Body Mass Index Has a Good Correlation with Proatherosclerotic Profile in Children and Adolescents

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Summary

Background: More recently, the association of different risk factors has been described as the metabolic syndrome. Different definitions are being used for the same syndrome. Regardless of the name or classification, it has been well established that a cardiovascular cluster including overweight/obesity, increased blood pressure, and lipid and glucose abnormalities are associated with an increased risk of atherosclerosis in adults.

Objective: The aim of this study was to correlate body mass index percentiles with blood pressure, insulin resistance index, and lipid profiles in children and adolescents, which characterize a proatherosclerotic profile.

Methods: Cardiovascular risk factor clusters were evaluated in 118 children and adolescents divided according to body mass index percentile (BMIP) quartiles: Q1 (n=23) with BMIP <50%, Q2 (n=30) with BMIP between 50 and 85%, Q3 (n=31) with BMIP between 85 and 93%, and Q4 (n=34) with the BMIP > 93%. Statistically significant differences were not observed for age (F=2.1; p=0.10); sex (chi-square test=3.0; p=0.38), and ethnicity (chi-square test=4.7; p=0.20) between different quartiles.

Results: A statistically significant difference was observed for systolic BP (F=15.4; p<0.0001), diastolic BP (F=9.5; p<0.0001), glycemia (F=9.6; p<0.0001), insulin (F=12.9; p<0.0001), HOMAir (F=30.8; p<0.0001), and triglyceride levels (F=2.7; p=0.05) between the different quartiles.

Conclusion: Excess weight evaluated by BMIP was associated with increased blood pressure, triglycerides, HOMAir index, and low HDL-cholesterol, a proatherosclerotic profile in children and adolescents.

Key Words: Body mass índex; child; adolescent; risk factors.

Abbreviations

BMIP - body mass index percentile

BP – blood pressure

HDL – high-density lipoprotein

HOMA-ir - homeostasis model assessment of insulin resistance

LDL – low-density lipoprotein

MS – metabolic syndrome

Introduction

According to the World Health Organization[1], obesity is assuming epidemic proportions all over the world and is considered a chronic pediatric disease, more dangerous than malnutrition, as it is associated with a large number of comorbidities. The problems associated with obesity include psychosocial problems (low self-esteem, affecting academic ability and relationships), social problems (prejudice), and culminate in the association of central obesity, insulin resistance, hypertension, and dyslipidemia, which characterize a cluster of cardiovascular risk factors also called metabolic syndrome (MS). Metabolic syndrome is associated with an increased chance of atherosclerotic disease, steatohepatitis, gallstones found in sedentary subjects with overnutrition and genetic predisposition[2]. The prevalence of this situation is increasing in children and adolescents, and type 2 diabetes is appearing in this population more frequently[3]. There are other clinical situations associated with this cardiovascular risk factor cluster that require attention: sleep apnea related to pulmonary hypertension, left ventricle hypertrophy, brain pseudotumor, and orthopedic disturbances[4]. Scientific evidence has revealed that high blood pressure and atherosclerosis begin in early childhood, when physical activity and food intake habits start[5].

This study describes the impact of excess weight, evaluated by body mass index percentile, and provides the results of blood pressure levels, insulin resistance index, and lipid

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Manuscript received on 08/20/08; revised manuscript received on 10/02/08; accepted on 10/21/08.

profile in children and adolescents considered to be clinically normal.

Our hypothesis is that the increase in the body mass index percentile will result in a higher probability of clustering of cardiovascular risk factors, regardless of age and clinical features.

Patients

This is a clinical controlled trial (transversal analytic study) that correlates the body mass index percentile (BMIP) with the cardiovascular and biochemical profile in a population of children and adolescents recruited sequentially between January and November 2005 from cardio-pediatric, endocrinology outpatient centers and private offices. A total of 118 subjects was included in the study. They were divided into quartiles according to their body mass index percentile: Q1 (n = 23) with BMIP <50%; Q2 (n=30) with BMIP between 50 and 85%; Q3 (n=31) with BMIP between 85 and 93%, and finally Q4 (n=34) with BMIP >93%. Clinical characteristics of the population are shown in Table 1.

Methods

All the anthropometric measurements were performed early in the morning, and the volunteers were fasting: a) Weight was measured with a digital Tech Line scale, model Tec 10L (Techline Asia, China). All the subjects wore light clothing, were barefoot, and were in an orthostatic position. b) Height was measured in a stadiometer fixed in the vertical position. Subjects were in the orthostatic position, barefoot, with feet together and bottom and shoulders touching the vertical axis of the stadiometer. They kept the arms close to the body, and the measurement was taken at the end of expiration. Weight and height were registered according to Tanner[6] curves. c) Body mass index (BMI) or Quetelet index = weight (kg) divided by height (m^2) was calculated. Because this was a population of children and adolescents, the BMI percentile was used according to the National Center for Health Statistics[7] and applied to divide them into different quartiles.

Blood pressure (BP) was measured according to the protocol recommended by the Update on the Task Force Report (1987) on High Blood Pressure in Children and Adolescents: A Working Group Report from the High Blood Pressure Education Program[8]. A calibrated mercury sphygmomanometer with appropriate-sized cuff was used. Subjects were in a sitting position for at least 10 minutes in a resting condition. Phase I of Korotkoff was adopted to define the systolic blood pressure and phase V of Korotkoff for diastolic blood pressure. There was a 2-minute interval between the measurements. Subjects were instructed not to take coffee, tea, nonsteroidal anti-inflammatory drugs, corticosteroids, or nasal vasoconstrictors for 12 hours before the blood pressure measurements. The mean of 3 consecutive measures was used. For both sexes, blood pressure was corrected according to height percentile.

For the biochemical evaluation, blood samples were drawn after a 12-hour fasting period. Blood plasma was separated and stored at -10°C in a freezer. Triglycerides were measured using the enzymatic Trinder-reagent Lab test – colorimetric method (commercial kit). HDL-cholesterol was measured with the COD-ANA Labtest Cat – 60 method (commercial kit). Fasting blood glucose was measured by the enzymatic colorimetric - Glucox 500/glucose oxidase (Selectra II, Brazil). Insulin was measured by the chemilumminescence method using an Immulite 2000 machine (DPC, USA). Fasting glucose and insulin were used to calculate the homeostasis model of assessment of insulin resistance (HOMA-ir) (glucose mg/dL x insulin μU/mL/22.5)[9]. The parents or a legal representative of all study patients signed a written informed consent. The Ethics Committee of the Federal University of Sergipe, Brazil, approved this research.

Statistical analysis

The SPSS package version 13.0 (SPSS, Chicago, IL) was used for the statistical analysis. Non-numeric data are summarized in proportions, with the respective confidence intervals of 95%. Numeric data are shown as means and standard deviations. Nominal variables are shown as frequencies. The normal distribution was tested by the Shapiro-Wilks test. Analysis of variance (ANOVA) was used to analyze the variation of variables associated with metabolic syndrome according to body mass index percentile. One-way ANOVA was used to compare different quartiles of the body mass index percentile; Bonferroni (equal variance) and Tamhne (different variance) were used as posttests. The trend analysis and evaluation for linear, cubic, and quadratic trends for different factors in each quartile was measured by the polynomial method. $P<0.05$ was adopted as statistically significant.

Table 1 - Population characteristics.

	Q1 (n=23)	Q2 (n=30)	Q3 (n=31)	Q4 (n=34)
BMIP (%)	<50	50 - 85	85 - 93	>93
Age, years	12.0±4.3	10.6±3.4	11.9±2.9	12.5±2.1
Sex (male/female)	11/12	19/11	15/16	22/12
Race (White/ Nonwhite)	13/10	22/8	17/14	16/18

Results

The population did not differ regarding mean age ($F=2.1$; $p=0.10$); sex distribution (chi-square test=3.04; $p=0.38$), and ethnicity (chi-square test=4.7; $p=0.20$) between the different quartiles (Table 1).

There was a statistically significant difference for systolic BP between different quartiles ($F=15.4$; $p<0.0001$): Q4 *versus* Q1 (32.8±4.1; $p<0.0001$); Q4 *versus* Q2 (23.0±4.0; $p<0.0001$); Q3 *versus* Q1 (13.5±3.9; $p=0.002$); Q3 *versus* Q2 (12.2±4.0; $p=0.02$). There was no difference between Q1 and Q2 (Figure 1). A statistically significant difference was observed for diastolic BP between quartiles ($F=9.5$; $p<0.0001$): Q4 *versus* Q1 (12.9±2.7; $p<0.01$); Q4 *versus* Q2 (10.8±2.5; $p<0.0002$) and Q4 *versus* Q3 (7.0±2.5; $p=0.04$) (Figure 2).

Regarding carbohydrate metabolism, a statistically significant difference was observed between the different quartiles for glycemia (F=9.6; p<0.0001); insulin (F=12.9; p<0.0001), and HOMA-ir (F=30.8; p<0.0001). For glycemia, a difference was observed between quartiles: Q4 *versus* Q1 (12.2±2.6; p<0.001); Q4 *versus* Q2 (10.3±2.4; p=0.0002), and Q4 *versus* Q3 (7.2±2.4; p=0.02) (Figure 3). A statistically significant difference was observed for insulin between quartiles: Q4 *versus* Q1 (7.4±1.4; p<0.0001); Q4 *versus* Q2 (6.9±1.4; p<0.0001); Q3 *versus* Q1 (3.5±1.1; p=0.01), and Q3 *versus* Q2 (3.0±1.1; p=0.01) (Figure 4). HOMA-ir differed significantly between quartiles: Q4 *versus* Q1 (46.3±6.0; p<0.0001); Q4 *versus* Q2 (45.6±6.0; p<0.0001); Q4 *versus* Q3 (21.5±7.2; p=0.02); Q3 *versus* Q1 (24.8±3.9; p<0.0001) and Q3 *versus* Q2 (24.2±3.9; p<0.0001) (Figure 5).

A statistically significant difference was observed for lipid profiles between the quartiles: Q4 *versus* Q1 (38.6±13.3; p=0.03) and for triglycerides (F=2.7; p=0.05) (Figure 6). A reduction in HDL-cholesterol levels was observed between quartiles; however, the difference was not statistically significant (F=1.9; p=0.14) (Figure 7).

An analysis for trends was performed and a linear and significant increase was observed for systolic BP (F=39.3; p<0.0001); diastolic blood pressure (F=24.7; p<0.0001); glycemia (F=26.5; p<0.0001); insulin (F=32.5; p<0.0001); triglycerides (F=7.9; p=0.006), and HDL-cholesterol (F=5.3; p=0.03), between the quartiles. A trend was also observed in the quadratic variation for HOMA-ir (F=6.5; p=0.01), between the quartiles.

Discussion

There have been several studies related to cardiovascular risk factors in adults. However, few studies have been related to the cluster of cardiovascular risk factors in children and adolescents. Among the studies that have addressed the associated cardiovascular risk factors in children and adolescents are the Bogalusa Heart Study[10], the Muscatine Study[11], and the PDAY[12]. These studies have shown the association between multiple risk factors and atherosclerosis in children and young adults. In our study, we observed the association between the body mass index percentile and a cluster of cardiovascular risk factors, such as increased blood pressure, low HDL-cholesterol, increased triglyceride levels, increase in glucose and insulin levels, as well as insulin resistance, evaluated by the HOMA-ir index in children and adolescents. It is well known that this cluster of cardiovascular risk factors that appear early in life will persist and worsen if primary prevention is not precociously adopted. Consequently, this cluster of cardiovascular risk factors will result in cardiovascular morbidity and mortality in young adults.

Anthropometry is considered a useful method to track excess weight, as it is not expensive and is universally applicable. The anthropometric indexes are obtained from 2 or more basic combinations (weight, sex, age, and height)[1]. Body mass index is calculated according to weight and height and is largely used and accepted to identify overweight and obese subjects. But the use of BMI in children and adolescents

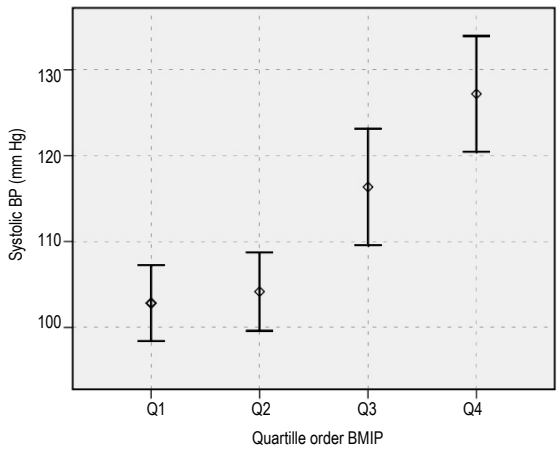

Figure 1 - Mean systolic blood pressure (95% CI) by quartille order among children and adolescents. BP indicates blood pressure. BMIP indicates body mass index percentiles.

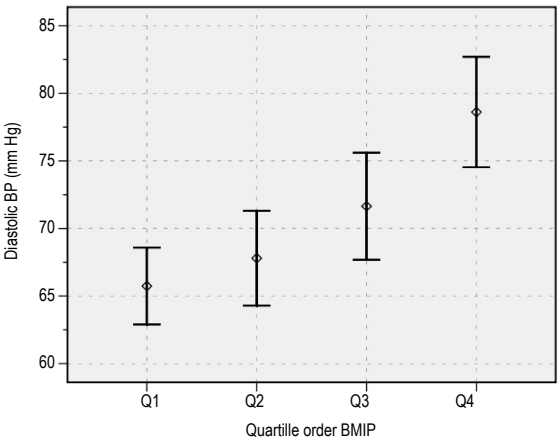

Figure 2 - Mean diastolic blood pressure (95% CI) by quartille order among children and adolescents. BP indicates blood pressure. BMIP indicates body mass index percentiles

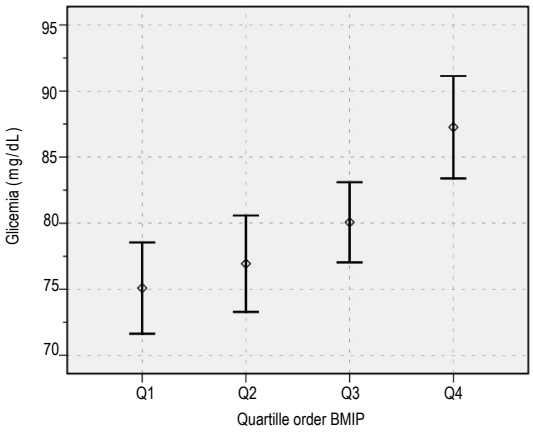

Figure 3 - Mean glicemia (95% CI) by quartille order among children and adolescents. BMIP indicates body mass index percentiles.

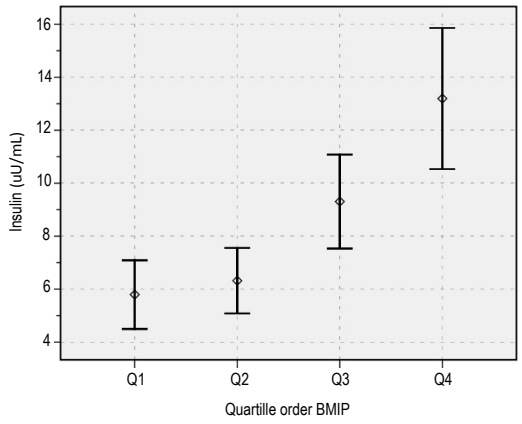

Figure 4 - Mean insulin (95% CI) by quartille order among children and adolescents. BMIP indicates body mass index percentiles.

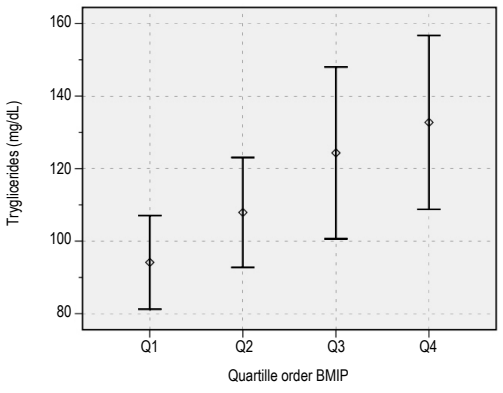

Figure 6 - Mean tryglicerides (95% CI) by quartille order among children and adolescents. BMIP indicates body mass index percentiles.

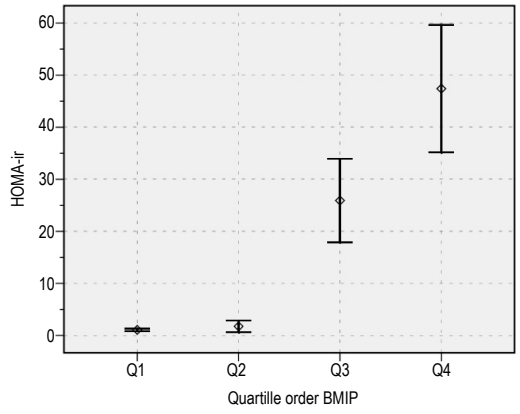

Figure 5 - Mean HOMA-ir (95% CI) by quartille order among children and adolescents. BMIP indicatesbody mass index percentiles

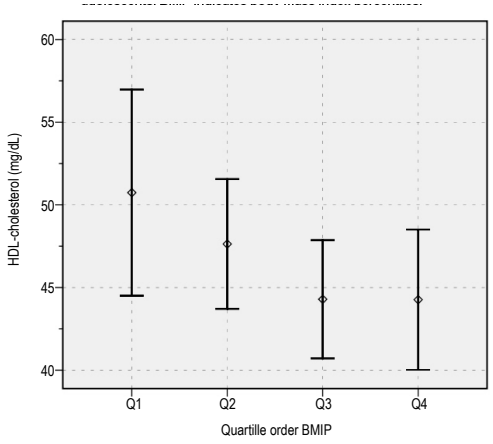

Figure 7 - Mean HDL-cholesterol (95% CI) by quartille order among children and adolescents. BMIP indicates body mass index percentiles

started after the study by Must et al[13], which reported reference values for percentiles according to age and sex, and those are currently considered as reference values by the World Health Organization. According to this study, subjects with BMI percentiles ≥85 and <95 are considered overweight, and subjects with BMI percentile ≥95 are considered obese. Although body mass index has been used to characterize obesity in children and adolescence, it has limitations. One limitation pointed out by Luukkaa et al[14] is that BMI does not discriminate lean mass from fat mass, and does not permit the separation of subjects with increased muscle mass from those with increased fat mass. However, even the low quartile (Q1) of the distribution of subscapular skinfold, when compared to upper quartile (Q4) is related to increased risk of elevated total cholesterol (TC) levels in children and adolescents[15]. Currently, it is important to know not just the fat mass, but also the fat distribution. Regarding the fat distribution, Fujioka et al[16] showed that abdominal fat is associated with a high risk of morbidity and mortality, mainly from cardiovascular disease. Lapidus et al[17] demonstrated that increased abdominal fat is associated with increased plasma insulin levels (hyperinsulinemia), and increased plasma insulin levels are predictive of future hypertension and dyslipidemia. In another study[18], the authors concluded that abdominal fat is an important predictor of an increase in triglycerides, a decrease in HDL-cholesterol, and an increase in left ventricular mass in children and adolescents. It is well known that systolic BP increases progressively from 1 year of age until adolescence and that diastolic BP increases after 5 to 6 years of age, proportionally to systolic BP. In young children, secondary hypertension is more frequent, and after 10 years of age, mainly in adolescents, the primary form of hypertension is more often observed[19]. In a review related to hypertension in obese children[20], 3 possible mechanisms have been discussed: autonomic function imbalance (hyperactivity of the sympathetic nervous system and/or an imbalance between the sympathetic and the parasympathetic nervous systems); insulin resistance; and abnormalities in vascular structure and function (decrease in vascular compliance). Possibly, the interaction among these different mechanisms

might result in hypertension in obese children and adolescents. Therefore, as demonstrated in the Rio de Janeiro study, early blood pressure level is a mark of familial aggregation of metabolic cardiovascular risk factors[21]. Even though the present study did not use central obesity or specifically the fat mass to classify the population of children and adolescents, blood pressure increased progressively with the increase in the body mass index percentile, strengthening the importance of the relation between obesity or the increase in body mass and hypertension. We can speculate that increased sympathetic activity, insulin resistance, and vascular abnormalities, cited as plausible mechanisms for hypertension in obese people, are related to the appearance of cardiovascular risk factor clusters, observed in the metabolic syndrome.

Becque et al[22] evaluated the incidence of risk factors for coronary artery disease in obese adolescents and showed that 80% had systolic hypertension, diastolic hypertension, or both. They also showed that 97% of this population had 4 or more clustered risk factors (hypertriglyceridemia, low HDL-cholesterol, hypercholesterolemia, and hypertension). Our population of children and adolescents had a significant association of increase in body mass index percentile with increased blood pressure and also with increased triglycerides, and decreased HDL-cholesterol. The HDL-cholesterol is a protective factor and has an inverse relation to cardiovascular risk as shown by Barter and Rye[23]. These authors showed an increase in 2 to 3% in cardiovascular risk for each 1% reduction in HDL-cholesterol level. They also showed that the lipid profile related to insulin resistance is low HDL-cholesterol, frequently associated with hypertriglyceridemia and increased low-density LDL-cholesterol particles (considered atherogenic). According to Weiss et al[24], there is a positive association between obesity and dyslipidemia in children and adolescents. A prevalence of dyslipidemia of up to 50% was found in children with body mass index percentile over 99. In this study, the authors used excess weight to classify the lipid profile. One possible mechanism to explain this association is the activation of AMP-dependent kinase that is induced by the increase in insulin and leptin and the reduction in adiponectin levels. Adiponectin, alone, increases fatty acid oxidation. Adiponectin also has a positive association with insulin sensitivity, HDL-cholesterol, and a negative association with triglyceride levels. On the other hand, dyslipidemia in infants can be associated with obesity in adult life, especially in females. Hyperinsulinemia is indicated as a possible common causal mechanism for metabolic abnormalities, including hypertriglyceridemia, low HDL-cholesterol, increased blood pressure, and type 2 diabetes. Sinha et al[25] found a high prevalence of glucose intolerance in obese children: 25% of 55 obese children between 4 and 10 years old and in 21% of 112 obese adolescents between 11 and 18 years old. In our study, we found a positive association between the increase in the body mass index percentile and increase in HOMA-ir, an insulin resistance index that commonly points toward hyperinsulinemia and consequently to hypertriglyceridemia, low HDL-cholesterol, and increased blood pressure, also found in the highest body mass index percentile in our population. Study limitation: the study population was selected among subjects who came to the clinic for medical check-ups and therefore, it is not necessarily a representative sample of the general population of the same age group.

In conclusion, this study characterized a proatherosclerotic profile in children and adolescents according to excess weight, although in the absence of cardiovascular symptoms.

Acknowledgments

The authors would like to thank the Heart Institute (InCor), University of São Paulo Medical School, Prof. José Antonio Franchini Ramires and Prof. Eduardo Moacyr Krieger for their support in developing this study.

What is already known about this topic:

- It is already known that abdominal fat and sedentary lifestyle are related to insulin resistance.

- Although diagnostic criteria for metabolic syndrome are already known, they are unclear even for adults. The best criteria are: Abdominal circumference, BMI, hip/abdominal circumference ratio?

- BMI and insulin resistance are associated with increased CVD risk in adolescents.

What this study adds:

- To the best of our knowledge, no study had analyzed the metabolic syndrome features in children and adolescents, including different anthropometric measurements.

- Our data were analyzed according to quartiles, suggesting an increase in the number of metabolic syndrome features according to the increase in BMI percentile.

- All metabolic syndrome components showed the same tendency according to the increase in the BMI percentiles, showing a good correlation between these components and the BMI percentile.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of Doctoral submitted by Geodete Batista Costa, from Instituto do Coração, Universidade Federal de Sergipe, Unidade Cardiotorácica de Sergipe.

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