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Metabolic syndrome components in obese Egyptian children

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BACKGROUND AND OBJECTIVES: Obesity is one of the most serious global health issues. The aim of this study was to assess the association between obesity and different components of metabolic syndrome among obese school children aged 7 to 9 years, and to identify associated clinical and biochemical characteristics.
DESIGN AND SETTING: Case-control study among children attending Al-Zahraa Hospital Outpatient Clinic March 2010.
SUBJECTS AND METHODS: The study included 60 obese children (28 boys and 32 girls) and 50 non-obese controls (25 boys and 25 girls). Anthropometry, fasting glucose, insulin concentrations, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, systolic and diastolic blood pressure (BP) were measured. Insulin resistance was determined by Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Subcutaneous and visceral fat thicknesses were measured ultrasonographically. Metabolic syndrome (MS) was defined according to the Cook criteria.
RESULTS: MS was found in 25% of obese cases. Obese children showed significantly higher values in waist circumference, waist-to-hip ratio, levels of systolic and diastolic BP, insulin, HOMA-IR and LDL compared to their lean controls. HDL was significantly lower in obese children compared to controls. Obese children with MS had significantly higher values of body mass index standard deviation score (SDS), skinfold thickness, visceral fat thickness, waist circumference, systolic and diastolic BP, HOMA-IR, insulin and triglycerides compared to obese children without MS, whereas HDL was significantly lower. Obese children with MS had a high prevalence of hypertension and dyslipidemia compared to children without MS. Results showed positive relationships between visceral fat and waist circumference as well as with insulin level in obese children ($P<.05$).
CONCLUSIONS: The prevalence of the MS is considerable among obese Egyptian children. Abdominal obesity and high HOMA-IR values were the most frequent components of this syndrome among obese children. The study suggests that increased degree of insulin resistance is associated with a heightened risk of suffering MS.

The prevalence of chronic or noncommunicable diseases is escalating much more rapidly in developing countries than in industrialized countries. According to WHO estimates, by the year 2020, noncommunicable diseases will account for approximately three quarters of all deaths in the developing world.[1] The prevalence of overweight and obesity among schoolchildren aged 6 to 10 years in the Eastern Mediterranean Region was 12% to 25%. Many developing countries, including the Middle East, have undergone epidemiologic and demographic transitions affecting their population's nutritional status and created environments that contribute to an increase in obesity, a health problem that often coexists with undernutrition in this type of nation.[2] As a major risk factor for chronic disease, the metabolic syndrome (MS) is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide. Few studies have estimated the prevalence of metabolic syndrome in children, and no international definition exists.[3] Studies from the past

years have reported an alarming increase in the prevalence of the MS among children and adolescents.[4,5] The MS is an aggregation of abnormalities in lipid and carbohydrate metabolism accompanied with hypertension, all of which are risk factors for cardiovascular disease.[4,6] Genetic predisposition or early-life adverse events may contribute to the insulin resistance and adverse body-fat patterning seen in MS and its related complications. MS is closely associated with obesity, especially with central distribution. Parameters associated with MS have been shown to originate early in life[7] and tend to track into adulthood.[3] The recognition of MS in obese children, who have not yet developed cardiometabolic disorders, is of great importance from a clinical and public health perspective.[8] Many studies have shown that high levels of body mass index (BMI) among children and adolescents were associated with adverse levels of lipids, insulin, and blood pressure, all components of the metabolic syndrome.[4,9] Insulin resistance (IR) and an altered plasma lipid pattern are common pathophysiological features of MS, not only in adults but also in children and adolescents.[9] The MS has been widely studied in adults, but there is little research focusing on younger children (<10 years old).[10] Moreover, the absence of studies on MS in the pediatric Egyptian population led us to design the current study. The aim of this study was to assess the association between obesity and the different components of MS among obese Egyptian schoolchildren aged 7 to 9 years old, and to identify clinical and biochemical characteristics associated with MS in our population.

SUBJECTS AND METHODS

We conducted a case-control study during March 2010. The subjects of this study comprised 110 children: 60 were obese (28 boys and 32 girls) and 50 were non-obese, normal healthy controls randomly chosen from both sexes (25 boys and 25 girls). All were attending the Pediatric Clinics of Al-Zahraa Hospital, Al-Azhar University, Cairo, Egypt. Their ages ranged from 7 to 9 years. A formal consent letter from the parents of each child included in the study was obtained after explaining the study to them. This study was approved by the Ethics Committee of the hospital. The nutritional diagnosis of obesity (BMI equal to or higher than the 95th percentile) was performed according to age and gender.[11] The obese children with a clinical history of other morbidities and undergoing medical treatment and clinical-nutritional follow-up for body weight reduction were excluded.

The anthropometric measurements and instruments followed the International Biological Programme (IBP).[12] Measurements were taken three times and the mean values used in the analysis included weight, height, waist and hip circumferences, triceps and subscapular skinfold thicknesses. Body weight was measured to the nearest 0.1 kg and height was measured to the nearest 1 mm. The skinfold thickness was measured to the nearest 1.0 mm. The triceps skinfold was measured parallel to the long axis of the arm midway between the acromion and the olecranon, with the arm slightly flexed, and the subscapular skinfold was measured below the lower angle of the left scapula at a diagonal in the natural cleavage of the skin. BMI in kg/m^2, and waist-to-hip ratio (WHR) were calculated. Age was calculated in decimal units based on the date of the examination relative to birth date. Physical growth was assessed for each child by determining the standard deviation scores (SDS) of weight, height, BMI, using the Egyptian growth reference data.[11] The SDS was calculated independent of sex and age that is, child measurement minus population mean/population SD. WHR ratio was also calculated and compared to the control group in the present study.

Medical assessments were performed, including a history of symptoms covering various systems, and a physical examination was performed looking for characteristic abnormalities, specifically acanthosis nigricans. Blood pressure was measured by the auscultatory method after the child had been sitting at rest for a minimum period of 5 minutes, and the cuff involved 80% of the right arm circumference. The arm rested on a support surface at the level of the precordium. Blood pressure was measured three times and was averaged for analysis. Blood pressure was measured three times in three different days only when the first measurement was above 95th percentile according to gender, age and height, based on The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents.[13] Fasting plasma glucose and serum lipids (total cholesterol, HDL, LDL, triglycerides) were measured by enzymatic colorimetric methods using a Hitachi autoanalyzer 704 (Roche Diagnostics. Switzerland).[14] Serum insulin concentration was analyzed by chemiluminescent immunoassay (Immulite 2000, Siemens, Germany).[15] Insulin resistance was then determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as the product of the fasting plasma insulin level (μU/mL) and the fasting plasma glucose level (mmol/L), divided by 22.5.[16] We used the Cook definition for MS,[17] which includes the presence of >3 of the following five conditions: (1) central obesity (waist circumference (WC) >90th percentile)[18] (2) fasting triglycerides >110 mg/dL, (3) HDL <40 mg/dL, (4) blood pressure >90th percentile for age, gender and height, and (5) fasting glu-

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cose >100 mg/dL.[17]

Ultrasonography (US) measurements of subcutaneous and visceral abdominal fat layers were performed using a 7.5 MHz linear-array probe; the rectus muscle to spine and rectus muscle to aorta distances was measured as indicative of visceral fat thickness, and the distance between skin to fat and fat to rectus muscle interfaces was indicative of subcutaneous fat thickness using VIVID Three (GE, Healthcare, United States) ultrasound scanner with a high resolution B-mode.[19]

Statistics were done by computing the mean and standard deviation (SD) for scale variables, or frequencies for nominal variables. To study the independence between nominal categorical variables the chi-square test was used. An independent samples t test was performed on scale variables to evaluate the differences between two groups. The normality of scale variables was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney test was used in ordinal variables to evaluate the differences between two groups. A HOMA-IR value of 3.4 was chosen as the cut-off point to define IR as it has been suggested that beyond this value, which corresponds to the 90th percentile of a population of healthy children, IR becomes a cardiovascular risk factor. Four categories were used for HOMA-IR percentiles: <25th, 25-49.9th, 50-74.9th, and ≥75th, to assess the risk of developing MS through logistic regression analysis. Statistically significant differences were assumed if the P value was <.05. Statistical presentation and analysis of the results were carried out using SPSS software version 11.

RESULTS

The anthropometric, clinical and biochemical characteristics of the 60 obese children (28 boys and 32 girls) are shown in **Table 1**. A statistically significant difference between genders was found for the sum of SDS for the skinfold thicknesses and ultrasound visceral fat thickness, with boys presenting higher values. **Table 2** shows comparison of the clinical and biochemical characteristics between the obese boys and girls and their normal weight control groups. Waist circumference, WHR, visceral and subcutaneous fat thickness, levels of systolic and diastolic BP, insulin, HOMA-IR and LDL were significantly higher in obese boys and girls compared to controls. On the other hand, HDL was significantly lower in both obese boys and girls compared to their normal weight children. Total cholesterol showed a trend towards higher levels in obese children.

Table 3 compares clinical and biochemical characteristics between obese children with and without MS. The mean (SD) age of children with MS was 8.43 (1.37)

Table 1. Anthropometric, clinical and biochemical characteristics of the obese children, according to gender.

Features	Boys Mean (SD)	Girls Mean (SD)
Age (years)	8.01 (0.64)	8.67 (0.72)
Duration (years)	3.55 (1.1)	3.80 (0.7)
Anthropometric measures		
Weight SDS	3.75 (1.94)	3.49 (2.01)
Height SDS	0.25 (3.59)	0.12 (2.12)
BMI SDS	5.25 (2.32)	4.78 (1.53)
Sum of skinfolds SDS	3.36 (1.52)[a]	2.33 (1.36)
Blood pressure (mm Hg)		
Systolic PB (mm Hg)	105.16 (12.54)	106.66 (7.61)
Diastolic PB (mm Hg)	72.96 (11.89)	71.25 (8.50)
Metabolic profile		
Glucose (mg/dL)	95.22 (7.84)	97.0 (9.36)
Insulin (μU/mL)	10.61 (6.98)	10.17 (8.20)
HOMA-IR	2.32 (1.59)	2.45 (1.86)
Total cholesterol (mg/dL)	162.59 (33.14)	168.50 (45.71)
HDL-C (mg/dL)	41.31 (13.27)	42.65 (16.24)
LDL-C (mg/dL)	116.73 (25.8)	122.12 (32.87)
Triglycerides (mg/dL)	82.25 (28.85)	81.75 (40.56)
Ultrasound		
Visceral fat (mm)	65.42 (15.97)[b]	52.70 (17.42)
Subcutaneous fat (mm)	23.76 (1.52)	21.08 (6.84)

[a]t-test, [b]Mann-Whitney, P<.05 for both.

compared to 8.60 (1.64) of children without MS (not statistically significant). Duration of obesity, BMI SDS, sum of skinfold thicknesses SDS, waist circumference, visceral fat thickness, systolic and diastolic BP, HOMA-IR, insulin and triglycerides were significantly higher in children with MS compared to children without MS. However, significantly lower HDL was found in MS children compared to non- MS children. Acanthosis nigricans was detected in 20% of obese children with MS. **Table 4** shows the prevalence of components of MS according to presence of metabolic syndrome. None of the children fulfilled the five criteria of the MS. The prevalence of the components of MS among obese children was as follows: abdominal obesity, 85%; high systolic BP, 8.3%; high diastolic BP, 5%; impaired fasting glucose, 8.3%; hyperinsulinemia, 25%; HOMA-IR values, 28.3%; high total cholesterol, 8.3%; hypertriglyceride-

Table 2. Descriptive clinical and biochemical characteristics of obese and control groups.

Features	Boys		Girls	
	Obese	Normal weight	Obese	Normal weight
Age (years)	8.01 (0.64)	8.353 (0.65)	8.67 (0.72)	8.67 (0.24)
Systolic BP (mm Hg)	105.16 (12.54)[b]	96.61(7.82)	106.66 (7.61)[b]	102.5 (6.12)
Diastolic BP (mm Hg)	72.96 (11.89)[b]	66.61 (7.82)	71.25 (8.50)[b]	67.77 (10.29)
Waist circumference (cm)	87.88 (14.02)[a]	63.89 (11.1)	89.95 (11.73)[a]	57.23 (8.71)
Waist to hip ratio	0.93 (0.05)[a]	0.87 (0.11)	0.90 (0.05)[a]	0.87 (0.04)
Glucose (mg/dL)	95.22 (7.84)	92.18 (8.48)	97.00 (9.36)	93.83 (9.21)
Insulin (µU/mL)	10.61 (6.98)[b]	6.29 (3.79)	10.17 (8.20)[b]	6.94 (5.23)
HOMA-IR	2.32 (1.59)[a]	1.41 (0.85)	2.45 (1.86)[a]	1.61 (1.23)
Total cholesterol (mg/dL)	162.59 (33.14)	155.64 (30.56)	168.50 (45.71)	166.91 (26.55)
HDL-C (mg/dL)	41.31 (13.27)[b]	50.21 (21.22)	42.65 (16.24)b	53.36 (22.28)
LDL-C (mg/dL)	116.73 (25.8)[b]	99.07 (36.38)	122.12 (32.87)[b]	112.02 (31.65)
Triglycerides (mg/dL)	82.25 (28.85)	80.82 (43.18)	81.75 (40.56)	79.82 (30.18)
Ultrasound visceral fat (mm)	65.42 (15.97)[b]	48.21 (13.39)	52.70 (17.42)[b]	45.73 (11.88)
Ultrasound subcutaneous fat (mm)	23.76 (1.52)[b]	13.20 (6.37)	21.08 (6.84)	17.86 (17.17)

Values are mean (standard deviation). [a] t test for the differences between obese and normal weight children, $P<.05$. [b] Mann-Whitney for the differences between obese and normal weight children, $P<.05$.
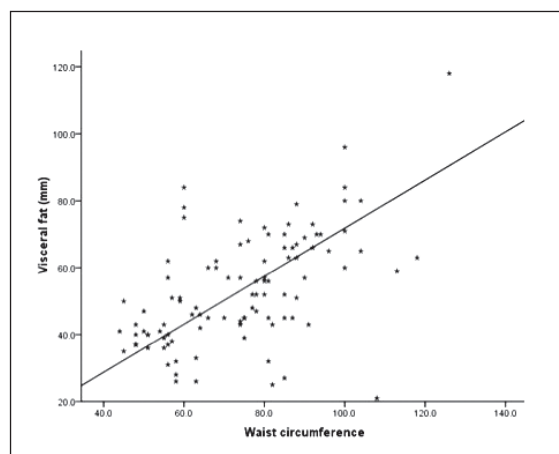

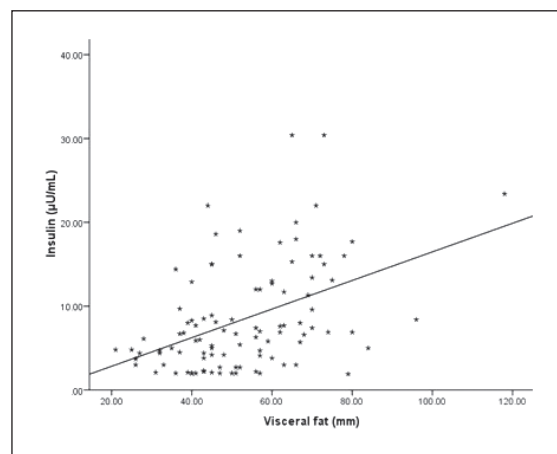**Figure 1.** Relationship between visceral fat and waist circumference in obese children.

Figure 2. Relationship between fasting serum insulin levels and visceral fat in obese children.

mia, 13.3%; high LDL, 8.3%, and low HDL-C, 20%. High frequency of high diastolic BP, insulin concentration level, HOMA-IR value, triglycerides and low HDL were observed in the obese children with MS compared to children without MS ($P<.001$).

Table 5 shows the ORs of suffering MS according to IR categories. From this table, it is apparent that the odds of developing MS (adjusted for gender and age) increases as a function of IR. Such OR is 5.7 (95% CI 2.34-11.55) times greater when IR is above the 75th percentile ($P<.001$). **Figure 1** shows positive significant relation between waist circumference and visceral

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Table 3. Descriptive clinical and biochemical characteristics of the obese children according to the presence or absence of metabolic syndrome.

Parameters	With MS (n=15)	Without MS (n=45)
Age (years)	8.43 (1.37)	8.60 (1.64)
Duration	4.07(1.01)[a]	3.18 (1.07)
Anthropometric Measures		
Weight SDS	4.07 (3.40)	3.78 (2.17)
Height SDS	0.18 (2.41)	0.25 (2.83)
BMI SDS	7.07 (2.22)[a]	3.35 (2.48)
Sum of skinfolds SDS	3.09 (1.46)[a]	2.97 (1.79)
Waist circumference (cm)	96.20 (12.99)[a]	84.03 (12.23)
Waist-to-hip ratio	0.94 (0 .03)	0.91 (0.06)
Blood Pressure		
Systolic (mmHg)	108.66 (14.45)[a]	101.0 (9.92)
Diastolic (mmHg)	76.67 (14.09)[a]	69.78 (10.44)
Metabolic Profile		
Glucose (mg/dL)	91.33 (9.81)	90.04 (8.02)
HOMA-IR	3.97 (1.77)[a]	1.58 (1.03)
Insulin (μU/mL)	17.52 (7.64)[b]	7.32 (4.55)
HDL-C (mg/dL)	37.80 (11.33)[b]	42.68 (16.18)
LDL-C (mg/dL)	124.0 (21.69)	117.31 (32.65)
Triglycerides (mg/dL)	110.33 (37.53)[b]	85.09 (84.31)
Total cholesterol (mg/dL)	168.73 (26.99)	157.82 (42.36)
Ultrasound		
Visceral fat (mm)	70.33 (18.07)[b]	54.59 (15.73)
Subcutaneous fat (mm)	24.93 (8.87)	21.43 (7.94)
Gender (M/F)	8/7	24/21
Acanthosis	3 (20%)	2 (4.4%)

Values are mean (standard deviation) or number (percent).

[a]t-test for the differences between absence or presence of MS, P<.05; [b]Mann-Whitney for the differences between absence or presence of MS, P<.05

Table 4. Prevalence of components of MS according to presence of metabolic syndrome.

Components of MS	Total Obese (n=60)	With MS (n=15)	Without MS (n=45)	P
Waist circumference ≥90 pc	85%	100%	80%	.09
Systolic BP ≥90 pc	8.3%	20%	4.4%	.09
Diastolic BP ≥90 pc	5%	20%	4.2%	.04
Glucose ≥100 (mg/dL)	8.3%	20%	4.4%	.09
Insulin ≥15 (μU/mL)	25%	73.3%	8.8%	.0001
HOMA-IR (≥3.4)	28.3%	73.3%	13.3%	.0001
Total cholesterol ≥200 (mg/dL)	8.3%	20%	4.4%	.09
Triglycerides ≥150 (mg/dL)	13.3%	40%	4.4%	.002
LDL- C ≥130 (mg/dL)	8.3%	20%	4.4%	.09
HDL-C <40 (mg/dL)	20%	53.3%	8.8%	.0007

Data are number (%).

Table 5. Risk of suffering from metabolic syndrome according to HOMA-IR percentile values by logistic regression analysis.[a]

HOMA-IR percentile (values)	Significance	OR	95.0% CI for OR	
			Lower	Upper
<25 pc (<2.4)	-	Referent	-	-
25-49.9 pc (2.4-3.3)	0.46	1.2	1.022	2.28
50-74.9 pc (3.4-4.9)	0.003	3.8	1.104	8.86
≥75 pc (≥5)	<0.001	5.7	2.34	11.55

[a]Values obtained through logistic regression analysis, adjusted for gender and age. OR: Odd ratio, Pc: Percentile, CI: Confidence interval

fat thickness in obese children (r=0.56, P<.05). **Figure 2** positive significant relations between fasting serum insulin level and visceral fat in obese children (r=0.41, P<.05).

DISCUSSION

Global analysis showed a rising trend in childhood overweightness in developing countries in more than one national survey.[20] In 38 countries for which secular data were available, 16 showed a rising trend in obesity prevalence over time, 16 were static, and only 8 showed falling rates in obesity prevalence.[7] Rates of increase seemed most marked in the countries of northern Africa, such as Morocco and Egypt. Generalized obesity in Egypt and its association with certain chronic diseases has been reported in the literature among adults.[21,22] The results of our study demonstrate that MS components, which until recently were associated with adult morbidity, are also found to be highly prevalent among obese children in our community. The present study revealed that the prevalence of MS was 25% in obese children with no sex tendency, 85% presented with abdominal obesity, a criterion of MS. The observed prevalence of MS in our study is higher than in European coun-

tries.[8,23,24] In Western countries, the incidence of childhood obesity has more than doubled over the past generation; as a consequence, the prevalence of MS and type 2 diabetes mellitus is rapidly increasing in the pediatric population.[25] A previous study on 4250 adolescents (from 10 to 18 years of age; male subjects comprised 42.5% of participants) from 7 governorates representing Egypt showed that MS was 7.4% with no sex or area of residence predilection and that more than one-third of obese Egyptian adolescents had criteria for MS.[2] The present study is the first Egyptian one on the frequency of MS and associated metabolic complications among obese children aged 7 to 9 years. In studies where the Cook criteria were applied, the prevalence of MS among North American obese adolescents was 27%.[17] In others studies following the III Adult Treatment Panel criteria, the prevalence was 26.1%.[26] However, there is no consensus about the definition of MS in pediatric populations.[23] Until recently, even if the MS was reported in children, several definitions were developed. The International Diabetes Federation (IDF) developed a simple unified definition for children over 10 years of age.[27] Many different MS criteria have been employed in children and adolescents, and the components and cut-offs used to diagnose this syndrome have varied considerably among studies.[17,23] The mean age of the children in this study was approximately 8 years, and as the IDF definition was proposed only for children over 10 years we used the the Cook definition.[17] Changes in growth and development during childhood and adolescence make it difficult to choose a cut-off for risk factors.[28,29] To ascertain the real prevalence of this syndrome among children, agreement is needed on the cut-off points for each of the syndrome components; likewise, categories for pubertal stage and gender need to be established.

Environmental factors, including health-related behaviors or lifestyle changes and economic disadvantage, contribute to some of the race or ethnic disparities in the prevalence of the diseases associated with obesity. In cross-sectional population studies, higher fasting serum insulin levels are directly related to increases in body fatness, particularly in those with central adiposity.[30,31] Obesity is an important factor in the development of hypertension in children.[32,33] In our study, BP measurements were significantly higher in both obese males and females compared to controls. The influence of obesity in Egyptian children may be affected by the specific genetic background of the population. Hispanic individuals have a greater risk of developing diabetes and insulin resistance

than other ethnic groups.[34,35] The present study clearly confirms that metabolic components are more common in obese children than in controls. Dyslipidemia is more prevalent in obese children with higher HOMA-IR and LDL and lower HDL than a normal weight group.

There was no significant correlation in the present study between regional fat accumulation and blood pressure in obese children. The study showed a significant positive association between waist circumference and visceral fat as well as between visceral fat and insulin level in obese children (**Figures 1, 2**) in accordance with previous studies indicating that WC provides a simple yet effective measure of truncal obesity.[36,37] WC in obese children was more related to US measurements when compared with that in the control group. No relationship between WHR and ultrasonographic fat thickness measurements was found in either group. These results suggest that WC, but not WHR, might be a useful index to show truncal obesity. In some studies in children and adolescents, there is no correlation between WHR and visceral fat measured by various techniques.[36,38]

Children with MS had significantly different higher levels of BMI SDS, sum of skinfolds thicknesses SDS, waist circumference, visceral fat thickness, systolic and diastolic BP, HOMA-IR, insulin and triglycerides compared to children without MS. However, significantly lower HDL was found in MS children compared to nonMS children. The reason why some obese children developed this syndrome, while others do not is still unknown.[10] This may be due to the presence of other underlying factors, such as IR. Indeed, IR seems to be an important pathophysiologic event contributing to MS, becoming more important than overall adiposity in the development of this syndrome.[4,9,39] In accordance with previous studies, the IR reported in this study was associated with the primary alterations in lipid profile; hyperinsulinism increases free fatty acid release and triglyceride synthesis, which results in hypertriglyceridemia.[40,41] The lipid profile can be considered more atherogenic in MS children, with higher TG, LDL, VLDL and apolipoprotein B, and lower HDL and apolipoprotein AI. Our results show that higher levels of IR are associated with a greater degree of alterations in the components of the MS in obese children. HOMA-IR values above 3.4, which correspond to the 50th percentile of this population, were associated with an increased risk of having MS, compared to the lowest percentile of HOMA-IR value. The most important finding in this study is that insulin resistance and obe-

sity are both strongly associated with MS in children. These findings are supported by the previous results of a multiple regression analysis with the use of insulin resistance and BMI as independent factors and with adjustment for other factors.[33] Consistent with several studies,[7,42,43] in our study, obese children with MS had higher frequencies of central obesity, high insulin, HOMA-IR, triglycerides, diastolic BP levels and low HDL level than nonMS obese children. Although the children in our sample were young, the children with MS already had acanthosis, elevated insulin and increased HOMA-IR. Despite this, fasting glucose levels were normal which reflects the range of abnormalities of glucose homeostasis associated with childhood obesity. Even in the obese, high fasting glycemia is not common in children.[44]

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