

# Cardiovascular Risks in Adolescents with Different Degrees of Obesity

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### **Abstract**

Background: There have been few studies on cardiovascular risk factors in adolescents with different degrees of obesity.

Objective: To evaluate metabolic effects associated with different degrees of obesity in adolescents and their impact on cardiovascular risks.

Methods: Cross-sectional study of 80 obese adolescents, divided in two groups: 2<z-BMI<2.5 and z-BMI ≥2.5, classified as obese with lower or higher degree of obesity, respectively. Physical examination was carried out, as well as biochemical and body composition assessment. The statistical analysis was performed with t-Student and Chi-square tests, aiming at comparing both groups. A multiple logistic model was used to verify the associations between the biochemical variables and the degree of obesity. Risk scores were developed for cardiovascular disease, according to the number of alterations found in the following variables: fasting glycemia, triglycerides, HDL and blood pressure. Association between these scores and degree of obesity were verified.

Results: The two groups differed regarding weight, waist circumference, fasting glycemia and insulin, HOMA-IR, triglycerides, HDL, blood pressure (BP) and body composition measurements (p<0.05). The adolescents with the higher degree of obesity presented higher frequencies of alterations for glycemia, HOMA-IR, triglycerides, HDL and BP (p<0.05). The logistic model showed associations between the degree of obesity and the variables: HDL (OR=5.43), BP (OR=4.29), TG (OR=3.12). The risk score demonstrated that 57.7% of the adolescents with higher degrees of obesity had two or more metabolic alterations versus 16.7% from the other group (p<0.001).

Conclusion: The degree of obesity influenced the onset of alterations that comprise the metabolic syndrome, increasing the cardiovascular risk. (Arq Bras Cardiol 2011;96(3):205-211)

Key words: Obesity; adolescent; risk factors; metabolic syndrome; body mass index.

### Introduction

Adolescence is one of the critical periods for the onset or persistence of obesity and for the development of its complications<sup>1</sup>. Although genetic factors predispose to the development of obesity, studies have highlighted the importance of environmental and behavioral factors - such as the decrease in physical activity together with the increase in sedentary activities<sup>2</sup> - associated with a higher consumption of food as the main causes of the increased prevalence of obesity.

The predominance of obesity in childhood and adolescence has increased drastically and represents a relevant public health problem in developed countries and in many developing ones. In the USA, during the last three decades, the prevalence of obesity in children and adolescents has more than doubled, with prevalences of 31.9% and 16.3% of overweight and obesity, respectively, between the years

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2003 and 2006<sup>3</sup>. In Brazil, the rates of excess weight among adolescents have followed the same tendency in the last 20 years, with a prevalence of 7.7% in the 80s<sup>4</sup> for both sexes. This rate increased to 17.9% in boys and 15.4% in girls at the last national survey in 2002 to 2003<sup>5</sup>.

Obesity is associated with relevant health problems in the pediatric population<sup>6,7</sup> and constitute a risk factor for many morbidities and mortality in adulthood<sup>8</sup>. The study by Freedman et al<sup>9</sup> using data from the Bogalusa Heart Study, correlated the body mass index (BMI) of childhood with that of adulthood and obtained a value of 0.58. This study demonstrated that 77% of the children with excess weight became obese adults. A cohort study carried out in Brazil, using three assessments during a 17-year period, which comprehended from childhood to the start of adulthood, verified that children with high BMI throughout all study phases, that is, permanently obese, presented higher prevalence of alterations in glycemia, blood pressure (BP) and HDL at adulthood, when compared to the group with normal BMI (p<0.05)<sup>10</sup>.

Comorbidities, such as arterial hypertension, dyslipidemia, type 2 diabetes mellitus (DM2) - increasingly more evident in the pediatric population<sup>11</sup> - affect around 40% of North-

American adolescents<sup>12</sup> and the coexistence of these metabolic alterations are up to 7-fold higher in obese individuals<sup>12,13</sup>.

The concomitance of metabolic alterations related to obesity and chronic diseases has been called metabolic syndrome. A comparative study of diagnostic criteria for metabolic syndrome in children and adolescents - Caucasians and African-Americans - showed variations in the prevalence rates of 18% to 25%. These numbers were significantly high in those individuals with excess weight (24% to 51%)<sup>14</sup>. Although the criteria used to characterize the metabolic syndrome were not necessarily the same among the studies, its prevalence gradually increased in parallel with the increase in obesity among the young population<sup>15</sup>.

However, there have been few studies on the metabolic risks and their consequences in adolescents with different degrees of obesity<sup>8,15,16</sup>. The present study analyzed the metabolic and cardiovascular complications associated with different degrees of obesity in adolescents, describing their impact on early cardiovascular and metabolic risk factors, as well as on metabolic syndrome.

### **Methods**

The present is a cross-sectional study, of which data are part of the study "Risk factors and comorbidities associated with obesity in adolescents from public schools in the city of São Paulo, Brazil", which evaluated obese (BMI> 95<sup>th</sup> percentile)<sup>17</sup> postpubertal adolescents<sup>18</sup> aged 14 to 19 years, that regularly attended school in the morning and afternoon periods, from 2006 to 2007. The exclusion criteria were: presence of acute diseases or other chronic diseases, drug or nutritional treatment status for weight loss and pregnant or nursing girls.

The sample size was calculated for  $\alpha$  0.05 and  $\beta$  0.20, consisting of two obese individuals with a lower degree of obesity. For each obese individual with a higher degree of obesity and an estimated OR of 3.00 for the metabolic alteration hypertriglyceridemia when comparing both groups and assuming a one-tailed test, the samples of values in the two groups would be 48 and 24, respectively.

The sample selection included 2,330 adolescents from four public schools in Vila Mariana, of which 150 (6%) were diagnosed as obese and among which 26 (17.33%) met the aforementioned exclusion criteria. Of the 124 remaining students, 42 (33.87%) refused to participate in the study and two individuals (1.61%) abandoned the project during the field study. A total of 80 obese adolescents (64.5% of the initial sample) completed the protocol. When the BMI means were compared - stratified by age and sex of the analyzed sample - with the BMI means of the 44 individuals who did not participate in the study, no significant differences were observed between the groups, evidence that the lost samples must not have introduced selection biases.

The adolescents were classified in z-scores of BMI (z-BMI) and all those > + 2.0 z-score remained with a diagnosis of obesity¹9. Based on the z-BMI, the adolescents were distributed in two groups: 2<z-BMI<2.5 and z-BMI≥2.5. This cutoff was used to differentiate obese adolescents with a higher or lower degree of obesity, as there are no established criteria to diagnose different degrees of obesity in adolescence.

The anthropometric assessment was carried out by two nutritionists, according to the recommended protocols<sup>20</sup>. Weight was measured in a Kratos™ digital scale, model "Linea", with minimum and maximum capacities of 1.25 kg and 150 kg, with a 50-g variation, placed on a solid and level surface. Height was measured with an Alturaexata™ portable anthropometer of which scales were in millimeters, placed on a solid and level surface. The waist circumference (WC) was measured using an inextensible measuring tape, at the midpoint between the last rib and the iliac crest<sup>21</sup>.

Blood pressure (BP) was measured by two appropriately trained physicians that belonged to the team, using a mercury sphygmomanometer (Thycos™) using an appropriate cuff for each individual. The mean value of three measurements was considered for the study<sup>22</sup>. Arterial hypertension (AH) was defined as systolic or diastolic BP ≥ 95th percentile for age, sex and height<sup>23</sup>. The adolescents aged 18 to 19 years were classified as hypertensive when they presented a mean BP ≥ 140/90 mmHg<sup>24</sup>. The blood samples were collected by venipuncture after a 12-hour fast. Conventional enzymatic and colorimetric laboratory techniques were used for the laboratory assessment, except for the LDL levels, which were calculated by Friedewald's equation<sup>25</sup>. Levels of total cholesterol (TC) and fractions, triglycerides (TG) and fasting glycemia were classified according to the I Guideline for the Prevention of Atherosclerosis in Childhood and Adolescence of the Brazilian Society of Cardiology<sup>26</sup>. Fasting insulin levels were considered altered when ≥ 20 mg/dl<sup>27</sup>. The HOMA-IR (homeostasis model assessment for insulin resistance) index, used for the classification of insulin resistance (IR), was obtained by calculating the product of fasting plasma insulin  $(\mu U/mL)$  and fasting glycemia (mmol/l) divided by 22.5. The cutoff used was  $\geq 3.43$  for both sexes<sup>27</sup>.

The evaluation of body composition by DXA (Dual X-ray Absorptiometry) in a LUNARTM DPX-L/PED equipment, Wisconsin, USA, (version 1.5), was performed by a single technician, who had been appropriately trained.

At the statistical analysis, the differences of the means of the independent variables between the two groups of obese adolescents were evaluated by the Student's t test. The Chisquare test was used to verify associations of the two groups with the dichotomized values. The multiple logistic regression analysis was performed, considering the variables that presented p<0.20 at the bivariate analysis. The final model included the variables that presented p<0.05. During the development of the model, no effect modifiers or confounding factors were identified among the dependent variables for the association with the degrees of obesity<sup>28</sup>.

A risk score was created for metabolic syndrome and associated cardiovascular diseases, which attributed values of 0 to 4 to each one of the obese individuals, according to the number of metabolic alterations observed: fasting glycemia, triglycerides, HDL and BP. Previous studies with adolescents<sup>8,12,16,29</sup> and metabolic syndrome were considered when choosing the variables used to create the scores, as well as the results of the bivariate analyses. The Chi-square test was used to evaluate the association of the number of metabolic alterations in the two groups of adolescents, according to the degree of obesity.

The level of significance was set at p < 0.05. The data were analyzed using the software Epi info release 6.04 (Atlanta, Georgia, USA: CDC; 1996) and Stata release 10.0 (College Station, Texas, USA: Stata Corporation; 2007).

The study was approved by the Ethics Committee in Research of *Universidade Federal de São Paulo* and the data were collected after the free and informed consent form had been signed by all adolescents and their parents/tutors. The adolescents were followed by the multidisciplinary team of the Ambulatory of Obesity of the Discipline of Nutrology of the Department of Pediatrics of *Universidade Federal de São Paulo*.

#### Results

The group that comprehended individuals with a higher degree of obesity (≥ 2.5 z-BMl) consisted of 26 adolescents - 15 (57.7%) of which were females. The other group consisted of 54 adolescents with lower degrees of obesity - 32 (59.3%) of which were females. The means of the anthropometric, metabolic and body composition variables for the two groups of obese adolescents with higher or lower degrees of obesity are shown in Table 1. The means of age, sex and height did not show any statistically significant difference. As expected, the weight, WC and body composition measurements (total body fat and truncal body fat in kg) presented significant difference. Regarding the metabolic variables, all of them presented significant differences between the degrees of obesity, except TC and LDL-cholesterol (Table 1).

As shown in Table 2, the adolescents, regardless of the degree of obesity, presented high percentages of metabolic effects that varied from 37.5% for insulin resistance to 15% for AH. As there were no significant differences between sexes in the frequencies of alterations, the data are not presented according to sex.

Among the adolescents from the group with BMI ≥ 2.5 z-BMI, 30% presented both hyperglycemia and hyperinsulinemia (OR 3.55 and 2.56), compared with 11% and 14% of the group with a lower degree of obesity, respectively. Half of the adolescents with BMI ≥ 2.5 z-BMI presented insulin resistance, whereas 30% of the adolescents from the other group presented this metabolic alteration. Regarding the lipid profile, the group with higher BMI values had 50% of altered results for triglycerides and 57% for HDL with OR of 3.5 and 4.3, respectively, when compared with the group with BMI < 2.5 z-BMI. The presence of AH was 26.9% in the group with the higher degree of obesity and 9.2% in the other group. Thus, the adolescents with higher degrees of obesity presented higher frequencies of the assessed alterations, with significant differences for fasting glycemia, insulin resistance, TG, HDL and BP.

The variables selected for the logistic model were: HDL, triglycerides and fasting glycemia, BP. Basal insulin and the HOMA-IR index were not included in the model, as it was decided to choose only one test related to the glycidic profile. Glycemia was chosen as it presented a stronger association with the degrees of obesity at the bivariate analysis. Table 3 shows the OR adjusted for metabolic alterations in adolescents with different degrees of obesity, disclosing a

Table 1 - Mean and standard deviation of clinical and biochemical variables and of body composition, according to the severity of obesity in postpubertal adolescents from public schools of the state of São Paulo. 2007

_	Sever	ity of Obesity (z-BM	I)
	< 2.5 (n=54)	≥2.5 (n=26)	p value*
Age	15.87 (1.05)	16.15 (1,29)	0.296
Male sex †	22 (40%)	11 (42%)	0.893
BMI kg/m²	30.28 (1.17)	37.22 (4.57)	0.000
Weight kg	86.14 (8.51)	105.34 (15.04)	0.000
Height m	1.68 (0.08)	1.68 (0.07)	0.874
WC cm	96.00 (5.52)	108.83 (10.7)	0.000
Glycemia mg/dl	91.61 (7.41)	96.27 (8.6)	0.001
Insulin µU/ml	12.88 (7.05)	17.89 (11.21)	0.017
Homa-IR	2.95 (1.66)	4.38 (3.09)	0.000
Total cholesterol mg/dl	154.41 (29.74)	150.42 (34.93)	0.508
HDL mg/dl	49.53 (7,95)	44.42 (10.88)	0.020
LDL mg/dl	89.11 (23.06)	85.46 (28.29)	0.540
TGL mg/dl	78.92 (39.37)	102.76 (39.53)	0.013
SBP mmHg	113.24 (11.78)	119.38 (9.82)	0.024
DBP mmHg	68.24 (8.21)	73.69 (9.04)	0.000
Total fat kg	31.83 (6.27)	45.46 (9.71)	0.000
Truncal fat kg	14.55 (2.63)	20.23 (4.61)	0.000

p value<0.05. † Chi-square.

strong association with HDL (OR= 5.43; CI: 1.80-16.39), followed by BP (4.29; CI: 1.06-17.28) and triglycerides (OR= 3.12 CI: 1.04-9.37). Glycemia did not remain the model, as it lost statistical significance when analyzed together with other independent variables.

Chart 1 shows the presence of at least one risk factor for cardiovascular disease (CVD) in more than 60% of the sample and 30% presented at least two alterations. More than 50% of the group of adolescents with higher degrees of obesity presented two or more positive tests (57.7%), whereas only 1/6 (16.7%) of the group with lower degrees of obesity presented the same result, with a statistically significant difference (p<0.001).

#### **Discussion**

Most of the studied metabolic effects present significant associations with the degree of obesity among postpubertal adolescents. The use of the BMI for the diagnosis of obesity in adolescents has been well-established in the literature, as it has good clinical applicability. Additionally, its use demonstrates an association with visceral fat, a better correlation than other anthropometric parameters with BP and blood levels of lipids<sup>30,31</sup>.

Previous studies have demonstrated the association between obesity and metabolic alterations<sup>13,14</sup>, but few have

Table 2 - Frequency and Odds ratio (OR) with respective confidence intervals (95%CI) for variables related to severity of obesity according to the Body Mass Index (BMI) of postpubertal adolescents from public schools of São Paulo, 2007

				Severity o	f obesity (z-	ВМІ)		
Variables	Tot	al (n=80)	< 2.	5 (n=54)	≥	2.5 (n=26)	OR (95%CI)	P∥
	n+	% +	n+	%+	n+	% +	-	
Glycemia ≥ 100 mg/dl*	14	17.5%	6	11.1%	8	30.8%	3.55 (1.08< OR <11.68)	0.020
Insulin ≥ 20 mg/dl*	16	20.0%	8	14.0%	8	30.0%	2.56 (0.72 <or<9.14)< td=""><td>0.090</td></or<9.14)<>	0.090
HOMA-IR ≥ 3,43†	30	37.5%	16	29.6%	14	53.8%	2.77 (1.05 <or<7.28)< td=""><td>0.040</td></or<7.28)<>	0.040
Triglycerides ≥100 mg/dl*	25	31.2%	12	22.2%	13	50.0%	3.5 (1.28 <or<9.52)< td=""><td>0.010</td></or<9.52)<>	0.010
HDL < 45 mg/dl*	28	35.0%	13	24.1%	15	57.7%	4.3 (1.58 <or<11.65)< td=""><td>0.002</td></or<11.65)<>	0.002
LDL ≥ 100 mg/dl*	27	33.7%	18	33.3%	9	34.6%	1.06 (0.35 <or<3.19)< td=""><td>0.900</td></or<3.19)<>	0.900
BP ≥ p95 <sup>‡, §</sup>	12	15.0%	5	9.3%	7	26.9%	3.61 (1.02 <or<12.78)< td=""><td>0.047</td></or<12.78)<>	0.047

<sup>%+ -</sup> percentage of adolescents with altered test results. \* SBC, 2005; † Cuartero, 2007; ‡ NHBP, 2004; § SBC, 2005; || p value < 0.05.

Table 3 - Multiple logistic regression with adjusted Odds Ratio (OR) for metabolic alterations associated with the degree of obesity in postpubertal adolescents from public schools of the state of São Paulo, 2007

Z-BMI					
Metabolic alterations	Adjusted OR (95%CI)	p Value *			
HDL < 45mg/dl <sup>†</sup>	5.434 (1.802-16.391)	0.003			
Triglycerides ≥ 100mg/dl <sup>†</sup>	3.124 (1.041-9.380)	0.042			
BP ≥ p95 <sup>‡, §</sup>	4.2953(1.067-17.284)	0.040			

Total number evaluated = 80. \* p value <0.05.  $^{\dagger}$  SBC, 2005;  $^{\ddagger}$  NHBP, 2004;  $^{\S}$  SBC, 2005.

correlated the degree of obesity with the presence of such alterations<sup>8,15,16</sup>. Our results showed that, the higher the degree of obesity, the higher the risk of glycidic, lipidic and BP alterations. As in the multivariate analysis, none of the variables were identified as a confounding factor or effect modifier. The identified risks can be attributed to each one

of the variables, regardless of the effects of the other variables included in the model.

Insulin resistance was the most common alteration among the obese adolescents of this study. Lee et al<sup>32</sup> analyzed a representative subsample of adolescents aged 12 to 19 years that participated in the 1999 to 2002 NHANES study and showed that obesity was the factor that most influenced the levels of insulin resistance (IR). In children and adolescents, IR has also been associated with dyslipidemia, DM2 and long-term cardiovascular complications<sup>33,34</sup>. Our results indicate, in concordance with previous studies<sup>16</sup>, that IR is strongly associated with the severity of obesity, which suggests a dose-response gradient in the association between IR and adiposity.

The severity of obesity in our sample also presented a significant association with other metabolic and clinical parameters, such as hypertriglyceridemia, altered HDL, fasting hyperglycemia and hypertension. Caranti et al<sup>16</sup> analyzed metabolic alterations in 509 Brazilian (n=110) and Italian (n=399) postpubertal obese adolescents and found similar results for altered HDL, IR and hypertension. A cohort study

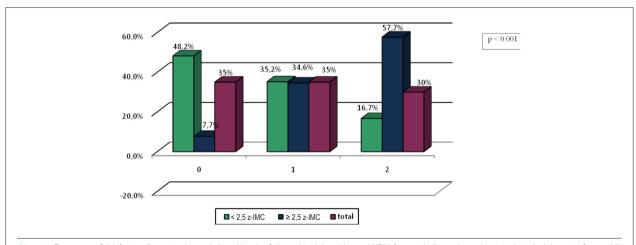


Chart 1 - Frequency of risk factors (hypertension and altered levels of glycemia, triglycerides and HDL) for metabolic syndrome in postpubertal adolescents from public schools of the state of São Paulo, Brazil, analyzed according to the obesity severity, 2007.

with 115 individuals from the city of Rio de Janeiro, Brazil, carried out in three assessments - a period that comprehended childhood, adolescence and start of adulthood - showed that the group with high BMI presented a higher prevalence of arterial hypertension (p<0.001) than the other groups consisting of adolescents with normal BMI or with a different BMI diagnosis during the study<sup>10</sup>.

Another study verified that the prevalence of glucose intolerance, hyperinsulinemia, hypertriglyceridemia, arterial hypertension and low HDL levels was significantly higher in severely obese individuals (>2.5-z), when compared to the individuals with moderate obesity, in agreement with the findings of the present study<sup>8</sup>.

Bell et al<sup>35</sup> studied the association between metabolic alterations and z-BMI increase in children aged 6 to 13 years. The regression with BP showed a linear aspect; the regression with TG and HDL showed a curve-shaped aspect, which indicates that the increase in the z-BMI in the upper extremity of the spectrum (> 2 z-BMI) has a higher impact on unfavorable lipid profiles. With this approach, the authors demonstrated that the risk of comorbidities during childhood increases continuously throughout the spectrum, with the increase of z-BMI and markedly so with > 2.0 z-BMI.

The logistic regression model shows a significant association of triglycerides, HDL and BP with the severity of obesity. Studies with populations that tested hypotheses that were similar to the ones in the present study did not develop multiple analysis models, which prevents the comparison of our results.

The presence of obesity seems to have a key-role in triggering of risk factors for the development of CVD and DM2. The parameters most often used to create the group of risk factors for CVD have been: obesity, hypertriglyceridemia, low HDL levels, arterial hypertension and some parameter related to the glycidic profile, in this study, fasting glycemia<sup>14</sup>.

In the present study, the severity of obesity had a positive and statistically significant association with the frequency of these risk factors. Other studies also evaluated the presence of cardiovascular risk factors in obese adolescents and the presence of two or more risk factors that also significantly associate to the degree of obesity<sup>15</sup>.

The concomitant presence of metabolic alterations and obesity was called metabolic syndrome, due to its interrelations and its importance as a risk factor for cardiovascular disease and DM2<sup>36</sup>. Although there has been no consensus to date that defined metabolic syndrome for children and adolescents, studies have demonstrated that the metabolic alterations, when established in childhood, tend to persist at adulthood, in addition to causing early cardiovascular injury<sup>37</sup>.

The group with metabolic syndrome was characterized by the presence of obesity and two more cardiovascular risk factors: high levels of TG, fasting glycemia, BP and low HDL levels. Therefore, 57.7% of the group of adolescents with severe obesity had metabolic syndrome (MS), in comparison with 16.7% of the other group. Another study with Brazilian and Italian obese adolescents, which adopted criteria that

were similar to ours, also verified a higher prevalence of MS in obese adolescents with higher z-BMI and the prevalence increased from 9.5% to 19.7% <sup>16</sup>.

In the study by Weiss et al<sup>8</sup>, which evaluated 439 obese children and adolescents from the USA, the MS components: obesity, BP, TG, fasting glycemia and HDL were established as the group of cardiovascular risk factors. The MS was also characterized by the presence of three or more risk factors (obesity plus two metabolic or clinical risks) and presented higher rates with the increase in the severity of obesity: 38.7% in individuals with moderate obesity and 49.7% in those with severe obesity.

In the study by Sen Y et al<sup>15</sup>, the number of obese adolescents with three or more risk factors increased in parallel with the degree of obesity. The adolescents with BMI > 3 z-BMI had a 2.6-fold higher risk of developing metabolic syndrome than those with BMI between 2 and 3 z-BMI.

Some studies have shown that, regardless of the used criteria, obesity was the most common characteristic of the MS in their populations<sup>14,15</sup> Additionally, they have suggested that obesity should be considered an essential component of the set of cardiovascular risk factors, in order to identify adolescents with a higher risk of developing comorbidities and early cardiovascular disease<sup>14</sup>.

As the BMI is an easy-to-obtain indicator using available equipment in schools, the identification of adolescents with z-BMI >2.0 or >2.5 could be used in screening tests to identify adolescents, aimed at establishing preventive and educational measures.

Due to the complexity of the etiology of obesity and its consequences throughout life, its treatment must occur with the help of a multidisciplinary team, including a physician, nutritionist/dietitian, psychologist and physical educator. Policies and programs promoting a healthy life style are necessary to disseminate the need for healthy diet choices and the practice of physical activity among the children, adolescents and their family members.

In spite of the improvement in the risk estimation precision, the limitations inherent to all cross-sectional studies remain, regarding the difficulties to determine the temporal sequence of the line of causality that was investigated.

#### **Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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#### **Study Association**

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