Relationship between obesity and biochemical markers in Brazilian adolescents

Relação entre obesidade e biomarcadores de risco cardiovascular em adolescentes de escolas públicas do Brasil

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Abstract – The aim of this study was to describe the prevalence of biochemical markers and associate with obesity in Brazilian adolescents enrolled in public schools in a rural area. The sample consisted of 199 adolescents between 10 to 14 years old from Piracicaba, Brazil. The obesity was measured by body mass index (BMI) and according to the World Health Organization curves. We collected blood for biochemical markers analysis (total cholesterol, high density lipoprotein, low density lipoprotein, triacylglycerol, insulin and glycemia). Mann Whitney test was used to compare continuous variables between sexes. Chi-square test was used to compare proportions. To investigate the association between the independent variables and biochemical markers a multiple logistic regression model was performed. Among 199 adolescents, 23.1% was obese and 65.8% were insufficiently active. A high prevalence of dyslipidemia (71.4%) was observed, whereas the low levels of high density lipoprotein (40.7%) were the most prevalent. An association between obesity and undesirable values for high density lipoprotein, triacylglycerol and insulin resistance was found. Obese adolescents were less likely to present a desirable value for high density lipoprotein. It is understood that obesity is detrimental to metabolic profile and should be prevented and treated even in adolescence.

Key words: Adolescents; Dyslipidemia; Obesity; Risk factors.

Resumo – *O objetivo desse estudo foi descrever a prevalência de marcadores bioquímicos e associar com a obesidade em adolescentes brasileiros de escolas públicas. A amostra consistiu de 199 adolescentes, de 10 a 14 anos de idade, da cidade de Piracicaba, Brasil. A obesidade foi medida pelo índice de massa corporal (IMC) de acordo com as curvas da Organização Mundial da Saúde. Coletamos amostra de sangue para analisar os marcadores bioquímicos (colesterol total, lipoproteína de alta densidade, lipoproteína de baixa densidade, triacilglicerol, insulina e glicemia). O teste Mann Whitney foi utilizado para comparar variáveis contínuas entre meninos e meninas. Para comparar proporções, utilizou-se o teste Qui-quadrado. Para investigar a associação entre as variáveis independentes e os marcadores bioquímicos, foi realizada a regressão logística multivariada. Dos 199 adolescentes, 23,1% eram obesos e 65,8% insuficientemente ativos. Uma alta prevalência de dislipidemia (71,4%) foi observada, enquanto baixos níveis de lipoproteína da alta densidade foram os mais prevalentes (40,7%). Uma Associação entre obesidade e valores indesejáveis de lipoproteína de baixa densidade, triacilglicerol, e glicemia foi encontrada. Adolescentes obesos tiveram menor probabilidade de apresentar valores adequados de lipoproteína de alta densidade. Os efeitos deletérios da obesidade no perfil metabólico são sabidos e devem ser prevenidos e tratados durante a adolescência.

Palavras-chave: Adolescentes; Dislipidemia; Fatores de risco; Obesidade.*

INTRODUCTION

Childhood obesity is an increasing problem worldwide[1]. In Brazil, over-weight and obesity prevalence in adolescents reached around 30% in 2009[2], with an important contribution of low income level group[3,4]. Among the many consequences, longitudinal studies has showed that higher body mass index (BMI) in childhood are associated with a greater risk of cardiovascular disease (CVD) in adulthood[5,6]. Consequently, CVD are one of the leading causes of death in adults, with a trend to commit younger people in developing countries[7].

In addition, unhealthy biochemical profile has showed to be independent associated with CVD[8]. Dyslipedemia, impaired glucose tolerance, insulinemia, hypertension, and vascular abnormalities are considered important surrogate markers for future CVD[9]. Despite the health importance, Brazilian school/based surveillance system has not assessed those biochemical markers.

Giving the increasing number of childhood obesity in Brazil, it is critical to incorporate biochemical markers in school/based surveillance in order to assess a robust data for estimation of current CVD risk. Furthermore, considering Brazil as a large, complex and diverse country[10], only few cities in Brazil have collected data about this issue in a pediatric Brazilian population. Therefore, the objective of this study is to describe the prevalence of biochemical markers and associate with obesity in Brazilian adolescents enrolled in public schools.

METHODOLOGICAL PROCEDURES

Participants

This work is part of the study entitled "Factors affecting the risk of obesity in adolescents from public schools in Piracicaba: a cross-sectional study as a first step of a cohort study" funded by FAPESP (Grant #2006/61085-0, São Paulo Research Foundation).

In the present study, adolescents older than 10 years, from both sexes enrolled in the fifth grade of elementary school, attending public schools in different regions of Piracicaba, São Paulo were included in our cross-sectional study.

Exclusions were base on current medicine use that could change the biochemical markers profile, students aged less than 10 years old or incomplete measures data. To calculate the sample size it was considered the universe of 45 public schools with 5th grade classes, distributed in six regions of the city, including rural area. Five random drawings of schools within each region were performed, considering the prevalence of over-weight/obesity between 20% and 32%, type I error of 5% and type II error of 10%[11]. Between the 45 public schools, 26 were selected to our study. The second stage of sampling consisted of the random draw of students within each school. The random draw was performed in a systematic manner with

a random start, determining the student and his/her substitutes. Considering a remission rate of 20%, 488 students were calculated to the final simple size. However, between 488 students, only 210 presented the signed informed consent form specific for blood collection. Finally, 11 students that did not presented complete anthropometric and demographic measures. Thus 199 adolescents between 10 to 14 years were included in our sample.

The data were collected from six previous trained students (Nutrition and Physical Education) between March and November 2009.

Biochemical markers and Anthropometric measures

Body mass was obtained in electronic scale, platform type, brand Tanita® with 150 kg capacity and 100 gram accuracy. Students were wearing light clothing and were barefoot. Height was measured with the aid of a rigid stadiometer, with scale in millimeters, brand Alturaexata®. From these measurements it was possible to calculate the body mass index (BMI) and classify adolescents as to their nutritional state, using the new growth curves of the World Health Organization[12].

Blood was collected after 12 hours of fasting. The biochemical collection was performed in an accredited laboratory in Piracicaba - SP. The fasting glucose, total cholesterol (TC), triglyceride (TG) and HDL (high density lipoprotein) were measured by automated enzymatic method. The LDL (low density lipoprotein) was obtained using FRIELDWALD calculation[13]. We collected one tube of five milliliters with yellow cap (no anticoagulant with separating gel) to measure the concentrations of serum TC and fractions, TG and insulin, and a one tube of five milliliters with gray cap (containing fluoride) for glycemia. Blood glucose was analyzed by colorimetric enzymatic method. For the classification of serum glucose concentration, we used the Standards of Medical Care in Diabetes reference, issued by the American Diabetes Association (ADA)[14].

To obtain the levels of insulin, a dosage was performed using the Radioimmunoassay (RIA) method. The insulin resistance (IR) assessment was performed using the HOMA (Homeostatic Model Assessment) method. Through this method we calculated the index (HOMA - IR) that aims to translate the insulin sensitivity[15].

Dyslipidemia was classified according to the Brazilian Cardiology Society[15]: $TC \geq 170$ mg/dL; $LDL \geq 130$ mg/dL; $HDL < 45$ mg/dL; $TG \geq 130$ mg/dL. And according to the ADA, blood glucose ≥ 126 was considered diabetes.

According to the Brazilian Cardiology Society[15] were considered increased values: $TC > 150$ mg/dL, $LDL > 100$ mg/dL, $TG > 100$ mg/dL, $TC/HDL > 3.5$, insulinemia > 20 μU/I and HOMA-IR > 3.16. For HDL, values lower than 45 mg/dL were considered below the desired. And according to the ADA, blood glucose ≥ 100 mg/dL was considered above normal.

The study was approved by the School of Public Health's Ethics Committee from University of São Paulo (FSP-USP) under protocol #1633. The research was conducted within the ethical standards required by the Declaration of Helsinki (1964) and in accordance with Resolution 196/96 of the Ministry of Health.

Covariates

The sexual maturation was performed through self-assessment of the stage of puberty, according to Tanner's worksheet[16].

Dietary intake was assessed through the application of computerized Simplified Food Frequency Questionnaire for Adolescents[17]. To calculate energy density (kcal/g) we used a method based on all solid foods and beverages containing calories[18].

The physical activity (PA) level was assessed using the Physical Activity Questionnaire for Adolescents Computerized Version[19]. We collected Information on type of PA, frequency and duration of weekly sports practice, physical exercise and PA for displacement. The score result was used as a dichotomous variable categorized as insufficiently active and active, with a cutoff of 300 minutes of weekly physical activities[20].

Statistical Analysis

In descriptive analysis, continuous variables are present in mean, median and standard deviations, while in categorical variables frequencies, percentage and 95% CI confident interval were used. The Kolmogorov-Smirnov test was used to test the distribution normality. We compared age, BMI, lipoproteins, lipids, blood glucose, insulin, TC/HDL and HOMA-IR between boys and girls using the Mann-Whitney test. We constructed multiple logistic regression models to examine association between the biochemical markers and obesity. The adjustment variables (PA, sexual maturation, energy density and sex) were inserted within the models through the "stepwise forward" procedure or because they were epidemiologically relevant to the study context. For all the statistical analyzes of interest, we established a significance level of 5%. The statistical analysis was performed with Statistical Package for the Social Sciences (SPSS, 2000), version 13.0.

RESULTS

From an initial sample of 488 students, only 40,8% (n=199) were included in our study. Between those students, 57% were girls, 21.1% overweight, and 23.1% obese (data not shown).

Table 1 shows girls were younger, and present higher levels of TG, insulinemia, and HOMA than with boys. In regards to age, although there is a statistically significant difference, values are very similar when compared among sexes.

In Table 2, shows the prevalence of dyslipidemia, increased level of glycemia (diabetes) and insulin, according to sex. Girls presented higher prevalences of CT/HDL, insulinemia and HOMA-IR when compared with boys (p<0.05).

In the crude analysis, obesity was associated only with low HDL levels. When potential confounders where included into the analysis, obese adolescents were more likely to present undesirable values of HDL, LDL, TG and insulin resistance when compared to non-obese adolescents .

Table 1. General characteristics of Brazilian adolescents from public schools, Piracicaba, 2009.

Variables	General n=199		Boys n=85		Girls n=114		p value*
	Mean(DP)	Mediana	Media(DP)	Mediana	Media(DP)	Mediana	
Age (years)	11.0 (0.7)	11.0	11.1 (0.8)	11.0	10.9 (0.6)	11.0	0.013
BMI	19.9 (4.6)	19.0	19.3 (4.1)	18.8	20.3 (5.0)	19.4	0.192
TC (mg/dL)	154.3 (28.6)	152.0	154.5 (31.1)	154.0	154.2 (26.8)	150.5	0.760
LDL (mg/dL)	89.0 (24.3)	87.0	90.1 (27.3)	90.0	88.2 (21.9)	85.0	0.489
HDL (mg/dL)	48.7 (11.1)	48.0	49.8 (11.0)	49.0	47.9 (11.1)	45.0	0.149
TC/HDL (mg/dL)	3.3 (0.8)	3.1	3.2 (0.9)	3.0	3.3 (0.8)	3.2	0.128
TG (mg/dL)	83.0 (45.1)	73.0	73.3 (43.3)	63.0	90.3 (45.2)	79.0	0.001
Glycemia (mg/dL)	90.0 (7.7)	90.0	90.7 (9.7)	90.0	89.6 (5.9)	89.0	0.474
Insulinemia (µU/l)	11.1 (11.2)	8.0	8.8 (11.1)	6.0	12.8 (11.1)	10.0	<0.001
HOMA-IR	2.5 (2.6)	1.8	2.0 (2.5)	1.3	2.9 (2.6)	2.8	<0.001

*Mann Whitney test; BMI- body mass índex; TC- total Cholesterol LDL – Low density Lipoprotein; HDL – High Density Lipoprotein; TG- triacylglycerol; HOMA-IR- Homeostasis model assessment of insulin resistance.

Table 2. Dyslipidemia, insulinemia and increased level of glycemia in adolescents from public schools, according to sex. Piracicaba, 2009.

Variables	General	Boys	Girls	p value[a]
	n(%)	n(%)	N(%)	
TC ≥170 mg/dL	55 (27.6)	25(12.6)	30 (15.1)	0,372
LDL ≥130 mg/dL	10 (5.0)	4 (2.0)	6 (3.0)	0,565
HDL-c <45 mg/dL	81(40.7)	29(14.6)	52 (26.1)	0,068
TG ≥100 mg/dL	22 (11.1)	7 (3.5)	15 (7.5)	0,194
TC/HDL >3.5	70 (35.2)	23 (27.1)	47 (41.2)	0,027
Glycemia ≥126 mg/dL	2 (1.0)	2 (1.0)	0 (0.0)	0,188
Insulinemia >20 µU/l	29 (14.6)	6 (3.0)	23 (11.6)	0,007
HOMA-IR >3.16	49 (24.6)	14 (16.5)	35 (30.7)	0,015

a Chi-square test; TC- total Cholesterol LDL – Low density Lipoprotein; HDL – High Density Lipoprotein; TG- triacylglycerol; HOMA-IR- Homeostasis model assessment of insulin resistance.

Table 3. Logistic regression to analyze the association between obesity and biochemical markers* in Brazilian adolescents from public schools. Piracicaba, 2009.

Variáveis	Crude Analysis	Adjusted Analysis
	Odds (IC 95%)	Odds (IC 95%)
CT >150 mg/dL		
No Obesity	1	1
Obesity	1,50 (0,76-2,93)	1,63 (0,82-3,25)
LDL >100 mg/dL		
No Obesity	1	1
Obesity	1,86 (0,94-3,69)	2,08 (1,02-4,22)
HDL <45 mg/dL		
No Obesity	1	1
Obesity	5,55 (2,68-11,49)	5,87 (2,72-12,67)
TG >100 mg/dL		
No Obesity	1	1
Obesity	3,59 (1,75-7,34)	3,34 (1,60-6,95)
Glicemia>100 mg/dL		
No Obesity	1	1
Obesity	1,02 (0,27-4,94)	1,78 (0,50-6,37)
HOMA-IR		
Menos ativo	1	1
Mais ativo	11,34 (5,30-24,28)	12,68 (5,61-28,65)

*Adjusted by: sex (male or female), sexual maturation (prepubertal or pubertal), physical activities (METs/min), and Energy density (kcal/g). TC- total Cholesterol LDL – Low density Lipoprotein; HDL – High Density Lipoprotein; TG- triacylglycerol; HOMA-IR- Homeostasis model assessment of insulin resistance.

DISCUSSION

Our study described the prevalence of biochemical markers and associate with obesity in Brazilian adolescents enrolled in public schools. We have found a high prevalence of undesirable biochemical markers values and overweight/obesity in our sample, especially in girls. In addition, obese adolescents are more likely to present undesirable biochemical markers values than non-obese.

Following the global tendency[1], the prevalence of obesity is increasing exponentially in Brazil[2-4]. In 2009, a overweight/obesity reached an epidemic proportion with about 30% of the adolescent population[2]. Our results corroborate with those findings once overweight/obesity reached 44.2% in our population.

In summary increased BMI was positively associated with unfavorable biomarkers, such as LDL, HDL and TG. Similar association between obesity and biochemical markers has been showed in multiple populations worldwide[9,21-22]. Although our study did not found a relationship between obesity and blood glucose levels, insulin resistance (HOMA-IR) was higher in obese individuals. Those results corroborate with a higher risk of developing type II diabetes in obese individuals presented in the literature[23,24]. In a large multiethnic, multiracial cohort of children and adolescents showed that obesity increased the risk of metabolic syndrome components[9]. In addition, obesity was associated with an increased C-reactive protein and decreased adiponectin levels in children and adolescents[9].

Given the importance of studies on biochemical markers in individuals at the beginning of adolescence in Brazil, the results of this study represent an important contribution a national scenario and can be used to policy markers. The mean values of lipids profile observed in this study are similar to those found in individuals aged 7 to 14 years old from Campinas/SP, which showed average TC, TG, LDL and HDL equal to 160, 79, 96 and 49 mg/dL, respectively[25].

Hypercholesterolemia prevalence (27.6%) in Piracicaba was higher than cities like Florianopolis/SC (22%)[26] and Itapetininga/SP (8,5%)[27].

HDL lower than 45mg/dL presented alarming results (40.7%). Other studies in Brazil has also showed a high prevalence (56.7%) of this type of dyslipidemia[21]. These results are worrying because HDL is an important CVD protective by removing cholesterol from peripheral tissues, avoiding atherosclerosis[24]. Our analysis showed that those undesirable HDL values may be explained mainly by low physical activity level (data not shown). Although the present study did not present significant prevalence of increased LDL, it is advisable to report that this lipoprotein is the main risk factor for DCV[28]; furthermore, there are LDL subfractions, such as small dense LDL, is more atherogenic by its ease of penetrating the vessel wall and being easily oxidizable[27]. Thus, even individuals with appropriate values for this lipoprotein may present high risk for CVD due to the type of LDL and not by its the amount.

Despite undesirable glucose and insulin values did not showed an increased prevalence, these indicators can vary significantly during the life course. It can be explained in part by sexual maturation[26]. However, monitoring the glucose and insulin levels in adolescence is critical, because those values tend to persist in the adulthood[27]. Moreover, elevated blood glucose levels and insulinemia found in our study, may indicate the presence of diabetes mellitus which is an important risk factor for cardiovascular disease[28]. In our study, childhood obesity was associated with HOMA-IR, which indicated an insulin resistance.

Therefore, our findings highlight the needed of including biochemical markers in the Brazilian National School-Based Adolescent Health Survey (PeNSE). This procedure would enhance the surveillance system in Brazil allowing an accurate metabolic health status in a national representative sample.

Our study was limited by its lower response rate (40.8%) that assigned the informed consent to biochemical markers analysis than were calculated initially. In this sense, our sample size may not be truly representative of general population in Piracicaba. We have not evaluated other measures of obesity such as waist circumference in the association with biochemical markers, which could provide a better characterization of body fat distribution than BMI. Strengths of this study is due to multiple biochemical markers assessment.

In an attempt to tackle obesity and metabolic unhealthy in Brazil, the Brazilian National Ministry of Health and Education has been implementing in 2007 the *Programa Saúde na Escola*. The program has the goal of promoting health and providing the school community a powerful weapon against vulnerabilities that compromise the development of children, adolescents and young Brazilians[29]. In addition, future representative studies should consider more cut points in BMI in order to identify possible differences in the association with biochemical markers.

In conclusion, overweight/obesity presented a high prevalence in Piracicaba. In addition, our data indicate an extremely high prevalence undesirable biochemical markers. Obesity was positively associated with unfavorable values of LDL, HDL, HOMA-IR and TG in Brazilian adolescents. Those results should be used to elaborate and put into practice policies in the areas of public health, education, socio-economic development, transport, sport and leisure aimed to tackle obesity and maintain a healthy metabolic profile.

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