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Metabolic syndrome in obese adolescents: a comparison of three different diagnostic criteria

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Abstract

Objective: To investigate the difference in the proportion of adolescents with metabolic syndrome diagnosed based on three different criteria, as well as the use of insulin resistance instead of fasting glucose.

Methods: Cross-sectional study with 121 obese adolescents, between 10 and 14 years old, from public schools of the city of Porto Alegre, Brazil, in 2011. Anthropometric, blood pressure, and biochemical variables were assessed. Metabolic syndrome was defined using three different diagnostic criteria: the International Diabetes Federation (IDF), Cook and de Ferranti. All of them include five components: waist circumference, blood pressure, high-density lipoprotein (HDL) cholesterol, triglycerides and fasting glucose, and there should be at least three abnormal results for the diagnosis of the syndrome. The Homeostasis Model Assessment - Insuline Resistance (HOMA-IR) was used for the characterization of insulin resistance. The analysis of agreement among the criteria was performed using Kappa statistics.

Results: Metabolic syndrome was diagnosed in 39.7, 51.2, and 74.4% of adolescents, according to the IDF, Cook and de Ferranti criteria, respectively. There was agreement for the three diagnostic criteria in 60.3% of the sample. Waist circumference was the most prevalent component (81.0, 81.0, and 96.7%), whereas high fasting glucose was the least prevalent (7.4, 1.7, and 1.7%). The use of HOMA-IR significantly increased the proportion of positive diagnoses for the syndrome.

Conclusion: The results showed significant differences between the three diagnostic criteria. While there is no consensus on the diagnostic criteria for metabolic syndrome, differences in the prevalence of the disease in pediatric population will be frequent.

J Pediatr (Rio J). 2012;88(4):303-9: Obesity, metabolic syndrome, insulin resistance, diagnoses.

Introduction

Adolescent obesity is currently one of the major public health problems, not only because of the possibility of having adult obesity,[1] but also because of the increased risk of early onset of metabolic complications associated with excess body fat,[2-4] such as metabolic syndrome.

Metabolic syndrome is the association of at least three of the following risk factors: abdominal obesity, hypertension, hypertriglyceridemia, high levels of fasting plasma glucose (FPG), and low levels of high density lipoprotein cholesterol (HDL-C); and this association is

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considered a precursor of cardiovascular disease and type 2 diabetes.[5]

In adults, the cutoff values for different components of the metabolic syndrome have been identified, but when it comes to children and adolescents no consensus has been reached in the literature.[6]

Several studies have investigated the prevalence of metabolic syndrome in children and adolescents, as well as its association with obesity[7-9]; however, disagreement regarding the diagnostic criteria hinders the comparison of the results obtained in different studies.[10] Such diagnostic disagreement has resulted in discrepancies ranging from 20 to 300% between the lowest and the highest prevalence in the same sample.[11-13]

Another issue that has an influence on the diagnosis is the choice of the metabolic syndrome components, because some authors have suggested the use of insulin resistance (IR), according to the Homeostasis Model Assessment: Insulin Resistance (HOMA-IR), instead of FPG.[14,15]

The objective of the present study was to investigate the difference in the proportion of adolescents with metabolic syndrome, whose diagnosis was based on three different criteria, as well as the use of IR instead of FPG.

Methods

We conducted a cross-sectional descriptive study with adolescents aged 10 to 14 years. The sample was selected using the database of the 2008 survey on the prevalence of overweight and obesity in students from 7 to 10 years old from public city schools of Porto Alegre (RS), Brazil.[16] This study used a cluster sample with equal inclusion probability calculated including 1,553 students; the prevalence of overweight was estimated to be 20%, 95%CI, and a margin of sampling error of 2%. Students were evaluated in 10 public city schools in 2007 and 2008, when their ages ranged between 7 and 10 years. The survey showed that 169 (11.2%) were classified as obese.

We contacted the schools and parents of these 169 obese students, whose ages ranged between 10 and 14 years old at the time of the study. For sample size calculation, we used the computer program G*Power 3.1.3, adopting effect size of 30%, α error of 0.05, and power of 80% ($1 - \beta$ error). The sample size was estimated at 108 subjects. Only those adolescents who agreed to voluntarily participate, whose parents signed the written consent form, and who attended school in fasting on one of the dates scheduled for data collection were included in the study.

The study was approved by the Research Ethics Committee at the Hospital de Clínicas de Porto Alegre, under no. 11-0149.

Data collection was performed at the students' schools always between 7 and 9 a.m. All anthropometric measurements were taken according to the recommendations by Costa.[17] Adolescents were barefoot and wearing light clothing while their body mass was measured using a 0.1 kg resolution Sanny® digital scale. Height was measured using a Sanny® stadiometer to the nearest 0.1 cm while adolescents were barefoot and standing erect. Waist circumference (WC) was measured using a Sanny® metal measuring tape, with 0.01 cm resolution, from the midpoint between the last rib and the iliac crest.

The oscillometric method was used to measure the blood pressure in the right arm only once using a Meditech ABPM-04 device while adolescents were sitting, after resting for 15 minutes.

A blood sample was collected by an experienced technician after a 12-hour fasting period. The following items were measured: FPG, fasting plasma insulin (FPI), and lipid profile, which included total cholesterol (TC), triglycerides (TG), HDL-C, and low density lipoprotein cholesterol (LDL-C). FPG was measured using the hexokinase method with Centra Link equipment; FPI was measured by chemiluminescence. TC and TG were measured using the enzymatic colorimetric method; whereas HDL-C was measured by the homogeneous enzymatic colorimetric method, all of them using Centra Link equipment. LDL-C was calculated using the Friedewald formula.

HOMA-IR, used to estimate IR, was calculated by multiplying the value of FPI (μU/mL) by the value of FPG (mg/dL) and dividing the product by 405. Values higher than 3.43 were considered indicators of IR.[15]

Nutritional status was defined using the body mass index for age and sex, as proposed by the World Health Organization,[18] adopting the 95th percentile as the cutoff point for identifying obese adolescents. Metabolic syndrome was diagnosed using three diagnostic criteria, two of them based on the National Cholesterol Education Program modified for children and adolescents by Cook et al.[19] and by de Ferranti et al.[20]; and the third based on the consensus proposed by the International Diabetes Federation (IDF)[5] (Table 1).

The statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 15.0 (SPSS Inc., Chicago, IL, USA). The assumption of normal data distribution was checked using the nonparametric Kolmogorov-Smirnov test. For continuous variables, we used descriptive analysis by means of mean (X) and standard deviation (SD). Comparisons of measurements were performed by Student's *t* test for independent samples, or by Mann-Whitney U test, according to data distribution. The chi-square test was used to compare the proportions of categorical variables. The Kappa index was used to check the agreement between the results achieved using different diagnostic criteria. Significance level was $p < 0.05$.

Results

Of the 169 adolescents eligible for the study, 48 did not participate. Thirteen of these were excluded because of parents' refusal; two adolescents also refused to participate; five adolescents could not take part in the study because they were not in fasting state; and 28 subjects were excluded because they missed the dates scheduled for data collection. Thus, the sample included 121 obese adolescents, and 62 (51.2%) of them were males. The characteristics of the sample are shown in Table 2.

When comparing sexes, we found no statistically significant difference regarding any of the variables; thus, the comparisons between the diagnostic criteria included the whole group, without stratification by sex (Table 3).

The proportion of positive diagnoses for metabolic syndrome based on different criteria is shown in Table 4.

The analysis of agreement between the criteria showed that in 73 subjects (60.3%) the diagnosis was the same for the three definitions of metabolic syndrome. When analyzing the criteria in pairs, the agreement between the IDF and Cook was 83.5% (Kappa = 0.704; p = 0.000); between the IDF and de Ferranti it was 62.0% (Kappa = 0.309; p = 0.000); and between Cook and de Ferranti it was 71.9% (Kappa = 0.465; p = 0.000). In 28 adolescents (23.1%), metabolic syndrome was only diagnosed by de Ferranti.

The comparison between the three criteria using the chi-square test showed that de Ferranti had a higher proportion of metabolic syndrome than the others (p = 0.000); whereas in the comparison between the IDF and Cook, although there was no statistically significant difference (p = 0.071), there was a tendency toward a higher proportion of adolescents with metabolic syndrome according to Cook's criteria.

The analysis of risk factors revealed that the IDF has a proportion significantly lower of positive diagnosis for metabolic syndrome than all other criteria in: HDL-C (p = 0.000), blood pressure (p = 0.000), FPG (p = 0.032), and TG (p = 0.001). In terms of WC, de Ferranti showed a proportion of positive diagnosis for metabolic syndrome significantly greater than the other two criteria (p = 0.000).

When we replaced FPG with IR, we found statistically significant increase in the proportion of cases of metabolic syndrome for the three criteria using the chi-square test. The proportion increased from 39.7 to 52.8% (p = 0.039) when the IDF criterion was used. In the criterion proposed by Cook, there was an increase from 51.2 to 65.4% (p = 0.024). Whereas in the criterion suggested by de Ferranti, the increase was from 74.4 to 86.0% (p = 0.022).

Discussion

Diagnostic disagreements regarding the metabolic syndrome in children and adolescents have been reported by several authors. Such divergences are considered to be primarily caused by the use of different cutoff points for the metabolic syndrome components based on different definitions of the syndrome.[10,21] A possible reason for this fact is that most definitions of these syndrome are based on criteria proposed for adults; thus, abnormalities that are less frequent in childhood and adolescence may be considered to establish the diagnosis of metabolic syndrome in this population, as it is the case of abnormal glucose level.[14]

Our study demonstrated that the prevalence of the metabolic syndrome among obese adolescents was high according to the three diagnostic criteria, showing a lower proportion based on the IDF criterion (39.7%) and a higher proportion according to de Ferranti (74.4%). Other studies have also shown a higher prevalence of metabolic syndrome using de Ferranti's criterion when compared to other criteria,[10-13] which can be explained by the fact that it has more strict cutoff values for WC, HDL-C, and TG levels.

WC was the component showing the highest prevalence in the sample considering the three diagnostic criteria, which has been found in several studies, regardless of the criterion used,[9,11,22-24] because abdominal obesity and metabolic syndrome are highly related.[12,25]

Table 1 - Variables and cutoff points according to the different classifications of the metabolic syndrome

Variables	Cook et al. (2003)	de Ferranti et al. (2004)	IDF (2007)
HDL-C	≤ 40 mg/dL	< 50 mg/dL	≤ 40 mg/dL
Blood pressure	≥ P90 (age/sex/height)	≥ P90 (age/sex/height)	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg
Glucose	≥ 110 mg/dL	≥ 110 mg/dL	≥ 100 mg/dL
Waist circumference	≥ P90 (age/sex)	≥ P75 (age/sex)	≥ P90 (age/sex)
Triglycerides	≥ 110 mg/dL	≥ 100 mg/dL	≥ 150 mg/dL

DBP = diastolic blood pressure; HDL-C = high-density lipoprotein; IDF = International Diabetes Federation; P90 = 90th percentile; P75 = 75th percentile; SBP = systolic blood pressure.

According to Weiss et al.,[26] abnormal FPG is rare in children and adolescents, even if they are overweight. This was confirmed in the present study, since this variable was the one showing the lowest proportions for the three criteria, 7.4% for the IDF and 1.7% for the other two criteria. In studies with obese children and adolescents, a low proportion of high FPG is a common finding in the literature.[9,12,27]

In this context, the use of blood glucose levels as a risk factor for the metabolic syndrome is questionable. An option that has shown good results is the use of IR, based on the HOMA-IR, as one of the components of the syndrome.[14,15,28,29]

A study conducted with obese adolescents aged between 14 and 19 years from São Paulo suggested a new diagnostic criterion for the metabolic syndrome, replacing FPG with IR according to HOMA-IR and including hepatic steatosis assessed by ultrasound.[14] The authors found a higher proportion of adolescents with metabolic syndrome according to the new criterion when compared to the other two criteria used.

In a study conducted with 105 African-American children and adolescents, aged between 9 and 13 years, the use of the HOMA-IR instead of FPG not only showed a higher proportion of positive diagnoses for the metabolic syndrome,

Table 2 - Description of the anthropometric, clinical, and laboratory characteristics of the sample

Variables	Mean ± SD	95%CI
Age (years)	11.1±1.6	10.81-11.39
Body mass (kg)	65.8±15.2	62.30-67.70
Height (cm)	150.4±10.1	148.58-152.22
BMI (kg/m²)	28.8±4.2	28.04-29.56
WC (cm)	88.3±10.3	86.45-90.15
SBP (mmHg)	131.4±20.8	127.66-135.14
DBP (mmHg)	71.8±10.4	69.93-73.67
Glucose (mg/dL)	91.0±6.1	89.92-92.08
Insulin (μU/mL)	28.0±19.5	24.49-31.51
HOMA-IR	6.4±4.9	5.52-7.28
TC (mg/dL)	159.2±28.5	153.07-163.33
LDL-C (mg/dL)	98.9±24.9	94.42-103.38
HDL-C (mg/dL)	39.9±7.5	38.55-41.25
Triglycerides (mg/dL)	102.4±52.9	92.64-111.36

BMI = body mass index; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein; HOMA-IR = Homeostasis Model Assessment - Insulin Resistance; LDL-C = low-density lipoprotein; SBP = systolic blood pressure; SD = standard deviation; TC = total cholesterol; WC = waist circumference; 95%CI = 95% confidence interval.

Table 3 - Comparison between sexes in terms of anthropometric measures, blood pressure, and metabolic profile of obese adolescents

	Mean ± SD		
Variables	Male (n = 62)	Female (n = 59)	p
Age	11.4±1.5	10.8±1.7	0.051*
Anthropometry			
Body mass (kg)	67.2±14.0	64.3±16.4	0.296*
Height (cm)	151.9±10.0	148.8±9.9	0.096*
BMI (kg/m²)	28.9±3.9	28.6±4.5	0.690*
WC (cm)	89.8±9.8	86.8±10.7	0.111*
Blood pressure (mmHg)			
Systolic	133.8±16.8	129.0±24.2	0.215*
Diastolic	72.6±11.0	70.9±9.8	0.385*
Metabolic profile			
Glucose (mg/dL)	91.8±6.3	90.1±5.8	0.102†
Insulin (μU/mL)	27.0±22.7	29.2±15.5	0.137†
HOMA-IR	6.2±5.8	6.6±3.7	0.225†
TC (mg/dL)	161.6±28.1	156.8±28.8	0.358*
LDL-C (mg/dL)	101.0±23.7	96.6±26.2	0.341*
HDL-C (mg/dL)	40.6±7.4	39.2±7.5	0.332*
Triglycerides (mg/dL)	100.1±50.0	104.9±56.1	0,669†

BMI = body mass index; HDL-C = high-density lipoprotein; HOMA-IR = Homeostasis Model Assessment: Insulin Resistance; LDL-C = low-density lipoprotein; SD = standard deviation; TC = total cholesterol; WC = waist circumference.
* Student's *t* test.
† Mann-Whitney U test.

Table 4 - Proportion of subjects regarding risk factors and metabolic syndrome considering three different diagnostic criteria

Variables	Cook et al. (2003)	de Ferranti et al. (2004)	IDF (2007)
Components			
HDL-C	54.5%	92.6%	54.5%
Blood pressure	76.0%	76.0%	54.5%
Glucose	1.7%	1.7%	7.4%
Waist circumference	81.0%	96.7%	81.0%
Triglycerides	34.7%	40.5%	16.5%
Metabolic syndrome	51.2%*‡	74.4%†‡	39.7%*†
Number of components			
0	2.5%	0.0%	5.8%
1	21.5%	4.1%	28.9%
2	25.6%	19.8%	25.6%
3	25.6%	42.1%	25.6%
4	24.0%	32.2%	9.9%
5	0.8%	1.7%	4.1%

HDL-C = high-density lipoprotein; IDF = International Diabetes Federation.
* Kappa = 0.704; p = 0.000.
† Kappa = 0.309; p = 0.000.
‡ Kappa = 0.465; p = 0.000.

but also demonstrated a reduction in the proportion of false-negative results from 94 to 13%.

The present study also showed a significantly greater proportion of positive diagnoses for the syndrome when FPG was replaced with IR. This fact can be explained by the earlier manifestation of IR than high glucose level in the evolution of the metabolic syndrome in pediatric populations.[14,15]

Conversely, low levels of HDL-C and high blood pressure are quite frequent risk factors in obese adolescents and in the composition of the metabolic syndrome in this stage of life,[9,28] which was also found in our sample.

In the comparison between the different criteria in terms of presence of high blood pressure, the IDF had a lower proportion (54.5%) than the other criteria (76.0% for both of them), which can be explained by the higher cutoff points of the IDF and by the fact that it did not classify adolescents according to age, sex, and height.

In relation to the number of risk factors, the absence of risk factors was not found in any adolescent based on de Ferranti's criterion and in only 2.5 and 5.8% according to the criteria of Cook and the IDF, respectively. The association between obesity in the pediatric population and the presence of risk factors for the metabolic syndrome has been widely demonstrated.[3,27,30-32]

The simultaneous presence of the five risk factors is also rare in this age group,[8,9,11] occurring in a small proportion and with no statistically significant difference between the criteria in the present study, but with a tendency toward a greater proportion based on the IDF. This can be explained by the small number of adolescents with high FPG and by the lower cutoff point than the other two criteria (100 vs. 110 mg/dL) for this variable in criterion proposed by the IDF.

Although the focus of the present study was the presence of the metabolic syndrome according to different diagnostic criteria, the proportion of adolescents showing one and two risk factors should be considered. Taking into consideration that our sample included only obese subjects, unless preventive measures are taken, other risk factors can develop, leading to the metabolic syndrome until adulthood.[1]

In a study conducted with 52 obese children from the city of Taguatinga (Federal District), Brazil, 17.3% of the children had metabolic syndrome. Of the 52 children, 44.2% had at least two risk factors, and 15% had hypertension. Hypertriglyceridemia was found in 50 and 70.8% of boys and girls, respectively. HDL-C below desirable levels were found only in girls.[8] Although these findings are different from our results as to the difference between sexes, as well as the low proportion of subjects presenting with the syndrome, it is worth noting that this condition in childhood can increase the metabolic risk in adolescence.[1]

In Mexico, a study using the IDF diagnostic criterion with 466 adolescents aged between 11 to 13 years, showed a prevalence of 20.0% for the metabolic syndrome, and 49.0% of the subjects had abdominal obesity, 69.0% had low HDL-C, and 29.0% had hypertriglyceridemia. In addition, high systolic and diastolic blood pressures were found in 8.0 and 13.0% of the adolescents, respectively.[28] Considering the high proportions of abdominal obesity, low HDL-C levels, hypertriglyceridemia, and taking into account that the cutoff points for this criterion are lower than for the other two criteria used in the present study, we can conclude that the prevalence of the syndrome would be much higher with the use of Cook or de Ferranti's criterion.

There was diagnostic agreement between the three criteria studied in 60.3% of the cases. Although the highest difference has been found between the IDF and de Ferranti, the syndrome was diagnosed only by the latter in 23.1% of the adolescents. Considering that the professional management for the prevention and treatment depends on the diagnosis, the choice of the criterion to be used can have an influence on the prescription of the intervention.

Our findings, which are in agreement with other studies,[10,11,13,14,22] suggest the need to establish a consensus as to the cutoff points for risk factors and a single diagnostic definition for the metabolic syndrome in the pediatric population in order to reduce the difficulties of interpretation and comparison of the data from different populations, as well as to support the preventive therapeutic management to be used.

Although the findings of our sample cannot be generalized to other populations, they were consistent with the results found in several recent studies. A limitation of the present study was the absence of assessment of the sexual maturation stage, because there are adolescents at different pubertal stages in the age group studied, and adolescence is a phase of significant metabolic changes.

Conclusion

Our findings showed a significant difference between the proportions found according to the three diagnostic criteria, and de Ferranti's criterion had the highest proportion. In addition, the use of IR instead of FPG significantly increased the proportion of positive diagnoses for metabolic syndrome.

While no consensus is reach on the diagnostic criteria for metabolic syndrome, disagreements regarding the prevalence of the disease in the pediatric populations will be frequent.

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