Characterization of the Metabolic Syndrome in a Multi-Ethnic Sample of Children: Is it Useful?

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Abstract: The pathophysiological relevance of the metabolic syndrome is not currently understood, particularly when attempting to apply the diagnosis to children with varying degrees of adiposity or from ethnically diverse populations. The aim of this study was to evaluate the applicability of the metabolic syndrome characterization when the associations are explored by sex, race/ethnicity, and weight status. Participants were 247 multi-ethnic (African American (AA); n=90; European American (EA); n=102; Hispanic American (HA); n=55) children aged 7-12y. Anthropometric measurements, body composition, blood pressure and fasting blood samples were obtained. Approximately 9% of the children met the criteria for a clinical diagnosis of the metabolic syndrome. There were no differences in prevalence by sex, nor were there differences between girls and boys for mean values of each component. However, there were ethnic differences in characterization of having the metabolic syndrome, with HA more likely to meet the criteria. HA had greater waist circumference, higher triglyceride and glucose concentration and lower HDL-C concentration; whereas AA had higher blood pressure. Weight status was also positively associated with mean values for each component. Due to inherent variations in body composition, physiology and genetics, the usefulness of a characterization of the metabolic syndrome may be limited in the pediatric population.

Keywords: Pediatric health, race/ethnicity, cardiometabolic outcomes, obesity.

INTRODUCTION

The concept of the metabolic syndrome was first introduced (as Syndrome X) by Reaven in 1988 [1], when he described metabolic risk factors that occur more often in a cluster than chance alone would predict. The central message surrounding a diagnosis of the metabolic syndrome is that meeting the criteria is a cause for concern related to progression of the development of type 2 diabetes (T2D) and cardiovascular disease (CVD). Although the association between the individual risk factors that comprise the metabolic syndrome is well-established, a clear demarcation as to whether the adverse effect of the sum (a characterization of the syndrome) is greater than the parts (health effects of each individual component) has not been identified. Further, the pathophysiological relevance is not currently understood, particularly when attempting to apply the diagnosis to children. In addition, the usefulness of clustered risk may be compromised when including children with varying degrees of adiposity or from ethnically diverse populations.

Recent research suggests that the clustered risk factors of the metabolic syndrome in childhood are, at least in part, causally related to excess adiposity [2]. It is well known that body composition differences exist between boys and girls [3-6] and between racial/ethnic groups [3, 7-9]. However, there may be a differential impact of long-term health effects, such that increased risk of morbidity and mortality conferred by increased adiposity may not necessarily apply equally to all individuals. For example, although girls have greater adiposity and are more insulin resistant than boys [10], these metabolic risks do not necessarily translate to an increased rate of T2D in adulthood [11, 12]. Further, whereas fat mass has been shown to be associated with the metabolic syndrome in European American (EA) and African American (AA) children [13-15], in a sample of Hispanic American (HA) children, fat mass was not independently associated with features of the metabolic syndrome [16]. Although it has not been documented, these differences in the role of adiposity in metabolic outcomes in children may suggest a differential impact according to race/ethnicity. Moreover, excess adiposity associated with hypertension among EA and AA children may not be associated with hypertension in HA children [16]. Additionally, the excess adiposity associated with dyslipidemia in EA and HA, may not be associated with an aberrant lipid profile in AA [17]. Taken together, it is plausible that the contribution of adiposity may differ by sex and racial/ethnic group.

In adults, the fact that some populations with a low prevalence of the metabolic syndrome have the highest prevalence for CVD and T2D challenges the concept that the sum of the metabolic syndrome components are greater than its parts and the raising questions on the clinical significance of diagnosing this entity. One factor may carry more weight and confer a greater risk than any clustering depending on the group in which the syndrome is being characterized. This limitation is likely to be more pronounced in children who exhibit risk factors that may (or may not) predispose them to future disease development. A greater understanding of how sex, adiposity and race/ethnicity may play roles in influencing a diagnosis of the metabolic syndrome in

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children is warranted. Therefore, the aim of this study was to evaluate the applicability of the metabolic syndrome characterization when the associations are explored by sex, race/ethnicity, and weight status in a multi-ethnic cohort of children aged 7-12 years.

METHODS

Participants

Participants were 247 children aged 7-12 years recruited as a part of an ongoing cross-sectional study which aims to identify racial and ethnic differences in metabolic outcomes among healthy children. Children were categorized according to parental self-report as AA (n=90), EA (n=102), or HA (n=55). The children were pubertal stage $\leq$3 (girls had not yet began menstruating) as assessed by a pediatrician according to the criteria of Marshall and Tanner [18], had no major illnesses or medical diagnoses (e.g. asthma, diabetes) and were not taking any medications contraindicated for study participation. The children and parents provided informed assent and consent, respectively, to the protocol, which was approved by the Institutional Review Board for human subjects at the University of Alabama at Birmingham. All measurements were performed at the General Clinical Research Center (GCRC) and the Department of Nutrition Sciences at UAB between 2005 and 2008.

Protocol

Participants completed two testing sessions. In the first session, pubertal status, anthropometric measurements, and body composition were assessed. In the second session, participants were admitted to the GCRC in the late afternoon for an overnight visit. Two blood pressure measurements (evening and morning) were obtained. All participants were given the same meal and snack foods. After 2000h, only water and/or non-caloric decaffeinated beverages were permitted until after the morning testing session. Upon completion of the overnight fast, blood samples were obtained for glucose and lipid analyses.

Anthropometric Measures

For all participants, anthropometric measurements were obtained by the same registered dietitian. Participants were weighed (Scale-tronix 6702W; Scale-tronix, Carol Stream, IL) to the nearest 0.1 kg in minimal clothing without shoes. Height was recorded without shoes using a digital stadiometer (Heightronic 235; Measurement Concepts, Snoqualmie, WA). BMI, calculated from measured height and weight, was categorized as: $<85^{th}$ percentile considered "normal weight; " 85^{th}-95^{th} percentile as "overweight; " and $\geq 95^{th}$ percentile as "obese"[19, 20] according to growth charts of the Center for Disease control.

Waist circumference was measured at the "narrowest part of the torso" or the area between the ribs and iliac crest as described by Lohman *et al.* [21]. Waist circumference measures were obtained using a flexible tape measure (Gulick II; Country Technology, Inc., Gays Mills, WI) and were recorded to the nearest 0.1 cm.

Assessment of Body Composition

Body composition (total body fat mass and non-bone lean tissue mass) was measured by dual-energy x-ray absorptiometry (DXA) using a GE Lunar Prodigy densitometer (GE LUNAR Radiation Corp., Madison, WI). DXA has been found to be highly reliable for body composition assessment in children [22]. In our laboratory, the coefficient of variation (CV) for repeated measures of total body fat mass was 6.55%. Participants were scanned in light clothing, while lying flat on their backs with arms at their sides. DXA scans were performed and analyzed using pediatric software (enCORE 2002 Version 6.10.029).

Assay of Glucose and Lipids

Fasting blood glucose was assayed using the glucose oxidase method using a SIRRUS analyzer (interassay CV 2.56%). Fasting triglycerides were assessed with the glycerylphosphate (GPO) method. HDL-cholesterol was analyzed using a two-reagent system involving stabilization of LDL, VLDL, and chylomicrons using cyclodextrin and dextrin sulfate, and subsequent enzymatic-colorometric detection of HDL-C.

Blood Pressure

Evening and morning blood pressure (Dinamap Pro 200 automated pediatric cuff, GE Medical Systems) was measured during the overnight inpatient stay. On each occasion, blood pressure was taken twice, 5 minutes apart, after 10 minutes of seated rest with legs uncrossed and feet flat on the floor. If the participant's feet did not reach the floor, books were placed under the feet to ensure they were flat. The evening measurements were taken at approximately 1800 h on the evening of the overnight stay. The morning measurements were taken shortly after awakening at approximately 0700 h of the overnight stay. The evening and morning measurements did not significantly differ from one another and therefore, were averaged to yield final blood pressure values.

Metabolic Syndrome Criteria and Definitions

A number of definitions and cut-off values exist that define criteria for the metabolic syndrome in the pediatric population [21, 23, 24] and debate over the most useful definition of the metabolic syndrome continues between organizations such as the American Diabetes Association, the International Diabetes Foundation, and the American Heart Association. Although a consensus has not been reached, the most frequently used definition is that of Cook *et al.* [23, 24]. This definition included waist circumference greater than the 90^{th} percentile (as defined by Maffeis *et al.* [25]), blood pressure greater than the 90^{th} percentile according to height, age, and sex (as defined by NHLBI National High Pressure Working Group Recommendations for Children and Adolescents) [26], triglyceride $\geq$ 110 mg/dL and HDL $\leq$ 40 mg/dL (as defined by the National Cholesterol Education Panel) [27], and glucose concentration > 110 mg/dL (as recommended by the American Diabetes Association). In 2003, the American Diabetes Association recommended lowering the value for impaired fasting glucose to >100 mg/dL [28]. In 2004, the work of Fernandez

et al. [29], demonstrated the importance of age, sex, and ethnic specific waist circumference values. The NHLBI also updated the blood pressure values for the 90th, 95th, and 97th percentiles in 2004 [30]. The Cook definition was revised in 2008 to include the recommendations of the American Diabetes Association, NHLBI, and Fernandez and colleagues [31]. For this analysis, we used the 2008 revised criteria of Cook and colleagues [31]. Individuals were categorized as having the metabolic syndrome if they possessed at least 3 of the 5 components.

Statistical Analyses

Differences in descriptive statistics by sex, race/ethnicity and weight status were examined using analysis of variance (ANOVA) with Duncan's post-hoc analysis. The prevalence of the metabolic syndrome and the mean and frequency of each component was compared in the total sample and according to sex, race/ethnicity, and weight status. Spearman correlations were calculated to determine the association between each of the individual components and the presence of the syndrome. Exploratory factor analysis was carried out using orthogonal varimax transformation; the number of principal factors determined by the amount of variance in relation to total variance (eigenvalue) greater than 1 using the PRIORS SMC command. Results are given as orthogonal score weights on principal components. Factor analysis values greater than 0.4 were deemed significant [32]. All data were analyzed using SAS 9.1 software.

RESULTS

Table **1** presents participant characteristics for the entire sample and by sex, race/ethnicity and weight status. Males and females differed only in body composition such that females had more total and percent fat, while males had more lean mass. There were also racial/ethnic differences in BMI and body composition. The BMI percentile and percent fat was greater in HA than EA and AA while AA were not different from EA or HA. AA had more lean mass than both EA and HA. In addition, differences in characteristics according to weight status were observed. As expected, children classified as obese had greater total adiposity, percent fat and lean mass than their normal and overweight counterparts.

In the total sample, approximately 9% of the children met the criteria for a diagnosis of the metabolic syndrome. Fig. (**1**) illustrates the prevalence of one, two, and three or more risk factors of the metabolic syndrome by sex, ethnicity, and weight status. There were no differences in prevalence according to sex, nor were there differences between girls and boys for mean values of each component (Table **2**). However, there were ethnic differences in characterization of having the metabolic syndrome, with HA more likely than EA and AA to meet the criteria (Fig. **1**). HA had greater waist circumference, higher triglyceride and glucose concentration and lower HDL-C concentration than EA and AA; whereas AA on average had higher systolic blood pressure than EA and HA. There were no differences in the presence of the metabolic syndrome detected according to weight status, but there were differences in meeting the criteria for the individual components. Weight status was positively associated with mean values for each component (albeit not significant for blood pressure and glucose concentration), and inversely associated with HDL-C. When the overweight and obese categories were pooled together, this group was significantly more likely to meet the criteria for the metabolic syndrome than the normal weight group ($p<0.05$) (data not shown).

Table 1. Population Characteristics (Mean (SE)) in the Total Sample and by Sex, Race/Ethnicity, and Weight Status

	Total Sample (n=247)	Male (n=127)	Female (n=118)	EA (n=102)	AA (n=90)	HA (n=55)	Normal Weight (n=172)	Over Weight (n=50)	Obese (n=25)
Sex (% male)	52.7			53.5	53.9	49.2	55.6	41.5	60.0
Age (yrs)	9.6 (0.1)	9.8 (0.1)	9.4 (0.1)	9.7 (0.1)	9.7 (0.2)	9.3 (0.2)	9.7 (0.1)^{e}	9.1 (0.2)^{f}	9.7 (0.3)^{e,f}
Height (cm)	140.1 (0.6)	140.4 (0.9)	139.4 (0.9)	139.7 (1.0)	141.7 (1.0)	138.1(1.3)	140.5 (0.8)	137.2 (1.4)	141.9(2.1)
Pubertal stage	1	1.4^{a}	1.6^{b}	1.4^{c}	1.7^{d}	1.4^{c}	1.5	1.5	1.6
BMI (kg/m^2)	18.4 (0.2)	18.2 (0.2)	18.6 (0.3)	17.8 (0.3)^{c}	18.5 (0.3)^{cd}	19.5 (0.4)^{d}	17.1 (0.1)^{e}	20.2 (0.2)^{f}	24.4 (0.4)^{e}
Percentile BMI	64.7 (1.6)	63.4 (2.2)	65.5 (2.4)	59.7 (2.4)^{c}	62.7 (2.5)^{c}	77.8 (3.3)^{d}	53.3 (1.4)^{e}	89.5 (2.7)^{f}	95.0 (4.0)^{e}
Total fat (kg)	8.71 (0.3)	7.9 (0.5)^{a}	9.6 (0.5)^{b}	8.01 (0.5)^{c}	8.36 (0.6)^{cd}	10.3 (0.7)^{d}	6.68 (0.3)^{e}	11.0 (0.6)^{f}	18.3 (0.8)^{g}
Percent Fat	23.0 (0.6)	20.4 (0.8)^{a}	25.8 (0.8)^{b}	22.1 (0.8)^{c}	20.8 (0.9)^{c}	27.7 (1.1)^{d}	19.6 (0.6)^{e}	28.1 (1.0)^{f}	36.2 (1.5)^{g}
Lean Mass (kg)	25.7 (0.7)	26.6 (0.4)^{a}	24.9 (0.5)^{b}	25.3 (0.5)^{c}	27.3 (0.5)^{d}	24.5 (0.7)^{c}	25.4 (0.4)^{e}	25.7 (0.7)^{e}	29.0 (1.0)^{f}

^{a,b} superscripts indicate mean value differences by sex ($P<0.05$)

^{c,d} superscripts indicate mean value differences by race/ethnicity($P<0.05$)

$^{e-g}$ superscripts indicate mean value differences by weight status($P<0.05$)

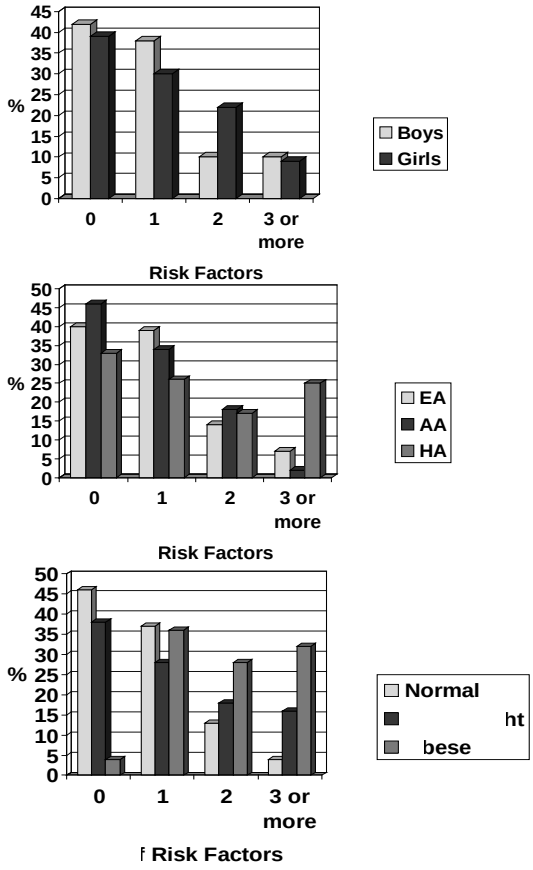


Fig. (1). Percentage of individuals meeting criteria for risk factors of the metabolic syndrome. **A**) Boys (light gray), girls (black) **B**) European Americans (light gray) African American (black), Hispanic American (dark gray); **C**) normal weight (light gray), overweight (black), obese (dark gray).

Table 2. Mean (SE) Values for Metabolic Risk Factors According to Sex, Race/Ethnicity, and Weight Status

	Total Sample (n=247)	Male (n=127)	Female (n=118)	EA (n=102)	AA (n=90)	HA (n=55)	Normal Weight (n=172)	Overweight (n=50)	Obese (n=25)
WC (cm^2)	64.0 (0.5)	64.2 (0.8)	63.9 (0.7)	63.8 (1.0)[a]	63.3 (3.1)[a]	67.8 (1.2)[b]	61.0 (0.4)[d]	67.6 (1.0)[e]	78.3 (2.4)[f]
%*	15	13.4	16.1	11.8[a]	12.2[a,b]	23.6[b]	2.9[d]	13[e]	18[f]
BP (mm Hg)	103.3 (0.7)	102.6 (0.9)	104.0 (1.0)	101.7 (1.0)[a]	106.5 (1.1)[b]	100.2 (1.2)[a]	102.7 (0.7	104.1 (1.7)	106.3 (2.8)
%*	19	17.3	21.2	14.7[a]	31.1[b]	7.3[a]	16.3)[d]	13[e]	6[e]
TG (mg/dL)	65.1 (2.1)	61.9 (2.7)	68.5 (3.3)	66.0 (3.1)[a]	54.8 (3.0)[b]	79.8 (5.5)[c]	60.3 (2.2)[c]	70.7 (5.1)[c]	86.4 (9.3)[d]
%*	9.0	7.9	10.2	8.8[a]	4.4[b]	16.4[a]	5.8[d]	12.0[e]	10.9[e]
HDL-C (mg/dL)	50.1 (0.8)	51.3 (1.1)	48.8 (1.1)	48.6 (1.1)[a]	54.3 (1.4)[b]	45.7 (1.6)[c]	52.2 (0.9)[c]	47.0 (1.6)[d]	42.2 (2.1)[d]
%*	9.0	18.1	23.7	21.6[a]	11.1[b]	34.5[a]	17.4[de]	15.4[d]	34.5[e]
Glucose (mg/dL)	96.8 (0.4)	97.1 (0.6)	96.5 (0.6)	96.7 (0.7)[a]	94.6 (0.7)[a]	99.9 (0.8)[b]	96.6 (0.5)	96.8 (0.9)	98.1 (1.3)
%*	22.7	27.6	17.8	21.6[a]	13.3[b]	40.0[a]	18.3	14.3	23.3

*Percentage of individuals with each component of the metabolic syndrome in the entire sample, and by sex, race/ethnicity and weight status.

[a,b,c] superscripts indicate differences by race/ethnicity (P<0.05)

[d,e, f] superscripts indicate percentage differences by weight status (P<0.05)

Note: Cut-off values for metabolic syndrome [31]; waist circumference (WC) $\geq 90^{th}$ percentile, systolic blood pressure (BP) $\geq 90^{th}$ percentile for age, height, and sex, triglyceride concentration (TG) >110 mg/dl, HDL-C <40 mg/dl, glucose concentration >100 mg/dl.

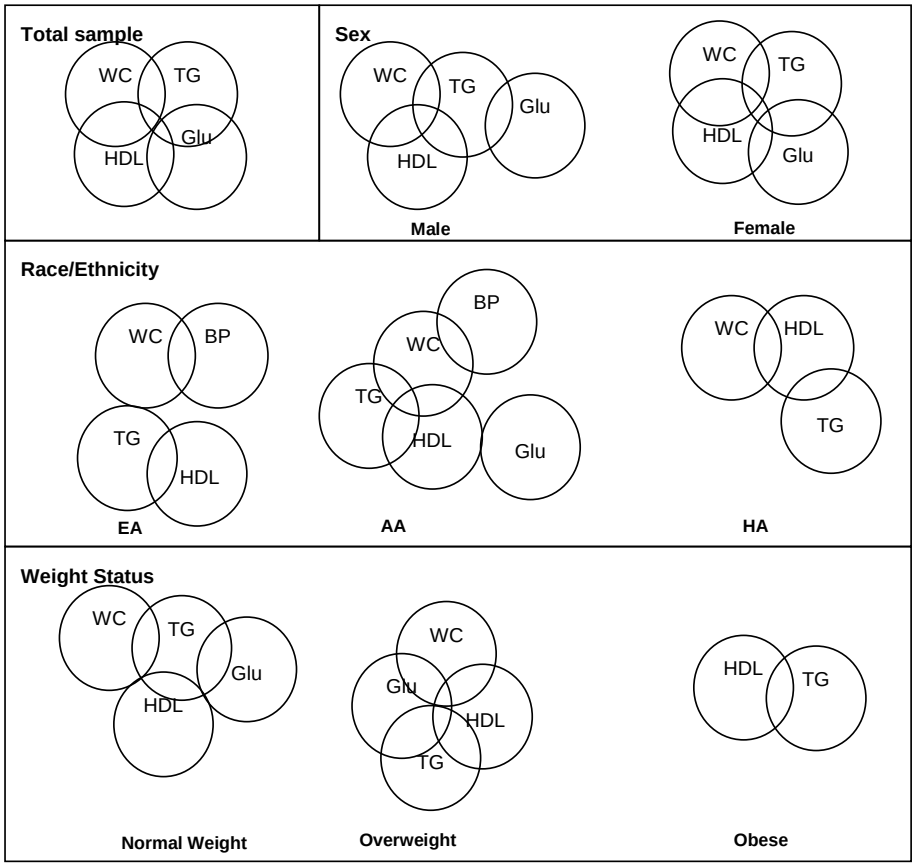
Table 3. Correlations Between the Individual Components and Characterization of the Metabolic Syndrome by Sex, Race/Ethnicity, and Weight Status

Metabolic Syndrome									
		Sex		Race/Ethnicity			Weight Status		
	Total n=247	**Male n=127**	**Female n=118**	**EA n=102**	**AA n=90**	**HA n=55**	**Normal n=172**	**Overweight n=50**	**Obese n=25**
WC	0.40	0.37	0.45	0.44	0.35	0.26	0.12	0.46	0.31
P-value	<0.001	0.001	<0.001	<0.001	0.001	0.068	0.112	0.001	0.159
BP	0.09	0.10	-0.10	0.12	0.06	0.10	0.03	0.04	0.20
P-value	0.952	0.207	0.293	0.258	0.387	0.492	0.562	0.760	0.423
TG	0.39	0.38	0.40	0.39	0.27	0.67	0.46	0.38	0.64
P-value	<0.001	<0.001	<0.001	0.005	0.020	<0.001	<0.001	0.005	0.001
HDL-C	-0.48	-0.46	-0.49	-0.32	-0.19	-0.52	-0.63	-0.61	-0.75
P-value	<0.001	<0.001	<0.001	0.001	0.189	<0.001	<0.001	<0.001	<0.001
Glucose	0.21	0.55	0.50	0.13	0.16	0.22	0.60	0.56	0.04
P-value	0.001	0.001	0.007	0.507	0.145	0.116	<0.001	0.001	0.107

Note: Cut-off values for metabolic syndrome [31]; waist circumference (WC) $\geq 90^{th}$ percentile, systolic blood pressure (BP) $\geq 90^{th}$ percentile for age, height, and sex, triglyceride concentration (TG) >110 mg/dl, HDL-C <40 mg/dl, glucose concentration >100 mg/dl.

Correlations between exceeding the cut-off for an individual component and being characterized as having the metabolic syndrome are presented in Table **3** for the total sample and by sex, race/ethnicity and weight status. In this sample, blood pressure was not associated with presence of the metabolic syndrome, regardless of the stratification. A high waist circumference was highly indicative of the presence of the metabolic syndrome in the total sample and by sex but the association differed by race/ethnicity and weight status.

Fig. (**2**) presents the clustering of the individual components of the metabolic syndrome with one another according to Spearman correlations. As noted in the figure,



WC= Waist circumference; BP= Blood pressure; TG= Triglyceride; HDL= High density Lipoprotein Cholesterol; Glu= Blood Glucose.

Fig. (2). Clustering of components of the metabolic syndrome based on correlation in the total sample and according to sex, race/ethnicity, and weight status. Overlapping circles represent significant correlation ($p<0.05$), circles that touch represent a correlative trend ($0.05<p>0.10$).

Table 4. Factor Analysis*

	Total	Male	Female	EA	AA	HA	Normal Weight	Over-weight	Obese	
									Factor 1	Factor 2
WC	**0.47**	**0.51**	**0.44**	**0.47**	**0.67**	0.31	0.20	**0.62**	**0.42**	**0.44**
BP	0.06	0.11	-0.01	**0.44**	0.29	-0.19	-0.03	0.15	-0.23	**0.48**
TG	**-0.63**	**-0.55**	**-0.70**	**-0.48**	**-0.59**	**-0.71**	**-0.52**	**-0.68**	**-0.84**	-0.01
HDL	**0.58**	**0.57**	**0.60**	**0.48**	**0.63**	**0.58**	**0.54**	**0.51**	**0.73**	-0.17
Glu	0.34	0.36	0.35	0.14	0.31	0.18	0.35	**0.47**	0.09	**0.45**

*Entries are orthogonal loadings, **values >0.4 in bold**.

WC= Waist circumference; BP= Blood pressure; TG= Triglyceride; HDL= High density Lipoprotein Cholesterol; Glu= Glucose concentration.

components differentially clustered based on sex, race/ethnicity and weight status. Principal components analyses revealed similar findings and assigned one factor for each analyses group, except for the obese group (Table **4**).

DISCUSSION

This study evaluated the applicability of the characterization of the metabolic syndrome in a cohort of children stratified by race/ethnicity, sex and weight status. In line with recent estimates [23, 33], in this sample of 247 children, the prevalence of the metabolic syndrome was ~9% (23 children). There were differences in the prevalence of the metabolic syndrome when analyzed by race/ethnicity (EA=7; AA= 2; HA= 11) and weight status (normal weight = 7; overweight= 9; obese = 7), but no differences detected by sex (boys = 12, girls = 11). Additionally, in this multi-ethnic cohort of children the way the components clustered differed according to sex, race/ethnicity and weight status.

The characterization of the metabolic syndrome (or syndrome X) is specific to the EA sample population from which it was derived [1]. Due to differences in genetic, socio-environmental, behavioral, and physiological differences, the risk for the development of chronic disease morbidity and mortality are not equally distributed across populations. As such there may be combinations of metabolic syndrome criteria that are more appropriate for one population than another in predicting future development of T2D and CVD. In adults, there are several examples of inadequate characterization of the metabolic syndrome in groups other than EA [16, 34]. In our sample, HA were more likely to be characterized as having the metabolic syndrome; they also had the highest rates of adiposity. NHANES analysis revealed the prevalence of the metabolic syndrome among obese adolescents to be approximately 30 times higher than among normal weight adolescents and approximately 4 times higher than overweight adolescents [17]. Conversely, the prevalence of the metabolic syndrome was low among AA, even when they were overweight. This is likely due to the favorable lipid profile [17] and lower glucose concentration [35] noted in this population, plausibly attributable to genetic background [17].

Nevertheless, the contribution to racial/ethnic differences in metabolic components cannot adequately be described without controlling for adiposity, which may have independent effects on the same metabolic outcomes. Although there were no differences detected in the prevalence of the metabolic syndrome by weight status when using 3 groups, when overweight and obese were pooled the overweight/obese group were more likely to meet the criteria than normal weight children ($P<0.05$). Further, an increased abnormality among three of the five components was identified with increasing weight. This finding is similar to the research of others [2, 15, 17] who have suggested the excess disease risk attributable to the diagnosis of the metabolic syndrome beyond the risk that is conferred by obesity is minimal.

However, there were differences in the way the components clustered when analyzed by weight status. In this sample, whereas components clustered similarly in normal and overweight children, they clustered uniquely in obese children. Among obese children, lipid profile measures were the only components that appeared to cluster. Factor analysis revealed two types of obese children 1) obese and dyslipidemic and 2) obese and normolipidemic. Population differences in terms of clustering according to race/ethnicity likely played a role in factor determination. Adiposity in EA and HA, may not confer the same aberrant lipid profile risks AA [17]. Because recruitment was focused primarily on normal weight healthy children sample size limitations restricted the analysis of an ethnicity by weight status interaction. The dyslipidemic characteristic may increase the risk of the development and future progression of cardiovascular disease, including atherosclerotic lesions [36].

Similarly, differences in fat deposition and distribution between the sexes may also influence health outcomes. During puberty, changes in the hormonal milieu impact boys and girls differently. There is evidence that hormonal shifts in girls may result in a greater magnitude of insulin resistance, but the extent to which adiposity differentially affects health outcomes between the sexes is not known. The long-term metabolic consequences of sex differences in body composition warrant further investigation.

The strengths of this study include utilization of a multiethnic sample of children with a wide range of body habitus. A limitation of this study was its cross-sectional nature preventing the establishment of cause and effect relationship; longitudinal data will be required to determine the long-term effects of the characterization of the metabolic syndrome and its components in children and future health

risks. Additionally, the sample was taken from the Southeast region of the United States and therefore, results may not be generalizable to the US population. For example, the HA children included in our study were primarily of Mexican descent and recent immigrants to the United States. Further, approximately 86% of the Hispanic children in our sample were first generation. Immigrant status may or may not have influenced their health status and warrants further investigation. In addition, there was skewness in the sample size by weight distribution. The inability to detect differences between individuals of varying weight status in our population does not infer that they do not exist, and differences may have been detected using a larger sample size. For example, when the overweight and obese children were pooled, a significant difference was noted between the lean and overweight/obese group.

Implications

In conclusion, this study contributes to our knowledge of the physiologic relevance of the differential clustering of cardiovascular risk factors by sex, race/ethnicity and weight status. Whether the metabolic syndrome is a useful clinical tool depends on its ability to indicate risk in the population that it is used. In this multi-ethnic cohort of children, both the meaning and the utility of characterization of the metabolic syndrome are further called into question. Due to inherent variations in body composition, physiology and genetics, the search for meaning of the metabolic syndrome using its currently "accepted" components and its applicability between ethnic groups may not be useful. Current criteria for the metabolic syndrome are established so that each component carries equal weight in a diagnosis. As such, there may be an underestimation of health risk due to the use of the incorrect combination of components used for a diverse population. Excess adiposity and metabolic health implications are a concern for the pediatric population. However, our evaluation of the utility in predicting the risk of individuals above that which is conferred by excess adiposity varied by the population for which it was used. The sum of individual risk factors may be useful in predicting future progression to T2D and CVD; however, the abnormalities among the parts should be targeted for treatment. Our findings suggest that regardless of meeting the criteria for 3 or more risk factors, physicians should evaluate all 5 criteria in overweight children with particular attention focused on lipid and glucose metabolism among EA and HA children and blood pressure among AA children. Further longitudinal research is needed to examine the utility of the metabolic syndrome and disease progression in a sample of children from multi-ethnic backgrounds or with varying degrees of adiposity.

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ABBREVIATIONS

AA = African American

BMI = Body mass index

CVD = Cardiovascular disease

DXA = Dual-energy X-ray absorptiometry

EA = European Americans

GCRC = General Clinical Research Center

GLU = Glucose concentration

HA = Hispanic Americans

HDL-C = High density lipoprotein cholesterol

T2D = Type 2 Diabetes

TG = Triglyceride concentration

WC = Waist Circumference

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