DEFINITION OF METABOLIC SYNDROME IN PREADOLESCENT GIRLS

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Objective To compare and contrast proposed definitions of metabolic syndrome in pediatrics, and to determine prevalence of metabolic syndrome in preadolescent females when applying different criteria.

Study design A literature review on definitions of metabolic syndrome and cardiovascular "risk factor clustering" in children and adolescents published in the past decade. Pediatric definitions of metabolic syndrome were then applied to a community-based study of 261 black preadolescent females (Girls Health Enrichment MultiSite studies [GEMS]) and a school-based, cross-sectional study of 240 ethnically-diverse preadolescent females (Girls Activity, Movement and Environmental Strategy [GAMES]) who had a baseline physical examination and fasting morning blood sample.

Results Agreement among pediatric definitions of metabolic syndrome was poor. The prevalence of MS and cardiovascular risk factor clustering ranged from 0.4% to 23.0% for GEMS and 2.0% to 24.6% for GAMES with definitions adapted from the National Cholesterol Education Program Adult Treatment Panel III, and 0% to 15.3% for GEMS and 0.4% to15.8% for GAMES using modified criteria from the World Health Organization.

Conclusions The prevalence of metabolic syndrome in preadolescent girls varies widely because of disagreement among proposed definitions of metabolic syndrome in pediatrics. Further investigation is needed to determine which metabolic factors and their respective cut points should be used to identify children at risk for development of clinical disease. *(J Pediatr 2006;148:788-92)*

Currently in the United States, 1 in 5 children is overweight.[1] Childhood obesity is significantly associated with hyperinsulinemia, dyslipidemia, and hypertension in adulthood.[2-4] The association between obesity and insulin resistance has been documented in several pediatric studies, in addition to clustering of adverse cardiovascular risk factors and insulin resistance.[5] In 1988, Reaven [6] first described the coexistence of multiple metabolic derangements—hyperinsulinemia, glucose intolerance, increased very low density lipoprotein triglycerides, decreased high-density lipoprotein (HDL) cholesterol, and hypertension—as syndrome X. Other metabolic abnormalities have been since observed in the setting of insulin resistance, including endothelial dysfunction, increased procoagulant factors, hyperuricemia, and inflammation.[7]

Multiple studies in adults have also shown a strong association between insulin resistance and increased risk of coronary artery disease and stroke.[8-10] The term "metabolic syndrome" was introduced into the medical community when the World Health Organization (WHO) formally recognized the clustering of cardiovascular risk factors associated with insulin resistance.[11] More recently, the National Cholesterol Education Program Adult Treatment Panel III (ATP III) has provided a new definition of the metabolic syndrome to identify individuals with increased risk for cardiovascular disease (CVD).[12] While the WHO definition of metabolic syndrome is primarily based on insulin resistance, the ATP III definition includes criteria predictive for CVD.[13]

Studies comparing the ATP III and WHO definitions of metabolic syndrome in adults have found similar results in total prevalence of metabolic syndrome but important differences in estimates among various ethnic groups.[13-15] To date, there is no universal definition of the metabolic syndrome in adults, thus making it difficult to compare results from different studies and characterize temporal trends in prevalence. Likewise, there is

ADA	American Diabetes Association	GEMS	Girls Health Enrichment MultiSite studies
ATP III	Adult Treatment Panel III	HDL	High density lipoprotein
BMI	Body mass index	NHANES	National Health and Nutrition Examination Survey
CDC	Center for Disease Control		
CV	Coefficient of variation	NHBEP	National High Blood Pressure Education Program
CVD	Cardiovascular disease		
GAMES	Girls Activity Movement and Environmental Strategy	WHO	World Health Organization

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no standard definition of the metabolic syndrome for children resulting in similar problems for epidemiologic studies and clinical practice. Several pediatric studies have shown an alarming increase in components of the metabolic syndrome, obesity and insulin resistance, during the past decades, using a variety of definitions. This suggests a growing prevalence of the metabolic syndrome in children and a new public health burden with serious adverse sequelae.

To estimate the prevalence of metabolic syndrome and cardiovascular risk factor clustering in children, we applied a number of the currently published criteria to 2 population-based samples of preadolescent girls. One sample was 8- to 10-year-old black girls whereas the other was 7- to 10-year-old girls of mixed ethnicity.

METHODS

Study Sample

The Stanford Girls Health Enrichment Multi-site Studies trial (Stanford GEMS) is an obesity prevention study in low socioeconomic, preadolescent black girls in Oakland, Calif. Participants were recruited from throughout the community, schools, and community centers in low-income areas of Oakland with high proportions of black people. Girls between the ages of 8.00 and 10.99 years with a body mass index (BMI) $\geq 50^{th}$ percentile for age on the 2000 growth charts of the Centers for Disease Control and Prevention [16] or with at least 1 parent/guardian with a BMI ≥ 25 kg/m^2 were eligible to participate. The Stanford Girls' Activity, Movement and Environmental Strategies study (Stanford GAMES) recruited preadolescent females between the ages of 7.00 to 10.99 years from 6 ethnically and socioeconomically diverse public elementary schools in South San Francisco, Calif, for an obesity prevention study. There were no minimum BMI or race-specific eligibility criteria for enrollment in GAMES. For both studies, girls were ineligible if they had a prior diagnosis of diabetes mellitus; a chronic illness that affects growth or weight (eg, hypothyroidism, inflammatory bowel disease), take a medication potentially affecting growth or weight, had a condition limiting participation in physical activity enough that they are not able to participate in Physical Education at school (eg, significant structural heart disease), were pregnant, or if the family expected to move away from the San Francisco Bay Area within the next 24 months. All measures were obtained in participants' homes to maximize the generalizability of the study samples, by not excluding families who would not have been able to make it to a medical center or clinical research center. This study uses data from the baseline measurements of both GEMS and GAMES. The protocols were approved by the Stanford University Panel for Protection of Human Subjects in Medical Research. Written consent was obtained from a parent or guardian and written assent was obtained from girls, before participation.

Anthropometric and Blood Pressure Measurements

Weight was measured in duplicate in light clothing to the nearest 0.1 kg using Seca 770 model scales (Vogel and Halke, Hamburg, Germany). Height was measured in duplicate to the nearest 0.1 cm using a Shorr Height Measuring Board (Shorr Productions Growth Unlimited, Olney, Md). BMI (kg/m^2) was calculated from measured body weight divided by squared height.[16] Waist circumference was measured in duplicate to the nearest 0.1 cm at the level of the umbilicus using a non-elastic fiberglass measuring tape (Tech-Med model 4414; Moore Medical Corp., New Britain, Conn). Triceps skinfold thickness of the right arm was measured in triplicate to the nearest 0.2 mm with a Harpenden caliper (British Indicators; St. Albans, United Kingdom). For physical attributes measured in duplicate, a third measurement was taken if the first 2 differed by 0.3 kg in weight, 0.5 cm in height, or 1 cm in waist circumference. The mean of the 2 or 3 measures was used for analysis. Resting systolic and diastolic blood pressures were measured after participants were seated quietly for 5 minutes with their arm supported at the level of the heart and feet flat on the floor using an automated blood pressure monitor (Dinamap Pro 100; GE Medical Systems Information Technologies, Inc., Milwaukee, Wisconsin). Three measures were completed at 1-minute intervals, and the mean of the 3 measures was used in the analysis.

Laboratory Assays

Fasting blood samples were obtained by venipuncture after an overnight fast of greater than 8 hours. Whole blood was collected in a 10-mL red and gray-stoppered tube containing a serum separator (BD Vacutainer Systems, Franklin Lakes, NJ). Serum was separated through centrifugation 30 minutes after collection, aliquoted, and held at 4° C for delivery to Stanford Hospital Clinical Laboratory (within 24 hours). Processed specimens were frozen at −70° C until analysis. Plasma glucose concentration was measured by an enzymatic method using the Vitros analyzer (Ortho Clinical Diagnostics, Rochester, NY), which has an intraassay coefficient of variation (CV) of 2% to 3% and an interassay CV of 3% to 5%. Insulin levels were obtained with an automated noncompetitive immunoassay (Immulite 2000; Diagnostic Products, Los Angeles, Calif). The intraassay and interassay CVs were 2% to 4% and 5% to 8%, respectively. HDL cholesterol was measured by direct coupled enzymatic colorimetric assay (Beckman Coulter, Brea, Calif) whereas triglyceride was measured by unbanked coupled enzymatic colorimetric assay (Ortho Clinical Diagnostics, Rochester, NY). The interassay CV was 2% to 3% for HDL and 1% to 2% for triglyceride.

Definitions of Metabolic Syndrome

The ATP III and WHO definitions are widely used in the adult population for defining metabolic syndrome.[11,12] Although they share some common criteria, the WHO definition requires insulin resistance, glucose intolerance, or diabetes as a necessary component for diagnosis.

We reviewed pediatric studies published in the past decade on the prevalence of metabolic syndrome. Although