percentile were classified as healthy weight, students with a BMI at the 85th percentile or higher but less than the 95th percentile were classified as overweight, and students at the 95th percentile or higher were classified as obese. All the students with a BMI at the 85th percentile or higher were approached to participate in the medical screening. A comparison group of healthy weight students, 1 for every 2 overweight or obese students participating in the project, was randomly selected. Eighty-seven percent of students approached for participation assented to participate. Sixty-three percent of assenters, unless they were older

than 18 years and could sign the consent form themselves, returned signed parental consent forms and participated in the medical screening. Among the students eligible for the study, no differences were observed between the participants and the nonparticipants in age, BMI, or BMI percentile. Although girls participated in slightly higher numbers than boys, no differences remained in age, BMI, or BMI percentile when the participants and the nonparticipants were compared separately by sex.

The participants were asked to arrive at the school-based health center between 7:30 and 8:30 AM after an overnight fast of 10 to 12 hours. A total of 1592 participants returned signed consent forms and completed the medical evaluation. We excluded 390 students from the final analyses for the following reasons: 359 had a systematic error in blood pressure measurement, 30 had missing data for 1 or more MetS components, and 1 had type 1 diabetes mellitus. In addition, 17 participants were excluded because they likely were not fasting (they had "fasting" insulin levels 2.5 SDs above the mean of the obese group); although all of their glucose levels were below 100 mg/dL (to convert glucose level to millimoles per liter, multiply by 0.0555), they had statistically significant elevations in fasting glucose levels but no elevations in glycated hemoglobin values. After these exclusions, 1185 students participating in The Banishing Obesity and Diabetes in Youth Project were included in the final analyses.

ANTHROPOMORPHIC MEASUREMENTS

Height, weight, and waist circumference were measured again on the day of the medical evaluation. Height was measured to the nearest 0.1 cm using a height rod (model 214; Seca), and weight was measured to the nearest 0.01 kg using a digital remote display scale (model 349KLX; Healthometer). With the participant standing and wearing a single layer of clothing, waist circumference was measured to the nearest 0.1 cm by placing the tape just superior to the iliac crest as per the Centers for Disease Control and Prevention's *Anthropometry Procedures Manual*.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)²⁸ 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 950 AT; Johnson & Johnson), and insulin was assayed using chemiluminescence (Advia Centaur; Bayer Corporation). Total cholesterol, HDL-C, and triglycerides levels were analyzed using chemistry slides (VITROS DT; Johnson & Johnson). The glycated hemoglobin level was mea-

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

Characteristic	Healthy Weight (n = 356)	Overweight (n = 387)	Obese (n = 442)
Female sex, %	57.3 ^a	61.5 ^a	46.4
Race/ethnicity, %			
Hispanic or Latino	74.7	74.2	74.7
Non-Hispanic African American	18.5	17.8	17.4
Other	6.7	8.0	7.9
Age, mean (SD), y	16.9 (1.2) ^{a,b}	16.7 (1.3)	16.6 (1.2)
Body mass index, mean (SD) ^{c,d}	21.9 (2.2)	26.6 (1.5)	33.8 (4.6)
Waist circumference, mean (SD), cm ^c	75.2 (8.4)	85.7 (6.6)	102.3 (11.7)
Blood pressure, mean (SD), mm Hg			
Systolic	114.4 (9.3) ^a	115.8 (9.9) ^a	121.8 (11.5)
Diastolic ^c	64.0 (7.7)	69.4 (9.3)	73.0 (10.4)
Fasting plasma glucose level, mean (SD), mg/dL	79.2 (7.0) ^a	79.4 (6.6) ^a	81.4 (7.6)
Fasting insulin level, mean (SD), μ IU/mL ^c	10.0 (5.7)	12.0 (6.7)	18.6 (9.3)
Homeostasis model assessment of insulin resistance, mean (SD) ^c	2.0 (1.3)	2.3 (1.4)	3.8 (2.0)
Glycated hemoglobin level, mean (SD), %	5.43 (0.31) ^c	5.35 (0.33)	5.40 (0.35)
Cholesterol level, mean (SD), mg/dL			
Low-density lipoprotein ^c	85.4 (22.0)	92.0 (24.6)	98.0 (24.9)
High-density lipoprotein ^c	52.5 (11.1)	48.4 (10.9)	43.4 (9.1)
Triglycerides level, mean (SD), mg/dL	66.2 (24.9) ^a	73.4 (45.7) ^a	90.6 (64.3)
C-reactive protein level, mean (SD), mg/L ^c	0.9 (1.4)	1.4 (2.1)	3.1 (3.2)

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.

^aSignificant difference from the obese group.

^bSignificant difference from the overweight group.

^cSignificant difference among all body mass index groups.

^dCalculated as weight in kilograms divided by height in meters squared.

sured using an automated method (HPLC; Tosoh Corporation) certified by the National Glycohemoglobin Standardization Program. HOMA-IR was calculated as the fasting blood glucose level (in milligrams per deciliter) times the fasting insulin level (in microinternational units per milliliter), divided by 405.²⁹ The high-sensitivity C-reactive protein (CRP) level was measured using an enzymatic immunoassay slide (VITROS CRP; Ortho Clinical Diagnostics).

DEFINITION OF MetS

We used 2 definitions of MetS. In the first definition of MetS, published by Cook et al³⁰ and used in other studies,^{31,32} the IFG level is the component measuring glucoregulatory control³³; 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 \geq 110 mg/dL [to convert triglycerides level to millimoles per liter, multiply by 0.0113]), (3) low HDL-C level (\leq 40 mg/dL [to convert HDL-C level to millimoles per liter, multiply by 0.0259]), (4) elevated blood pressure (for children \leq 18 years, a systolic or diastolic blood pressure exceeding the 90th percentile adjusted for age, sex, and height or \geq 130/85 mm Hg, whichever is lower; for those older than 18 years, \geq 130/85 mm Hg),³⁴ and (5) IFG level (fasting blood glucose level \geq 100 mg/dL).

In the second definition of MetS, we constructed an alternate criterion; MetS based on this definition is referred to as MetS_{HOMA-IR}, substituting the IFG level with an elevated HOMA-IR. As has been previously described in adolescent populations,³⁵ 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.

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 $\alpha = .05$.

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

Table 2. Point Prevalence of MetS Using Homeostasis Model Assessment of Insulin Resistance (MetS_{HOMA-IR}) vs Impaired Fasting Plasma Glucose (MetS_{IFG}) Level by Sex and by Body Mass Index Group

Variable	MetS _{HOMA-IR}			MetS _{IFG} Level		
	Male (n = 538)	Female (n = 647)	Total (N = 1185)	Male (n = 538)	Female (n = 647)	Total (N = 1185)
No. with MetS/total No. in group						
Healthy weight	0/152	1/204	1/356	0/152	1/204	1/356
Overweight ^a	9/149	14/238	23/387	4/149	6/238	10/387
Obese ^a	85/237	70/205	155/442	62/237	39/205	101/442
Total No. (%)^a	94 (7.5)	85 (13.1)	179 (15.1)	66 (12.3)	46 (7.1)	112 (9.5)

Abbreviation: MetS, metabolic syndrome.

^aSignificant difference in point prevalence between MetS_{HOMA-IR} and MetS_{IFG} for total and sex groups separately.

Table 3. Point Prevalence of Metabolic Syndrome (MetS) Components by Body Mass Index Group Among 1185 High School Students

MetS Component	Healthy Weight, %	Overweight, %	Obese, %	P Value
Hypertension	11.8	25.6	30.3	<.001
Hypertriglyceridemia	6.7	13.2	23.3	<.001
Low high-density lipoprotein cholesterol level	13.2	23.8	38.9	<.001
Central adiposity	2.2	23.8	72.6	<.001
Insulin resistance	4.5	12.4	37.8	<.001
Impaired fasting glucose level	0.6	0.3	2.0	.03

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} 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

Table 4. Linear Regression Analyses Demonstrating the Ability of Various Metabolic and Anthropomorphic Variables to Predict Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) vs Impaired Fasting Plasma Glucose (IFG) Level^a

Dependent Variable	HOMA-IR			IFG Level		
	β Coefficient	Adjusted R^2	P Value	β Coefficient	Adjusted R^2	P Value
Body mass index	0.488	0.256	<.001	0.159	0.057	<.001
Blood pressure						
Systolic	0.301	0.099	<.001	0.166	0.056	<.001
Diastolic	0.199	0.056	<.001	0.067	0.036	.02
Waist circumference	0.498	0.263	<.001	0.171	0.060	<.001
Triglycerides level	0.336	0.128	<.001	0.107	0.043	<.001
High-density lipoprotein cholesterol level	0.223	0.064	<.001	-0.055	0.034	.06
C-reactive protein level	0.326	0.122	<.001	0.154	0.052	<.001

^aAll 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.

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.

COMMENT

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,^{19,20,36-38} 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. In our sample, MetS prevalence also increased with higher BMI. Healthy weight seemed to be protective of MetS, with only 1 adolescent (0.3%) in that study group meeting the criteria for MetS_{HOMA}. This is in agreement with Cook and colleagues,³⁰ who described the prevalence of MetS among adolescents of normal weight to be 0% to 1.6%.

MetS is a useful clinical and research construct for identifying individuals at increased risk for type 2 diabetes mellitus, cardiovascular disease, and osteoarthritis,³⁹ among other chronic illnesses.^{40,41} In children, a MetS diagnosis can be a particularly valuable catalyst for an intensive diet and exercise intervention targeted at preventing further disease progression.⁴² However, our work highlights that a definition of MetS that uses an IFG threshold may fail to identify children with significant insulin resistance and hyperinsulinemia. Children can mount compensatory insulin secretion to maintain normoglycemia, while demonstrating evidence of significant insulin resistance and remaining at increased risk for developing numerous chronic conditions later in life.¹³ In our sample of more than 1000 adolescents, we found marked differences in the prevalence of IFG thresholds relative to that of a HOMA-IR of 3.99 or higher by BMI percentile categories. The IFG threshold was met by only 2.0% of our participants in the obese group (Table 3); alternatively, using a conservative HOMA-IR cut point of 3.99 or higher as an estimate of insulin resistance,^{21,36} this criterion was fulfilled by 37.8% of

adolescents in our obese group. The increased prevalence of an elevated 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 al³⁰ 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 colleagues³⁶ 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-workers¹⁸ 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 μ U/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.⁴³

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,²¹ who suggested that the incorporation of HOMA-IR into a pediatric MetS definition cre-

ates a more consistent construct that is more likely to reflect a cohesive underlying physiological basis than a MetS definition that uses the IFG adult standard.

Although the mean (SD) age of our participants was 16.7 (1.2) years, we did not ascertain sexual development stage, and the possibility exists that some of our participating students were prepubertal. Insulin resistance increases during early teenage years until sexual development Tanner stage 3 and eventually normalizes by the completion of puberty.^{1,44,45} However, Lee and colleagues³⁵ noted that in a nationally representative sample of US adolescents, HOMA-IR demonstrated limited variability by age in normal and overweight adolescents and showed high variability in obese adolescents. Moreover, insulin resistance also varies by sex and race/ethnicity⁴⁶; therefore, future work should determine appropriate age, sex, and race/ethnicity cutoffs for estimates of insulin resistance.⁴⁷

While IFG level is a significant risk factor for a host of diseases,⁴⁸ 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.⁴⁹ 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.⁵ 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.

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