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The Metabolic Syndrome in Overweight Hispanic Youth and the Role of Insulin Sensitivity

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The prevalence of the metabolic syndrome is highest among Hispanic adults. However, studies exploring the metabolic syndrome in overweight Hispanic youth are lacking. Subjects were 126 overweight children (8–13 yr of age) with a family history for type 2 diabetes. The metabolic syndrome was defined as having at least three of the following: abdominal obesity, low high-density lipoprotein (HDL) cholesterol, hypertriglyceridemia, hypertension, and/or impaired glucose tolerance. Insulin sensitivity was determined by the frequently sampled iv glucose tolerance test and minimal modeling. The prevalence of abdominal obesity, low HDL cholesterol, hypertriglyceridemia, systolic and diastolic hypertension, and impaired glucose tolerance was 62, 67, 26, 22, 4, and 27%, respectively. The presence of zero, one, two, or three or more features of the metabolic syndrome was 9, 22, 38, and 30%, respectively. After controlling for body composition, insulin sensitivity was positively related to HDL cholesterol ($P < 0.01$) and negatively related to triglycerides ($P < 0.001$) and systolic ($P < 0.01$) and diastolic blood pressure ($P < 0.05$). Insulin sensitivity significantly decreased ($P < 0.001$) as the number of features of the metabolic syndrome increased. In conclusion, overweight Hispanic youth with a family history for type 2 diabetes are at increased risk for cardiovascular disease and type 2 diabetes, and this appears to be due to decreased insulin sensitivity. Improving insulin resistance may be crucial for the prevention of chronic disease in this at-risk population. (*J Clin Endocrinol Metab* 89: 108–113, 2004)

THE RECENTLY RELEASED Adult Treatment Panel III provided a definition of the metabolic syndrome in adults and drew attention to the importance of the syndrome as an entity that places individuals at risk for type 2 diabetes and cardiovascular disease (1). The age-adjusted prevalence of the metabolic syndrome was recently found to be 23.7% among 8814 U.S. adults participating in the National Health and Nutrition Examination Survey (NHANES) III (2). Hispanics had the highest age-adjusted prevalence of the metabolic syndrome (31.9%). The high prevalence of the metabolic syndrome in Hispanics is probably linked to the higher prevalence of obesity (3).

The prevalence of being overweight in Hispanic youth has approximately doubled in the last 10 yr, such that 21.8% of young Hispanics are now overweight (4). The increased prevalence of being overweight in childhood has been paralleled by an increase in the incidence of type 2 diabetes (5) and impaired glucose tolerance (6). The link between obesity and disease risk is thought to be explained by insulin resistance and its associated metabolic abnormalities. It is now clear that increased adiposity, including increased visceral fat, in childhood is associated with lower insulin sensitivity (7–9). In epidemiological studies, insulin resistance (measured indirectly through fasting insulin) has been shown to cluster with several features of the metabolic syndrome in both White and Black children (10–13). However, studies designed to explore the prevalence of features of the metabolic syndrome in Hispanic youth are lacking. An evaluation of the relationship between directly measured insulin sensitivity and features of the metabolic syndrome is also required. These issues are important because children of Hispanic ethnicity have a higher prevalence of obesity (14) and are more insulin resistant than Caucasian children independent of adiposity (8). Therefore, the objectives of this study were to 1) establish the prevalence of the metabolic syndrome and its individual components in overweight Hispanic youth, 2) establish the relative role of insulin sensitivity (independent of body composition) on the metabolic syndrome, and 3) explore the association between insulin sensitivity and the individual components of the metabolic syndrome in this population.

Abbreviations: BMI, Body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NHANES, National Health and Nutrition Examination Survey; VLDL, very LDL.

Subjects and Methods

Subjects

The present study included 126 children and adolescents (73 boys, 53 girls). Thirty-eight percent (Tanner stage 1) were prepubertal, 40.5% were pubertal (Tanner stage 2–3), and 21.4% were postpubertal (Tanner stage 4–5). All subjects were part of the University of Southern California (USC) Study of Latino Adolescents at Risk for Diabetes (SOLAR Diabetes Project), an ongoing longitudinal study to explore risk factors for the development of type 2 diabetes in at-risk youth during adolescence. Subjects at high risk for type 2 diabetes were recruited through clinics and word of mouth and were selected based on the following inclusion

criteria: 1) Hispanic origin, 2) a family history for type 2 diabetes (at least one parent, grandparent, or sibling), 3) age 8–13 yr, 4) body mass index at least 85th percentile (15), and 5) absence of diabetes, established by an oral glucose tolerance test (5). Children were of Mexican-American (71%), Central American (16%), or mixed Mexican/Central American (13%) descent and lived in the county of Los Angeles. This study was approved by the USC Institutional Review Board. Written informed consent was obtained from all parents and subjects. Preliminary data have been previously reported from this cohort (9).

Protocol

Outpatient visit: oral glucose tolerance test. Children arrived at the USC General Clinical Research Center (GCRC) at approximately 0800 h after an overnight fast. Subjects ingested 1.75 g of oral glucose solution/kg body weight (to a maximum of 75.0 g). Blood samples were taken via antecubital vein catheter for measurement of glucose before (fasting) and 2 h after the glucose load. Impaired glucose tolerance was defined as a 2-h postchallenge plasma glucose value at least 140 and less than 200 mg/dl (16). In this cohort, 27% of subjects had impaired glucose tolerance (21 boys, 13 girls), and none had diabetes.

Inpatient visit. Children were admitted to the GCRC in the afternoon. A whole-body dual-energy x-ray absorptiometry scan was used to determine whole-body composition using a Hologic QDR 4500W. Children were fasted between 2000 h and testing the following morning.

Insulin-modified frequently sampled iv glucose tolerance test

At approximately 0730 h, flexible iv catheters were placed in both arms. Two fasting blood samples were collected for determining basal glucose and insulin concentrations. At time zero, glucose (25% dextrose, 0.3 g/kg body weight) was administered iv. Blood samples were then collected at the following time points: 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min. Insulin [0.02 U/kg body weight; Humulin R (regular insulin for human injection; Eli Lilly, Indianapolis, IN)] was injected iv at 20 min. Plasma was analyzed for glucose and insulin and values were entered into the Minmod Millenium 2003 computer program (version 5.16, Richard N. Bergman, USC) for determination of insulin sensitivity (17–19).

Anthropometry and blood pressure. Height, weight, and waist circumference (at the umbilicus) were recorded to the nearest 0.1 cm, 0.1 kg, and 0.1 cm, respectively. Body mass index (BMI) and BMI percentiles for age were determined based upon established Centers for Disease Control normative curves (15) using computer software EpiInfo 2000, version 1.1. Sitting blood pressure was measured on two separate days using the right arm after the subject had rested quietly for 5 min. On each occasion, three readings of blood pressure were obtained, and the average was recorded (20).

Definition of the metabolic syndrome. According to the Adult Treatment Panel III (1), the presence of the metabolic syndrome is defined as having at least three of the following abnormalities: abdominal obesity measured via waist circumference, triglycerides at least 150 mg/dl, high-density lipoprotein (HDL) cholesterol less than 40 mg/dl in men and less than 50 mg/dl in women, blood pressure at least 130/85 mm Hg, and a serum fasting glucose at least 110 mg/dl. Because there is no current definition of the metabolic syndrome in children, we defined metabolic syndrome as the presence of at least three of the following abnormalities: abdominal obesity [waist circumference ≥90th percentile for age, gender, and Hispanic ethnicity from NHANES III data kindly provided by J. R. Fernandez, D. Redden, A. Piertrobelli, and D. B. Allison (unpublished data)], hypertriglyceridemia (triglycerides ≥90th percentile for age and gender) (21), low HDL cholesterol (HDL cholesterol ≤10th percentile for age and gender) (21), hypertension (systolic or diastolic blood pressure >90th percentile adjusted for height, age, and gender (20), and finally, impaired glucose tolerance (16).

Assays. Blood samples taken during the oral glucose tolerance were separated for plasma and immediately transported on ice to the Los Angeles County-USC Medical Center Core Laboratory where glucose was analyzed on a Dimension clinical chemistry system and an *in vitro* hexokinase method (Dade Behring, Deerfield, IL). Blood samples taken during the inpatient visit were centrifuged immediately to obtain plasma, and aliquots were frozen at –70 C until assayed. Glucose was assayed in duplicate using a Yellow Springs Instrument 2700 Analyzer (YSI Inc., Yellow Springs, OH) and a glucose oxidase kit. Insulin was assayed in duplicate using a specific human insulin ELISA kit from Linco (St. Charles, MO). Fasting triglycerides and HDL and total cholesterol were measured using the Vitros chemistry DT slides (Johnson and Johnson Clinical Diagnostics Inc., Rochester, NY). Low-density lipoprotein (LDL) was calculated using the Friedwald formula.

Statistical analysis

Gender differences in physical and metabolic characteristics were examined using a general linear model. Variables that were not normally distributed (age, weight, height, Tanner stage, total fat mass, total lean mass, BMI, blood pressure, triglycerides, HDL cholesterol, fasting insulin, and insulin sensitivity) were log transformed. The prevalence of individual components of the metabolic syndrome was calculated as the total number of subjects with abdominal obesity, low HDL cholesterol, hypertriglyceridemia, hypertension, and impaired glucose tolerance expressed as a percentage of the total group. Subjects were then classified into one of four groups depending on whether they had zero, one, two, or three or more components of the metabolic syndrome.

Simple and partial Pearson correlation analysis was used to establish associations between insulin sensitivity and features of the metabolic syndrome alone and after adjustment for gender, age, Tanner stage, and body composition. Multivariate linear regression analysis was used to establish the independent contribution of insulin sensitivity on 1) log HDL cholesterol, 2) log triglycerides, 3) log systolic blood pressure, 4) log diastolic blood pressure, and 5) 2-h glucose, after adjustment for gender, age, Tanner stage, total fat mass, and total lean mass. For these analyses, the dependent variable was log HDL cholesterol, log triglycerides, log systolic blood pressure, log diastolic blood pressure, or 2-h glucose and the independent variable was insulin sensitivity. To establish differences in mean insulin sensitivity across groups that had zero, one, two, or three or more components of the metabolic syndrome, we performed analysis of covariance with Bonferroni adjustments for multiple comparisons, adjusting for gender, age, Tanner stage, total fat mass, and total lean mass. Results are presented as differences in the estimated marginal mean for insulin sensitivity. All analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, IL) with a type I error set at $P < 0.05$.

Results

Physical characteristics of subjects

Despite similar age, girls were more sexually mature than boys, as determined by Tanner stage (Table 1). Boys had higher fasting blood glucose ($P < 0.01$) and diastolic blood pressure ($P < 0.05$) than girls. Approximately 82% of subjects had a BMI at least 95th percentile for age and gender (15).

Prevalence of features of the metabolic syndrome

The prevalence of abdominal obesity, low HDL cholesterol, hypertriglyceridemia, hypertension, and impaired glucose tolerance as defined in *Subjects and Methods* is shown in Fig. 1. Approximately 90% of participants had at least one component of the metabolic syndrome (Fig. 2). The presence of one, two, or three or more components associated with the metabolic syndrome was 22, 38, and 30%, respectively (Fig. 2). Approximately 10% of subjects had four or five features of the metabolic syndrome. There was a tendency for postpubertal children to have greater number of features of the metabolic syndrome than pubertal and prepubertal children, but this did not reach statistical significance ($P = 0.09$). Similarly, boys tended to have a higher prevalence of features of the metabolic syndrome compared with girls. How-

TABLE 1. Physical and metabolic characteristics of subjects

	Boys (n = 73)	Girls (n = 53)	Total (n = 126)
Age (yr)	11.0 ± 1.7	10.7 ± 1.8	10.9 ± 1.7
Height (cm)	149.2 ± 10.9	147.4 ± 12.3	148.4 ± 11.5
Weight (kg)	62.8 ± 17.2	63.8 ± 22.7	63.2 ± 19.6
Tanner	1.8 ± 1.1[a]	2.8 ± 1.4	2.2 ± 1.3
BMI (kg/m^2)	27.7 ± 4.7	28.6 ± 7.1	28.1 ± 5.8
BMI percentile	97.3 ± 2.9	97.1 ± 3.0	97.2 ± 2.9
Waist circumference (cm)	88.9 ± 11.4	85.9 ± 14.5	87.7 ± 12.8
Total fat mass (kg)	23.2 ± 8.4	25.0 ± 10.9	24.0 ± 9.6
Total lean tissue mass (kg)	37.3 ± 9.5	35.3 ± 10.8	36.4 ± 10.8
Fasting glucose (μU/ml)	93.5 ± 6.1[b]	90.1 ± 7.9	92.1 ± 7.1
2-h Glucose (mg/dl)	127.0 ± 19.0	125.5 ± 16.4	126.4 ± 17.9
Fasting insulin (μU/ml)	19.0 ± 11.1	19.2 ± 10.3	19.1 ± 10.8
Insulin sensitivity [$\times 10^{-4}$ min^{-1}/(μU/ml)]	2.01 ± 1.12	2.24 ± 1.52	2.10 ± 1.30
Acute insulin response [(μU/ml × 10 min]	1873 ± 164	1561 ± 158	1742 ± 117
Systolic blood pressure (mm Hg)	111 ± 11	109 ± 10	110 ± 11
Diastolic blood pressure (mm Hg)	62 ± 6[c]	60 ± 5	61 ± 6
Cholesterol total (mg/dl)	159.2 ± 26.8	153.0 ± 26.9	156.6 ± 26.9
LDL cholesterol (mg/dl)	95.4 ± 22.6	92.4 ± 22.1	94.2 ± 22.4
HDL cholesterol (mg/dl)	38.1 ± 8.9	39.1 ± 8.2	38.5 ± 8.6
Triglycerides (mg/dl)	128.4 ± 74.2	106.2 ± 46.1	119.1 ± 64.6

Values are means ± SEM. For gender: [a] $P < 0.001$; [b] $P < 0.01$; [c] $P < 0.05$.

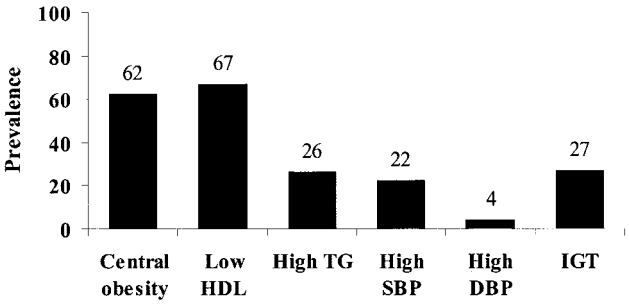

FIG. 1. Prevalence of the individual components of the metabolic syndrome in overweight Hispanic youth. SBP, Systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; IGT, impaired glucose tolerance.

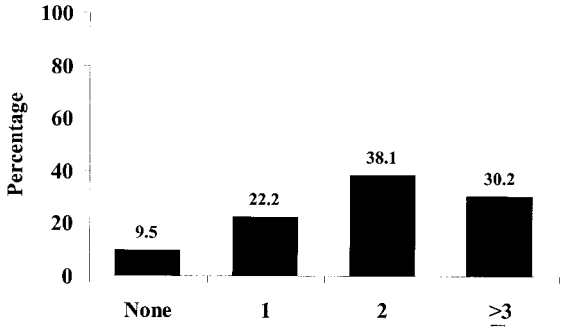

FIG. 2. Percentage of overweight Hispanic subjects with zero, one, two, or three or more components of the metabolic syndrome.

ever, significant differences between boys and girls were evident only for hypertriglyceridemia (15 *vs.* 9%, respectively; $P < 0.001$). Compared with subjects at risk of overweight (BMI ≥ 85th and <95th percentile), overweight subjects (BMI ≥ 95th percentile) had abdominal obesity (0 *vs.* 76%), low HDL cholesterol (48 *vs.* 71%), and high systolic blood pressure (0 *vs.* 27%), respectively ($P < 0.05$). Finally, 6% of all subjects had elevated plasma total cholesterol and 10% had elevated LDL cholesterol.

Simple and partial correlation between insulin sensitivity and features of the metabolic syndrome

Pearson correlation analysis showed that log insulin sensitivity was correlated positively with log HDL cholesterol and negatively with log waist circumference, log triglycerides, log systolic blood pressure ($P < 0.001$), and log diastolic blood pressure ($P < 0.01$). However, log insulin sensitivity did not correlate with 2-h glucose. As expected log insulin sensitivity was not correlated with total or LDL cholesterol (results not shown). After adjustment for age, gender, total fat mass, and total lean mass, log insulin sensitivity remained significantly related to all components of the metabolic syndrome and the correlation between log insulin sensitivity and 2-h glucose became significant ($P < 0.05$) (Table 2).

Multiple linear regression analysis to assess the independent contribution of insulin sensitivity to the separate components of the metabolic syndrome

Results from the multiple linear regression showed that insulin sensitivity, adjusted for gender, age, total fat mass, and total lean mass, was positively and significantly related to log HDL cholesterol (Table 3, model 1) and negatively related to log triglycerides (Table 3, model 2). Furthermore, insulin sensitivity remained significantly and negatively related to log systolic blood pressure (Table 3, model 3), log diastolic blood pressure (Table 3, model 4), but not to 2-h glucose (Table 3, model 5). Total fat mass was not independently related to any components of the metabolic syndrome (Table 3, models 1–5).

Figure 3 shows the estimated marginal means for insulin sensitivity (after adjustment for gender, age, Tanner stage, total fat mass, and total lean mass) in subjects grouped by the number of components of the metabolic syndrome. In general, insulin sensitivity decreased as the number of components of the metabolic syndrome increased ($P < 0.001$; Fig. 3). Mean insulin sensitivity was significantly higher in subjects with zero and one component of the metabolic syndrome compared with subjects with two and three or more

TABLE 2. Pearson correlation coefficients

	Waist	Log HDL	Log triglycerides	Log SBP	Log DBP	2-h Glucose
Log insulin sensitivity	−0.69[a]	0.41[a]	−0.41[a]	−0.50[a]	−0.25[b]	0.10
Log insulin sensitivity (adjusted for gender, age, and body composition)		0.23[b]	−0.30[a]	−0.24[b]	−0.22[c]	−0.19[c]

[a] $P < 0.001$; [b] $P < 0.01$; [c] $P < 0.05$. SBP, Systolic blood pressure; DBP, diastolic blood pressure.

TABLE 3. Multiple linear regression to assess the contribution of insulin sensitivity to the separate components of the metabolic syndrome after adjusting for confounding variables

Dependent variable	Independent variables	$\beta \pm$ SEE	P value
Model 1, $R^2 = 0.20$			
Log HDL cholesterol	Gender	0.04 ± 0.18	NS
	Age	0.01 ± 0.02	NS
	Tanner stage	−0.01 ± 0.02	NS
	Total fat mass	−0.0002 ± 0.003	NS
	Total lean mass	−0.01 ± 0.004	NS
	Insulin sensitivity	0.05 ± 0.02	0.004
Model 2, $R^2 = 0.23$			
Log triglycerides	Gender	−0.04 ± 0.35	NS
	Age	0.04 ± 0.04	NS
	Tanner stage	0.01 ± 0.06	
	Total fat mass	−0.01 ± 0.01	NS
	Total lean mass	0.02 ± 0.01	NS
	Insulin sensitivity	−0.18 ± 0.04	0.001
Model 3, $R^2 = 0.31$			
Log systolic blood pressure	Gender	−0.01 ± 0.02	NS
	Age	0.002 ± 0.007	NS
	Tanner stage	0.02 ± 0.01	NS
	Total fat mass	0.003 ± 0.002	NS
	Total lean mass	0.001 ± 0.002	NS
	Insulin sensitivity	−0.020 ± 0.01	0.01
Model 4, $R^2 = 0.12$			
Log diastolic blood pressure	Gender	−0.04 ± 0.02	0.03
	Age	−0.0002 ± 0.008	NS
	Tanner stage	0.02 ± 0.01	
	Total fat mass	0.02 ± 0.02	NS
	Total lean mass	−0.003 ± 0.002	NS
	Insulin sensitivity	−0.020 ± 0.01	0.021
Model 5, $R^2 = 0.04$			
2-h Glucose	Gender	−0.33 ± 3.4	NS
	Age	2.1 ± 1.5	NS
	Tanner stage	2.6 ± 2.3	NS
	Total fat mass	−0.19 ± 0.33	NS
	Total lean mass	−0.48 ± 0.42	NS
	Insulin sensitivity	−2.1 ± 1.6	NS

NS, Not significant.

($P < 0.001$ and $P < 0.01$, respectively) components (Fig. 3). There were no significant differences in insulin sensitivity between subjects with zero *vs.* one component or between subjects with two *vs.* three or more components of the metabolic syndrome (Fig. 3).

Discussion

The purpose of this study was 3-fold. The first objective was to establish the prevalence of the metabolic syndrome and of its individual components in overweight Hispanic youth at high risk for type 2 diabetes. The second objective was to establish the relative role of insulin sensitivity (independent of body composition) on the metabolic syndrome and third to establish the relationship between insulin sensitivity and the individual components of the metabolic syndrome. Our results show that 90% of overweight Hispanic children have at least one feature of the metabolic syndrome. Furthermore, when we used a similar definition of the metabolic syndrome as that described in the Adult Treatment Panel III (1), 30% of our subjects had the metabolic syndrome. In this cohort, directly measured insulin sensitivity was associated with HDL cholesterol, triglycerides, and blood pressure but not with 2-h glucose, and these relationships were independent of body fat. Finally, insulin sensitivity progressively decreased as the number of components of the metabolic syndrome increased. Our results suggest that insulin resistance is a central component of the metabolic syndrome in overweight Hispanic youth with a family history for type 2 diabetes and that insulin resistance is associated with an adverse metabolic profile.

The high prevalence of the metabolic syndrome in the current cohort of overweight Hispanic youth does not appear

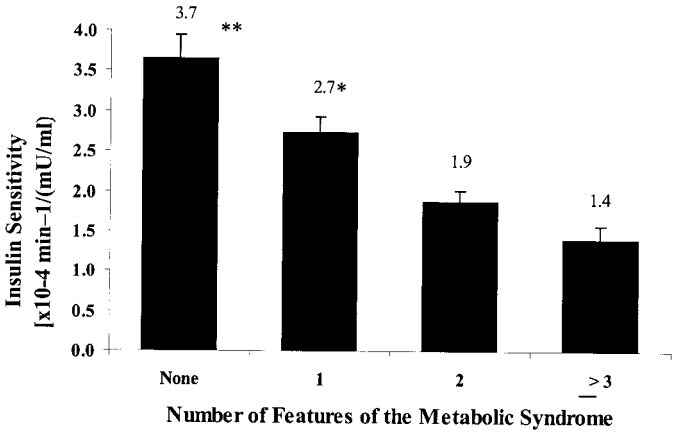

FIG. 3. Estimated marginal means for insulin sensitivity in overweight Hispanic youth according to number of features of the metabolic syndrome. For clarity of interpretation, data are presented using the non-log-transformed insulin sensitivity. However, statistical analysis was performed on log-transformed insulin sensitivity. Data were adjusted for gender, age, Tanner stage, total body fat, and total lean mass. Log insulin sensitivity was different between subjects with zero ($P < 0.001$) and one ($P < 0.01$) feature of the metabolic syndrome *vs.* those with two or three or more features. Log insulin sensitivity was not different between children with one *vs.* two features or between those with two *vs.* three features.

to be unique to this at-risk group. In a recently published study, the prevalence of the metabolic syndrome (based on Adult Treatment Panel III definition) in overweight U.S. adolescents (BMI ≥ 95th percentile) participating in NHANES III was 28.7% compared with 0.1, and 6.8% in normal-weight (BMI < 85th percentile) and at-risk of overweight (BMI ≥ 85th < 95th percentile) adolescents. Therefore it appears that in general a high proportion of overweight youth may be at increased risk for type 2 diabetes and cardiovascular disease.

The dyslipidemia characteristic of the metabolic syndrome may increase cardiovascular disease risk through mechanisms different from those associated with high total or LDL cholesterol. Autopsy studies in youth have shown that cardiovascular risk factors are related to the early stages of coronary atherosclerosis (22) and more importantly that the extent of lesions increases markedly with multiple risk factors In children, as in adults (23, 24), the presence of multiple risk factors for type 2 diabetes and cardiovascular disease in the same individual has been linked to obesity (25) and hyperinsulinemia (13, 26). Furthermore, high insulin levels have been shown to precede the development of the atherogenic profile characterized by low HDL cholesterol, high triglycerides, and high systolic blood pressure (13). Only a handful of studies in children have explored the relationship between directly measured insulin sensitivity and features of the metabolic syndrome (7, 27–29). In one study, which included a multiethnic group of Black and White children (n = 357, mean age ~13 yr), insulin sensitivity measured via the insulin clamp was significantly correlated with fasting triglycerides and HDL cholesterol after adjusting for BMI (29). We found that insulin sensitivity measured via the frequently sampled iv tolerance test was negatively associated with systolic blood pressure in a mixed cohort of Black and White prepubertal children (28). Our results are in agreement with previous reports in Black and White children (28, 29) and extend these findings to Hispanic youth. Our data support the view that insulin resistance is at the core of the metabolic syndrome in overweight Hispanic youth. The fact that fat mass was not independently related to features of the metabolic syndrome in our multivariate regression analysis suggests that the effect of overall adiposity on lipids and blood pressure control is mediated by insulin resistance, as has been previously reported in adults (30) and children (28). However, it remains to be established whether visceral fat, which we have recently shown to be negatively and independently related to insulin sensitivity in a subsample of overweight Hispanic youth from this cohort (9), has an independent effect on some of the features of the metabolic syndrome through increased delivery of free fatty acids to the portal circulation.

The relationship between insulin resistance and fasting lipids can be explained through the effect of insulin on lipoprotein metabolism. Insulin plays a central role in determining triglyceride clearance from the blood via activation of lipoprotein lipase and triglyceride output through effects on the synthesis and secretion of very LDL (VLDL) by the liver (31). Furthermore, insulin controls the output of free fatty acids from adipose tissue (32). It is thought that in the insulin-resistant state, triglyceride-rich lipoproteins accumulate in the circulation due to decreased activity of lipoprotein lipase (33), increased lipolysis in adipose tissue (32), and increased output of VLDL particles from the liver (31). The delay in plasma lipoprotein triglyceride clearance allows for cholesterol esters to be passed on from HDL to triglyceride-rich particles, which results in potentially atherogenic lipoproteins particles (34).

The mechanism through which insulin resistance and the accompanying hyperinsulinemia may alter blood pressure is less clear but may relate to direct effects on the sympathetic nervous system and renal sodium reabsorption (35). High blood pressure may develop due to the lack of resistance to these secondary effects of insulin (36) or alternatively, insulin resistance may lead to endothelial dysfunction through the nitric oxide pathway (37).

The lack of association between insulin sensitivity and 2-h glucose in this cohort may be due to the fact that the concentration of glucose in the blood is not only dependent on insulin sensitivity but also on β-cell secretory capacity (38, 39). In adults, a failure of the β-cells to adequately compensate for the degree of insulin resistance underlies the transition from insulin resistance to overt type 2 diabetes (38, 39). In children, these relationships are less well established, although early reports suggest a similar pathophysiology (6). We are currently investigating the relative contributions of insulin sensitivity and insulin secretion in the state of impaired glucose tolerance in overweight Hispanic children and adolescents with a family history for type 2 diabetes.

In summary, approximately 90% of overweight Hispanic children with a family history for type 2 diabetes have at least one feature of the metabolic syndrome and 30% possess the metabolic syndrome. Insulin sensitivity decreased as the number of features of the metabolic syndrome increased. Furthermore, insulin sensitivity was independently related to adverse lipids, blood pressure, and abdominal obesity. Collectively, our findings suggest increased risk for both cardiovascular disease and type 2 diabetes in overweight

Hispanic youth with a family history for type 2 diabetes. Our results support the view that improving insulin resistance may be crucial in the prevention of both type 2 diabetes and premature cardiovascular disease in this at-risk subpopulation of Hispanic youth. Research efforts should be made to address this issue specifically. For instance, insulin sensitivity may be improved through specific exercise modalities (*e.g.* resistance training), dietary interventions (*e.g.* polyunsaturated fatty acids), and/or through pharmacological agents (thiazolidinediones). Results from these studies will help us implement effective interventions for the prevention of chronic disease in the young.

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