Racial/Ethnic and Sex Differences in the Ability of Metabolic Syndrome Criteria to Predict Elevations in Fasting Insulin Levels in Adolescents

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Objective To evaluate racial/ethnic and sex differences in the relationship between metabolic syndrome (MetS) diagnosis and fasting insulin in adolescents.

Study design We analyzed data from the National Health and Nutrition Evaluation Survey 1999-2008 for 3693 non-Hispanic-white, non-Hispanic-black, and Hispanic adolescents (12 to 19 years of age). We used linear regression to evaluate differences in fasting insulin levels between those with and without an adolescent adaptation of ATPIII-MetS in a sex- and race/ethnicity-specific basis.

Results Females had higher insulin levels than males, and non-Hispanic blacks and Hispanics had higher levels than non-Hispanic whites. Adolescents with MetS had higher insulin levels than those without MetS. The difference in insulin levels between those with and without MetS was greater in non-Hispanic blacks than in non-Hispanic whites ($P < .05$) but not Hispanics ($P = .10$). The sensitivity of MetS in detecting elevated insulin levels was lower in non-Hispanic blacks and females than in other ethnicities and males, respectively. Correlations between insulin and individual MetS components were similar among ethnicities.

Conclusion MetS diagnosis performed more poorly in predicting elevated insulin levels in non-Hispanic blacks and in females. These data support the hypothesis that non-Hispanic blacks do not meet current criteria for MetS until they have reached a more advanced degree of insulin resistance. *(J Pediatr 2011;159:975-81)*.

Metabolic syndrome (MetS) was first described as a cluster of clinical findings strongly associated with insulin resistance.[1,2] Nevertheless, measurements of insulin itself are not criteria for diagnosis of MetS, which is instead based on specific cutoff values used to identify elevated waist circumference (WC), hypertension, low high-density lipoprotein-cholesterol (HDL-C), hypertriglyceridemia, and elevated fasting glucose.[1,2] Although multiple sets of criteria have been proposed for classifying MetS in children—including one by the International Diabetes Federation[3-5]—the majority of research in this area has used criteria based on the Adult Treatment Panel III (ATPIII) criteria,[2,6,7] with cutoff levels adjusted to be more consistent with adolescent ranges.[1,8-10] The utility of MetS as a clinical tool in pediatrics has been shown; children with MetS have an OR of 11.5 for developing type 2 diabetes mellitus (T2DM) within 30 years,[10] and in adults MetS predicts earlier cardiovascular disease (CVD).[6] This makes a diagnosis of MetS an appealing trigger for early intervention among at-risk youths.[5]

Non-Hispanic-black adolescents have lower rates of MetS diagnosis than Hispanics and non-Hispanic whites[4,7,9] despite having a higher degree of insulin resistance than is seen in non-Hispanic whites[11,12] and higher rates of T2DM and CVD as adults.[13,14] Similarly, adolescent females have lower rates of MetS,[4,9] and comparisons of insulin resistance between sexes have been mixed.[12,15] Thus, the value of MetS in identifying females and non-Hispanic-black adolescents with insulin resistance is unclear.

Our goal was to determine whether the relationship between insulin resistance and MetS varied by sex and race/ethnicity among non-Hispanic-white, non-Hispanic-black, and Hispanic adolescents who participated in the National Health and Nutrition Evaluation Survey (NHANES) 1999-2008. On a sex- and race/ethnicity-specific basis, we compared: (1) the degree of insulin resistance (estimated as either levels of fasting insulin or the homeostasis model of insulin resistance (HOMA-IR) in the presence and absence of MetS; and (2) the sensitivity of a MetS diagnosis to detect elevations in fasting insulin. In doing so, we aimed to identify sex- and racial/ethnic-oriented variations in the ability of a diagnosis of MetS to identify insulin resistance in adolescents.

ATPIII	Adult Treatment Panel III
BMI	Body mass index
BP	Blood pressure
CVD	Cardiovascular disease
MetS	Metabolic syndrome
HDL-C	High-density lipoprotein-cholesterol
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Evaluation Survey
SBP	Systolic blood pressure
T2DM	Type 2 diabetes mellitus
WC	Waist circumference

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Supported by NIH grants (5K08HD060739-02 to M.D. and 1R21DK085363 to M.G., L.D., and M.D.). The authors declare no conflicts of interest.

 10.1016/j.jpeds.2011.05.023

Methods

Data were obtained from NHANES (1999-2008), a complex, multistage probability sample of the US population. These annual cross-sectional surveys are conducted by the National Center for Health Statistics of the Centers for Disease Control, with subjects undergoing anthropometric and blood pressure (BP) measurements, answering questionnaires, and undergoing phlebotomy (http://www.cdc.gov/nchs/nhanes.htm). The National Center for Health Statistics ethics review board reviewed and approved the survey, and participants were provided with informed consent forms prior to participation. WC, BP, and laboratory measures of triglycerides, HDL-C, and glucose were obtained using standardized protocols and calibrated equipment.[1,16] All blood samples used for analyses were obtained from participants asked to fast for 8 hours or longer prior to the blood draw.

MetS was defined by a commonly used pediatric/adolescent adaptation of the ATPIII criteria.[1,8,9] Participants had to meet 3 or more of the following 5 criteria: (1) concentration of triglycerides 110 mg/dL or higher; (2) HDL-C 40 mg/dL or lower; (3) WC 90th percentile or higher for age/sex (or ATPIII limit of 102 cm for males and 88 cm for females, whichever was lower)[2,17]; (4) glucose concentration 100 mg/dL or higher; and (5) systolic or diastolic BP in the 90th percentile or above (age-, height-, and sex-specific).[18]

Data from non-Hispanic-white, non-Hispanic-black, and Hispanic (Mexican-American/other Hispanic) adolescents between 12 and 19 years of age were analyzed. Children younger than 12 years of age were excluded because fasting values for triglycerides and glucose were obtained only in participants 12 years old or older. Subjects were excluded if they had known diabetes or unknown diabetes (fasting glucose > 125 mg/dL), because each of these factors can result in limitations in insulin release,[19] which would have confounded our evaluation of the relationships between MetS and insulin levels. Also excluded were pregnant women and individuals taking antihyperlipidemic or antidiabetic medications because they are all likely to alter lipid and insulin levels in a manner that may not reflect baseline MetS-insulin correlations. Individuals taking antihypertensive medications were classified as having hypertension.

High fasting insulin levels were determined to be the 95th percentile of insulin in normal-weight individuals (body mass index [BMI] < 85th percentile) in the sample (16 IU/mL), given the influence of highly prevalent obesity on "normal" insulin values overall. The HOMA-IR was calculated as fasting insulin in mU/mL × fasting glucose in mmol/L/22.5.

Statistical Analysis

Statistical significance was defined as a P value of less than .05. Statistical analysis was performed using SAS (version 9.2, Cary, North Carolina) and SUDAAN (version 10; Research Triangle Institute, Research Triangle Park, North Carolina), which accounts for the survey design when estimating standard errors to obtain population-based estimates. We combined all data sets from the four 2-year cycles (1999 to 2008) for statistical analyses to increase our total sample size. The prevalence of MetS was calculated by sex, race/ethnicity, and time period of data collection and was compared via chi-square tests. Mean fasting insulin was also compared among these groups using either unpaired t-tests or ANOVA. Pearson r correlation coefficients were computed to assess the degree of linear association between each MetS component and ln(insulin) by race/ethnicity. Linear regression was then used to assess the effect of sex, race/ethnicity, and MetS status on levels of ln(insulin). The natural log transformation of fasting insulin was used to achieve normality. All interactions of the three covariates (sex, race/ethnicity, and MetS status) were initially included in the model but were removed in a stepwise fashion if the associated interaction P value was less than .15. Because of the known effects of poverty,[20] education,[20] and smoking[21] on insulin levels, each of these covariates was included in the model. Education was classified as the highest level obtained for any household member and was categorized as follows: less than high school, high school, and greater than high school. Income-to-need ratio was used to measure poverty. Because of the poor reliability of self-reporting of smoking among adolescents,[22] serum cotinine was used to identify smokers, with a cutoff of 15 ng/mL, as recommended.[23] Geometric means of fasting insulin from the final model were estimated and compared according to sex and race/ethnicity, as applicable. The sensitivity of MetS for identifying elevated fasting insulin (16 IU/mL, the 95th percentile among normal-weight adolescents) was computed by sex and race/ethnicity. With the exception of the correlation estimates, all analyses incorporated the sampling weights included in NHANES.

Results

The sample of participants consisted of 3693 non-Hispanic blacks, non-Hispanic whites, and Hispanics between 12 and 19 years old. Data for all variables were tested, and 119 subjects were excluded based on the criteria listed earlier. Analyzing Mexican Americans as a separate group did not yield results different from those that were obtained when they were combined with other Hispanics. Among US adolescents, the prevalence of MetS was greater in males than females (11.1% vs. 5.9%; $P < .05$) and was greater in non-Hispanic whites and Hispanics than in non-Hispanic blacks (8.8% and 11.2% vs. 4.7%, both $P < .05$) (**Table I**; available at www.jpeds.com).The prevalence of MetS did not differ over the test period, and there were no consistent trends in MetS-associated variables over the study period (data not shown).

Individual components of MetS are shown in **Table I**. Compared with non-Hispanic whites and Hispanics, non-Hispanic blacks had lower triglycerides and fasting glucose levels and had higher high-density lipoproteins and systolic BP (SBP). Hispanics had the highest WC but otherwise did not exhibit differences in individual MetS components compared with non-Hispanic whites.