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Association between nutritional status, C-reactive protein, adiponectin and HOMA-AD in Brazilian children

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Abstract

Introduction: In children, the presence of obesity is a major risk factor for the occurrence of cardiovascular diseases on the adulthood.

Objective: To evaluate the association of anthropometry, body composition, clinical variables and biochemical profile with C-reactive protein and adiponectin levels, and insulin resistance in children in the municipality of Nova Era, Brazil.

Methods: Nested case-control study following a cross-sectional study. We evaluated 178 children, 57 of them classified as obese and 121 as normal-weight from a population of 1024 schoolchildren 6 to 10 years old: Blood samples were collected after 12-hour fast to obtain serum and plasma. We collected anthropometric and body composition measures, systolic and diastolic blood pressure data. Sexual maturation was assessed according to the stage of sexual development. We performed Student's t-test, Mann-Whitney U test, Pearson's correlation, Spearman's test and multiple linear regression analysis. Independent variables with $p < 0.05$ were included in the multiple regression model. Residual analysis was performed to assess model validity.

Results: Among obese children, C-reactive protein levels were associated with triacylglycerol levels and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 27.6%, $p < 0.001$). Adiponectin was associated with HOMA-IR, HOMA-AD and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 75.5%, $p < 0.001$). HOMA-AD index was associated with HOMA-IR, adiponectin, systolic blood pressure and weight ($R^2_{adjusted}$ = 90.7%, $p < 0.001$).

Conclusion: Significant associations were found between body composition, anthropometry, clinical variables, biochemical profile and adiponectin and C-reactive protein levels and insulin resistance in obese and normal-weight children.

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Key words: *Inflammation. Child. Insulin resistance. Obesity. Biological markers.*

ASOCIACIÓN ENTRE ESTADO NUTRICIONAL, PROTEÍNA C REACTIVA, ADIPONECTINA Y HOMA-AD EN NIÑOS BRASILEÑOS

Resumen

Introducción: En niños, la obesidad es um factor de riesgo para enfermedades cardiovasculares en la edad adulta.

Objetivos: Asociaciar la antropometría, composición corporal, variables clínicas y bioquímicas con la proteína C reactiva (PCR), adiponectina y resistencia a la insulina en niños de Nova Era, Brasil.

Métodos: Estudio de casos y controles anidado en un transversal. Se evaluaron 178 niños, 57 obesos y 121 eutróficos en una población de 1.024 escolares de 6 a 10 años. Las muestras de sangre se recogieron después de 12 horas de ayuno. Recogimos las medidas antropométricas, de composición corporal y presión arterial. La madurez sexual fue evaluada de acuerdo con el desarrollo sexual. Se realizo las pruebas t de Student y U de Mann-Whitney, las correlaciones de Pearson y Spearman y el análisis de regresión lineal múltiple. Se incluyeron en el modelo de regresión, las variables independientes con $p < 0,05$. Se realizo el análisis residual para evaluar la validez del modelo.

Resultados: Entre los niños obesos, los niveles de PCR se asociaron con los triglicéridos y el porcentaje de grasa corporal (%GC) estimada por los pliegues cutáneos ($R^2_{ajustado}$ = 27,6%, $p < 0,001$). La adiponectina se asoció con HOMA-IR, HOMA-AD y % GC estimada por los pliegues cutáneos ($R^2_{ajustado}$ = 75,5%, $p < 0,001$). El HOMA-AD se asoció con HOMA-IR, adiponectina, presión arterial sistólica y peso ($R^2_{ajustado}$ = 90,7%, $p < 0,001$).

Conclusiones: Se encontraron asociaciones entre la composición corporal, antropometría, variables clínicas, perfil bioquímico, adiponectina, PCR y la resistencia a la insulina en niños obesos y eutróficos.

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Palabras clave: *Inflamación. Niño. Resistencia a la insulina. Obesidad. Marcadores biológicos.*

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Abbreviations

BF: Body Fat.
BIA: Bioelectrical Impedance Analysis.
BMI: Body Mass Index.
BP: Blood Pressure.
C INDEX: Conicity Index.
CRP: C-Reactive Protein.
DP: Standard Deviation.
HDL-C: High-Density Lipoprotein Cholesterol.
HOMA-AD: Homeostatic Model Assessment-Adiponectin.
HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.
IL-1: Interleukin 1.
IL-10: Interleukin10.
IL-6: Interleukin 6.
LDL-C: Low-Density Lipoprotein Cholesterol.
MUAC: Mid-Upper Arm Circumference.
ND: Not Detected.
SBP: Systolic Blood Pressure.
SST: Subscapular Skinfold Thickness.
TBIA: Tetrapolar Bioelectrical Impedance.
TC: Total Cholesterol.
TFM: Trunk Fat Mass.
TNF-α: Tumor Necrosis Fator-alpha
TST: Triceps Skinfold Thickness.
VIF: Variance Inflation Factor.
WC: Waist Circumference.

Introduction

Obesity is a chronic multifactorial and complex disease, a low-grade chronic inflammatory state resulting from altered secretion of cytokines, chemokines and hormones[1]. Studies show that prevalence of overweight and obesity in children has increased significantly in many countries, including Brazil[2].

Importantly, excess body fat is a possible risk marker for cardiovascular disease, metabolic syndrome, insulin resistance, and dyslipidemia. It is noteworthy that atherosclerotic process arising from the combination of endothelial dysfunction and inflammation may begin with the development of fatty streaks in childhood[3].

It is essential to analyze obesity as an inflammatory state, as research proves its direct association with markers of angiogenesis and inflammation even in children and adolescents[4].

Thus, studies associate measures of adiposity and biochemical profile with cytokines that modulate the inflammatory state, such as IL-1, IL-6, IL-10, TNF-α, C-reactive protein (CRP), leptin, resistin and adiponectin even in apparently healthy individuals[5]. CRP, an acute phase protein produced primarily in hepatocytes, has been used in clinical and epidemiological studies as inflammation marker and risk factor for acute myocardial infarction, ischemic stroke, and death from various cancers and pulmonary diseases[6,7].

Even a low-grade inflammatory process is probably related to CRP levels in overweight or obese children[8].

Among adipokines, adiponectin stands out as one of the most abundant hormones secreted by adipocytes, and its expression decreases as adipose tissue increases. In addition, adiponectin levels are inversely proportional to insulin resistance, type 2 diabetes, cardiovascular diseases, hypertension, atherosclerosis and triglycerides, and directly proportional to HDL cholesterol levels[9].

Adiponectin has antiatherogenic, anti-inflammatory and insulin sensitizer properties. Thus, this hormone protects vascular endothelium against processes involved in the pathogenesis of atherosclerosis and diabetes[10]. In addition, hypoadiponectinemia may be considered an independent biomarker of metabolic syndrome and atherosclerosis even in overweight young people[11].

As nutritional status is correlated with inflammatory markers, studies indicate that weight reduction in children can decrease CRP and increase adiponectin levels[12].

Since insulin resistance plays a major role in obesity complications, it should also be investigated for being associated with central adiposity, lipid profile and blood pressure in various age groups[13].

From the assumptions mentioned above, this study evaluated associations of body composition, anthropometry, clinical and biochemical variables with adiponectin and C-reactive protein levels and insulin resistance in children aged 6 to 10 years old.

Materials and methods

Study design and subjects

In 2009 we conducted a nested case-control study following a cross-sectional study with 1024 children aged 6 to 10 years old from public municipal schools in Nova Era, state of Minas Gerais, Brazil. In the first stage of the study we found a prevalence of 2.3% underweight, 11.2% overweight and 6.4% obesity by calculating z-score of body mass index for age (BMI-for age)[14] (fig. 1).

In the second stage we selected two normal-weight children (n = 130) for each obese child (n = 65) making a total sample of 195 students.

Children with acute, chronic, degenerative diseases, changes in the gastrointestinal tract (e.g. diarrhea), weight loss in the past six months, under special diets, medication that alters metabolism or affects inflammation pathways, showing values of C-reactive protein above 10 mg/L and elite athletes were excluded from the study. Finally we included 57 obese and 121 normal-weight children in the sample.

The study followed the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Federal University of Ouro Preto (2007/93).

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C-reactive protein, adiponectin
nd HOMA-AD in Brazilian children

Nutr Hosp. 2014;30(1):66-74

67

Consent was written and signed in duplicate by those responsible.

Anthropometry and blood pressure

Students were instructed not to perform intense workouts before anthropometry and body composition assessment, to attend school with light clothing, not to ingest large volume of water in the 24 hours before the tests, and be fasting for at least 4 hours. All measurements were performed on the right side of the students' bodies.

Weight (Tanita® BC554 Ironman, Illinois, USA) and height (Alturexata®, Belo Horizonte, Brazil) were measured and body mass index (BMI) was calculated by dividing weight by the square of height. Circumferences were measured with a tape measure to the nearest 0.1 cm. Mid-upper arm circumference (MUAC) was measured in duplicate at the midpoint between the acromion process of the scapula and the olecranon. Waist circumference (WC) was measured in triplicate at the midpoint between the anterior superior iliac crest and the last rib, then we calculated the Conicity index (C index)[15].

$$\text{Conicity index} = \frac{\text{Waist circumference (m)}}{0.109\sqrt{\dfrac{\text{Weight (kg)}}{\text{Height (m)}}}}$$

We also measured triceps skinfold thickness (TST) and subscapular skinfold thickness (SST) using a Cescorf® skinfold caliper (Cescorf Equipamentos Ltda, Porto Alegre, Brazil) in triplicate and not consecutively. TST was measured at the midpoint between acromion and olecranon on the posterior arm, and SST on the 45° diagonal line formed by the skinfold, 2 cm below the inferior angle of the scapula. Trunk fat mass (TFM) was obtained with the formula TFM = SST (mm)/TST (mm)[16].

Blood pressure (BP) was measured by oscillometry and Doppler ultrasound with Omron® HEM 705 CP and Doppler DV 610. The procedure was performed three times at 2-minute intervals and after a 5-minute rest period before the first blood pressure measurement. Values were replaced by averages.

Body Composition Assessment

Body fat percentage (% BF) was assessed by bipolar bioelectrical impedance analysis (bipolar BIA) using a Tanita® BC554 scale with body fat rate 0.1% and tetrapolar bioelectrical impedance (TBIA) using the Bioscan Maltron® BF-916. We also used an equation to predict body fat percentage by summing triceps and subscapular skinfolds (Body fat from skinfold)[17].

Biochemical Assessment

After a 12-hour fast, 10 mL blood was collected from the median cubital vein into disposable tubes, then fractionated in vials either containing sodium fluoride for glucose analysis or no anticoagulant for assessing total cholesterol and its fractions.

Samples were processed using an Excelsa Baby® 206-2 centrifuge (FANEM, São Paulo, Brazil). After centrifugation, serum was aliquoted into three amber microtubes and stored at -80°C for later analysis.

Blood glucose was measured by the enzymatic-colorimetric method and insulin by chemiluminescence. Levels of triglycerides and total cholesterol (TC) were determined in an CM 200 analyzer (WIENER LAB, Rosario, Argentina) by the enzymatic colorimetric method using Triglycerides Liquicolor mono and Cholesterol Liquicolor test kits (Human do Brazil, Itabira, Brazil). High-density lipoprotein cholesterol (HDL-C) was measured by the enzymatic colorimetric direct HDL-PP method (Analisa, Gold Analisa Diagnóstica Ltda, Belo Horizonte, Brazil) and levels of Low-density lipoprotein cholesterol (LDL-C) were calculated using the Friedewald equation. Subsequently, the atherogenic index was obtained by dividing Total cholesterol by HDL-C[18].

Levels of C-reactive protein were assessed with an Immage® 800 analyzer (Beckman Coulter, Fullerton, California, USA) by nephelometry with a detection limit of 0.1 mg/dL. Adiponectin levels were measured by the sandwich ELISA method in a Human Adiponectin ELISA kit (Liconplex Kit, EZHADP-61K, Linco Research - St Charles Missouri-USA).

Subsequently, we calculated the homeostatic model assessment for insulin resistance (HOMA-IR) from the equation HOMA-IR = (fasting insulin (μUI/mL) × fasting glucose (mmol/mL)/22.5).[19] Homeostatic model assessment-adiponectin (HOMA-AD) was obtained by using the formula HOMA-AD = insulinemia (mU/L) × glicemia (mg/dL)/adiponectina (μg/mL).[20]

Pubertal development

Development stages of the children's pubic hair were analyzed, based on the stages proposed by Tanner. Students were classified as prepubertal (stage 1), pubertal (stages 2, 3 and 4) and postpubertal (stage 5).

Statistical analysis

Identification of probability distributions is relevant, as depending on the distribution that best fits the data set choices concerning which inferential procedures will be applied may vary. In this study the Anderson-Darling test was employed. This test examines whether a data sample comes from a population with specific distributions. For the present study, tests were conduc-

ted to verify whether the data came from a normally distributed population. A normal distribution was obtained for the samples, whereas for others it was not. Variables were presented as mean ± standard deviation for the samples with normal distribution and median and interquartile range for samples was not. For comparison between groups were performed T-tests and Wilcoxon-Mann-Whitney a test fitting non-parametric data. For this study an α-level of 0.05 was used across all statistical tests.

As dependent variable we consider the concentrations of CRP, adiponectin and HOMA-AD. Tests were performed Pearson correlation and Spearman, to verify the associations between each of the independent variables and the dependent. Multiple linear regression models were estimated, and the independent variables that showed p-value less than 0.05 were considered significant, which were the "biological plausibility" and "epidemiological relevance"[21].

Analyses of waste each model in order to check the validity of the assumptions of normality, homoscedasticity and independence between observations. The statistics "Cook's distance" and "Variance Inflation Factor (VIF)", were used to identify outliers and verification of possible multicollinearity of the independent variables. For statistical analyzes we used the statistical software R. 2.13.1.

Results

We evaluated a sample of 178 children, 104 females (58.4%) and 74 males (41.6%). Comparing the two groups of obese and normal-weight children, there were no statistical differences between medians of age, HDL-C, adiponectin, and systolic blood pressure (SBP Omron). However, obese children had significantly higher mean and median values of the other variables compared to normal-weight group (table I).

Table I
Demographic, anthropometric, body composition, biochemical and clinical characteristics of schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	All (n = 178)	Normal (n = 121)	Obese (n = 57)	p-value
Age (years)	8.0 (7.0-9.0)[b]	8.0 (7.0-9.0)[b]	8.0 (7.0-9.0)[b]	0.618
Weight (kg)	29.80 (25.40-37.30)[b]	27.7 (24.0-30.6)[b]	40.9 (36.1-48.3)[b]	**<0.001**
Height (cm)	132.2 ± 9.68[a]	130.83 ± 9.52[a]	135.98 ± 9.45[a]	**0.006**
MUAC (cm)	20.05 (18.5-23.92)[b]	19.3 (18.0-20.2)[b]	25.7 (24.05-27.65)[b]	**<0.001**
Waist circumference (cm)	60.52 (56.98-71.5)[b]	58.4 (55.7-61.0)[b]	76.5 (70.87-83.0)[b]	**<0.001**
Triceps skinfold (mm)	10.20 (7.77-17.57)[b]	8.63 (7.13-10.56)[b]	21.13 (16.23-24.11)[b]	**<0.001**
Subscapular skinfold (mm)	7.43 (5.68-16.57)[b]	6.03 (5.23-7.6)[b]	19.46 (12.83-24.86)[b]	**<0.001**
BF from skinfolds (%)	16.41 (13.02-27.46)[b]	14.22 (11.96-17.33)[b]	32.08 (27.11-36.94)[b]	**<0.001**
BF bipolar (%)	19.25 (16.67-29.77)[b]	17.61 (15.2-19.7)[b]	32.67 (30.4-35.00)[b]	**<0.001**
BF tetrapolar (%)	19.24 (15.35-26.63)[b]	16.79 (13.89-20.67)[b]	29.45 (23.80-32.24)[b]	**<0.001**
BF tetrapolar (kg)	5.47 (3.86-9.38)[b]	4.24 (3.40-5.83)[b]	12.34 (8.58-15.58)[b]	**<0.001**
BMI (kg/m²)	16.55 (15.4-20.75)[b]	15.7 (15.1-16.6)[b]	22.4 (21.05-25.25)[b]	**<0.001**
Conicity index	1.19 (1.16-1.24)[b]	1.17 (1.14-1.20)[b]	1.26 (1.22-1.29)[b]	**<0.001**
Trunk adiposity index	0.79 (0.67-0.90)[b]	0.76 (0.65-0.84)[b]	0.92 (0.77-1.06)[b]	**<0.001**
Fasting glucose (mg/dL)	84.33 ± 7.42[a]	83.48 ± 7.45[a]	86.14 ± 7.08[a]	**0.002**
Fasting insulin (µU/mL)	5.42 (3.85-7.81)[b]	4.72 (3.25-6.42)[b]	7.61 (5.34-13.13)[b]	**<0.001**
Total cholesterol (mg/dL)	152.26 ± 28.96[a]	147.75 ± 27.08[a]	161.84 ± 30.68[a]	**0.004**
HDL cholesterol (mg/dL)	56.0 (49.0-65.0)[b]	57.0 (50.0-66.0)[b]	54.0 (48.0-64.0)[b]	0.159
LDL cholesterol (mg/dL)	78.84 ± 23.94[a]	74.82 ± 23.00[a]	87.38 ± 23.86[a]	**0.001**
Triacylgcerols (mg/dL)	69.5 (53.0-108.25)[b]	63.0 (48.5-99.0)[b]	94.0 (65.0-118.5)[b]	**<0.001**
Atherogenic index	2.69 ± 0.53[a]	2.58 ± 0.50[a]	2.94 ± 0.49[a]	**<0.001**
C-reactive protein (mg/dL)	ND (ND-0.172)[b]	ND (ND-0.051)[b]	0.148 (ND-0.449)[b]	**<0.001**
Adiponectin (µg/mL)	26.75 (18.95-38.28)[b]	26.89 (18.23- 39.66)[b]	26.30 (19.74-35.11)[b]	0.471
HOMA-IR index	1.14 (0.83-1.68)[b]	0.96 (0.69-1.32)[b]	1.64 (1.13-2.76)[b]	**<0.001**
HOMA-AD index	16.97 (9.95-29.83)[b]	14.01 (8.42-24.21)[b]	25.21 (16.37-51.0)[b]	**<0.001**
Systolic BP Dopller (mmHg)	94.84 (89.25-103.33)[b]	92.67 (87.33-98.34)[b]	103.33 (94.84-111.67)[b]	**<0.001**
Systolic BP Omron (mmHg)	102 (96.59-112.0)[b]	102.0 (96.33-107.84)[b]	104.50 (98.67-114.67)[b]	0.097
Diastolic BP Omron (mmHg)	58.00 (54.67-62.54)[b]	58.0 (53.83-60.0)[b]	62.0 (56.0-68.50)[b]	**<0.001**

a: Values presented as mean ± standard deviation. b: Values presented as median and interquartile range. T-tests and Test of Mann-Whitney U significant with p-value less than 0.05.
Abbreviations used: MUAC: Mid-upper arm circumference, BF: body fat, BMI: body mass index, HDL: high-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-AD: homeostatic model assessment-adiponectin. BP: blood pressure, ND: not detected.

Sexual maturation assessment based on pubic hair growth 55% of children diagnosed with obesity were prepubescent, 43.3% pubescent and 1.7% postpubescent. Regarding normal-weight children, 66.9% were classified as prepubertal and 33.1% as pubescent. No statistical differences were found between degree of sexual maturation between obese and normal-weight groups (data not shown).

We performed Pearson's correlation and Spearman's correlation tests with independent variables. CRP and adiponectin levels and HOMA-AD index are shown in table II.

Transformations were performed on dependent variables for constructing the final multiple regression model. These changes were necessary to ensure that residual assumptions were met.

Among normal-weight children, variables associated with CRP levels were blood glucose, age, arm circumference, HDL-C and weight ($R^2_{adjusted}$ = 16.1%, p < 0.001), whereas in the group of obese children associations occurred with body fat percentage estimated by skinfold thickness and triacylglycerol levels ($R^2_{adjusted}$ = 27.6%, p < 0.001) (table III).

In normal-weight children, adiponectin was associated with HOMA-AD (log) HOMA-IR and height ($R^2_{adjusted}$ = 87.4%, p < 0.001), whereas in obese children adiponectin levels were associated with HOMA-IR, HOMA-AD (log) and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 75.5%, p < 0.001) (table IV).

HOMA-AD was associated with adiponectin and waist circumference ($R^2_{adjusted}$ = 55.5%, p < 0.001) in normal-weight children. Among obese children, associated independent variables were HOMA-IR, adiponectin, systolic blood pressure (Doppler) and weight ($R^2_{adjusted}$ = 90.7%, p < 0.001) (table V).

Discussion

In this study, body composition, anthropometry, biochemical and clinical profiles of normal-weight and obese children were associated with adiponectin, C-reactive protein levels and HOMA-AD.

As noted, CRP levels were associated with blood glucose levels, age, arm circumference, HDL-C, and weight in normal-weight children ($R^2_{adjusted}$ = 16.1%, p < 0.001). Among obese children, association was found with triacylglycerol levels and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 27.6%, p < 0.001) thus highlighting the role of adipose tissue in subclinical inflammation.

Progressive increases in body adiposity may result in cellular hypoxia, adipocyte death by necrosis or apoptosis, and increased secretion of cytokines and proinflammatory chemokines, which favors states of insulin resistance. High levels of insulin and blood glucose increase free fatty acid levels, which are associated with high levels of triglycerides and low HDL-C levels[22].

CRP has been used in studies with different age groups as a marker of inflammatory processes. In a 2004 study with children and adolescents, Lambert et al. showed that BMI and insulin levels were the main determinants of altered CRP levels. In addition, individuals with the highest quartile of CRP levels had 1.4, 1.7, and 2.3 times higher chance of having high systolic blood pressure, high triglycerides, and low HDL-C levels compared with those with levels below the 75th percentile[23].

A study of obese and normal-weight adolescents found a positive association between CRP levels and obesity. Along with the sum of skinfolds, the z-score of BMI explained 42.1% of variation in protein levels[24].

Furthermore, another cross-sectional study showed relationship between adipose tissue and inflammation in children and adolescents. Overweight and obese individuals had lower HDL-C and higher triglycerides, CRP, and insulin levels. Thus, the authors concluded that overweight and obese adolescents had higher prevalence of cardiovascular risk factors shown by early signs of atherosclerosis[25].

In the present study, we found no statistical difference in adiponectin levels between obese and normal-weight groups. This result can also be explained by the low number of postpubertal children since this stage has significant influence on adiponectin levels, which decrease with sexual maturation[26].

However, adiponectin was associated with HOMA-AD, HOMA-IR and height in normal-weight children ($R^2_{adjusted}$ = 87.4%, p < 0.001) and HOMA-AD, HOMA-IR and body fat percentage estimated by skinfold thickness in obese children ($R^2_{adjusted}$ = 75.5%, p < 0.001).

Through intracellular signaling pathways, adiponectin promotes activation of glucose transport, fatty acid oxidation in muscles, and inhibition of liver gluconeogenesis, which decreases blood glucose levels thus reducing insulin[27]. In addition, adiponectin inhibits the expression of cell adhesion molecules, scavenger receptors, and inflammatory proteins such as TNFα, IL-6 and IL-1[28].

A cross-sectional study evaluated obese and overweight children. The authors found that HOMA-IR index, age, and HDL-C were associated with adiponectin levels[29]. When comparing obese children and adolescents, and their respective controls, Panagopoulou et al in 2008 found that gender and body fat percentage measured by tetrapolar bioimpedance were important determinants of adiponectin levels[30].

Reinehr et al. in 2004 evaluated influence of age, gender, puberty, weight loss, and adiponectin levels. The authors concluded that adiponectin levels in obese children were negatively correlated with age, body fat, and insulin resistance, and decreased at puberty. Conversely, significant weight loss increased adiponectin levels and improved insulin resistance[10].

In our study, HOMA-AD was associated with adiponectin and waist circumference among normal-weight children ($R^2_{adjusted}$ = 55.5%, p < 0.001) and with

Table II

Correlation between concentrations of C-reactive protein, adiponectin and HOMA-AD with anthropometric, body composition, biochemical, clinical and demographic in children aged 6 to 10 years of city of Nova Era, Mina Gerais, Brazil, 2009

	CRP (mg/dL)			Adiponectin (µg/mL)			HOMA-AD		
	All	Normal	Obese	All	Normal	Obese	All	Normal	Obese
	r	r	r	r	r	r	r	r	r
Age (years)	0.149	0.207*	0.111	-0.089	-0.060	-0.137	0.198*	0.287*	0.186
Weight (kg)	0.375*	0.081	0.425*	-0.127	-0.021	-0.391*	0.474*	0.345*	0.436*
Height (cm)	0.120	0.057	0.060	-0.146	-0.540	-0.331*	0.244*	0.160	0.281*
MUAC (cm)	0.432*	0.174	0.428*	-0.151*	-0.110	-0.397*	0.465*	0.339*	0.417*
Waist circumference (cm)	0.423*	0.121	0.469*	-0.104	-0.025	-0.349*	0.434*	0.256*	0.442*
Triceps skinfold (mm)	0.419*	0.140	0.422*	-0.055	-0.085	-0.365*	0.372*	0.118	0.466*
Subscapular skinfold (mm)	0.441*	0.204*	0.445*	-0.096	-0.004	-0.409*	0.410*	0.198*	0.510*
BF from skinfolds (%)	0.432*	0.169	0.483*	-0.065	0.074	-0.393*	0.384*	0.136	0.508*
BF bipolar (%)	0.380*	0.052	0.272*	-0.066	0.024	-0.322*	0.379*	0.158	0.351*
BF tetrapolar (%)	0.387*	0.094	0.381*	-0.042	0.083	-0.339*	0.373*	0.170	0.393*
BF tetrapolar (kg)	0.407*	0.112	0.426*	-0.081	0.028	-0.392*	0.453*	0.313*	0.453*
BMI (kg/m²)	0.399*	0.069	0.489*	-0.107	-0.050	-0.362*	0.428*	0.244*	0.468*
Conicity index	0.362*	0.028	0.310*	-0.040	0.077	-0.216	0.253*	-0.049	0.310*
Trunk adiposity index	0.294*	0.107	0.215	-0.115	-0.077	-0.199	0.241*	0.080	0.270*
Fasting glucose (mg/dL)	0.177*	0.211*	0.092	0.031	0.006	0.156	0.036	-0.001	-0.011
Fasting insulin (µU/mL)	0.221*	-0.011	0.241	-0.107	-0.097	-0.052	0.779*	0.738*	0.770*
Total cholesterol (mg/dL)	0.006	-0.122	-0.066	-0.119	-0.109	-0.094	0.168*	0.117	0.123
HDL cholesterol (mg/dL)	-0.203*	-0.180*	-0.124	-0.097	-0.158	-0.022	0.028	0.188*	-0.172
LDL cholesterol (mg/dL)	0.076	-0.100	0.054	-0.125	-0.111	-0.157	0.108	0.091	0.075
Triacylgicerols (mg/dL)	0.127	0.111	-0.196	0.117	0.247*	-0.157	0.140	-0.004	0.209
Atherogenic index	0.142	0.033	0.039	-0.042	0.039	-0.156	0.090	-0.056	0.123
C-reactive protein (µg/mL)	–	–	–	0.049	0.096	0.033	0.147*	-0.049	0.141
Adiponectin (µg/mL)	0.049	0.096	0.033	–	–	–	-0.651*	-0.691*	-0.610*
HOMA-IR index	0.244*	0.016	0.248	-0.112	-0.102	-0.037	0.787*	0.749*	0.758*
HOMA-AD index	0.147*	-0.049	0.141	-0.651	-0.691*	-0.610*	–	–	–
Systolic BP Dopller (mmHg)	0.268*	0.031	0.269*	0.047	0.181*	-0.284*	0.157*	-0.068	-0.068
Systolic BP Omron (mmHg)	0.007	-0.040	0.162	0.062	0.139	-0.103	0.046	-0.050	-0.050
Diastolic BP Omron (mmHg)	0.185*	0.006	0.194	-0.051	-0.038	-0.061	0.140	0.107	0.107

Abbreviations used: MUAC: Mid-upper arm circumference, BF: body fat, BMI: body mass index, HDL: high-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, CRP: C-reactive protein, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-AD: homeostatic model assessment-adiponectin. BP: blood pressure, Obese (n = 57), Normal (n = 121). *Significant correlations with p-value less than 0.05.

Table III
Multiple linear regression analysis of the association between concentrations of C-reactive protein (mg/dL) and demographic, anthropometric, body composition and biochemical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	Normal (n = 121)	
	$\beta \pm SE$	p-value
Constant	-1.1652 ± 0.3616	**0.002***
Glucose (mg/dL)	0.005771 ± 0.002731	**0.037***
Age (years)	0.06287 ± 0.02192	**0.005***
MUAC (cm)	0.07001 ± 0.02164	**0.002***
HDL-c (mg/dL)	-0.004973 ± 0.001803	**0.007***
Weight (kg)	-0.027750 ± 0.008352	**0.001***
	Obese (n = 57)	
	$\beta \pm SE$	p-value
Constant	-0.1416 ± 0.1355	0.301
BF from skinfolds (%)	0.018483 ± 0.003871	**<0.001***
Triacylglycerols (mg/dL)	-0.0022375 ± 0.0009861	**0.027***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: MUAC: Mid-upper arm circumference, HDL-c: high-density lipoprotein cholesterol, BF: body fat. $R^2_{adjusted}$ Normal = 16.1%; $R^2_{adjusted}$ Obese = 27.6%. *p< 0.001, α of 0.05.

Table IV
Multiple linear regression analysis of the association between concentrations of Adiponectin (µg/mL) and anthropometric, body composition and biochemical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	Normal (n = 121)**	
	$\beta \pm SE$	p-value
Constant	1.8895 ± 0.1023	**<0.001***
HOMA-AD (log)	-0.90026 ± 0.03171	**<0.001***
HOMA-IR	0.32761 ± 0.01962	**<0.001***
Height (cm)	0.0017363 ± 0.0008174	**0.036***
	Obese (n = 57)	
	$\beta \pm SE$	p-value
Constant	74.052 ± 3.885	**<0.001***
HOMA-IR	9.0229 ± 0.9629	**<0.001***
HOMA-AD (log)	-39.459 ± 3.645	**<0.001***
BF from skinfolds (%)	-0.24045 ± 0.09465	**0.014***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: HOMA-IR: homeostatic model assessment for insulin, HOMA-AD: homeostatic model assessment-adiponectin, BF: body fat. $R^2_{adjusted}$ Normal = 87.4 %; $R^2_{adjusted}$ Obese = 75.5%; *p< 0.05, α of 0.05 **Log adiponectin.

Table V
*Multiple linear regression analysis of the association between HOMA-AD** and anthropometric, biochemical and clinical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009*

	Normal (n = 121)	
	$\beta \pm SE$	p-value
Constant	0.5095 ± 0.2408	**0.037***
Adiponectin (µg/mL)	-0.016429 ± 0.001497	**<0.001***
WC (cm)	0.019297 ± 0.003984	**<0.001***
	Obese (n = 57)	
	$\beta \pm SE$	p-value
Constant	1.3413 ± 0.1513	**<0.001***
HOMA-IR	0.21589 ± 0.01268	**<0.001***
Adiponectin (µg/mL)	-0.018188 ± 0.001350	**<0.001***
Systolic BP Dopller (mmHg)	0.003466 ± 0.001366	**0.014***
Weight (kg)	-0.004666 ± 0.001485	**0.003***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: HOMA-IR: WC: Waist circumference, homeostatic model assessment for insulin, BP: blood pressure. $R^2_{adjusted}$ Normal = 55.5 %; $R^2_{adjusted}$ Obese = 90.7%; *p< 0.05, α of 0.05 **LogHOMA-AD.

HOMA-IR, adiponectin, systolic blood pressure, and weight in obese children ($R^2_{adjusted}$ = 90.7%, p < 0.001).

Few published studies have used HOMA-AD to assess insulin resistance. However, Makni et al. in 2012 found a significant correlation between HOMA-AD and waist circumference, blood glucose, HDL-C, and blood pressure in obese Tunisian children[31].

We emphasized the association of waist circumference with HOMA-AD in normal-weight children. Abdominal obesity, assessed in our study by measuring waist circumference, is associated with visceral fat accumulation, insulin resistance, elevated blood glucose, dyslipidemia, and hypertension[32].

Adiponectin levels are inversely proportional to body fat, and low levels promote lower glucose oxidation and increased activation of hormone-sensitive lipase[33].

Regarding blood pressure, adiponectin increases nitric oxide production by activating endothelial nitric oxide synthase. Moreover, low adiponectin levels reduce nitric oxide production and vasoconstriction. Also, high insulin levels stimulate endothelin, a powerful vasoconstrictor[9].

The present study has some limitations. Our sample consists of children aged 6 to 10 years from a specific municipality, which limits generalizability of results outside this population. In addition, the study design allowed associations to be determined, but not cause-effect results. Therefore, longitudinal studies are needed.
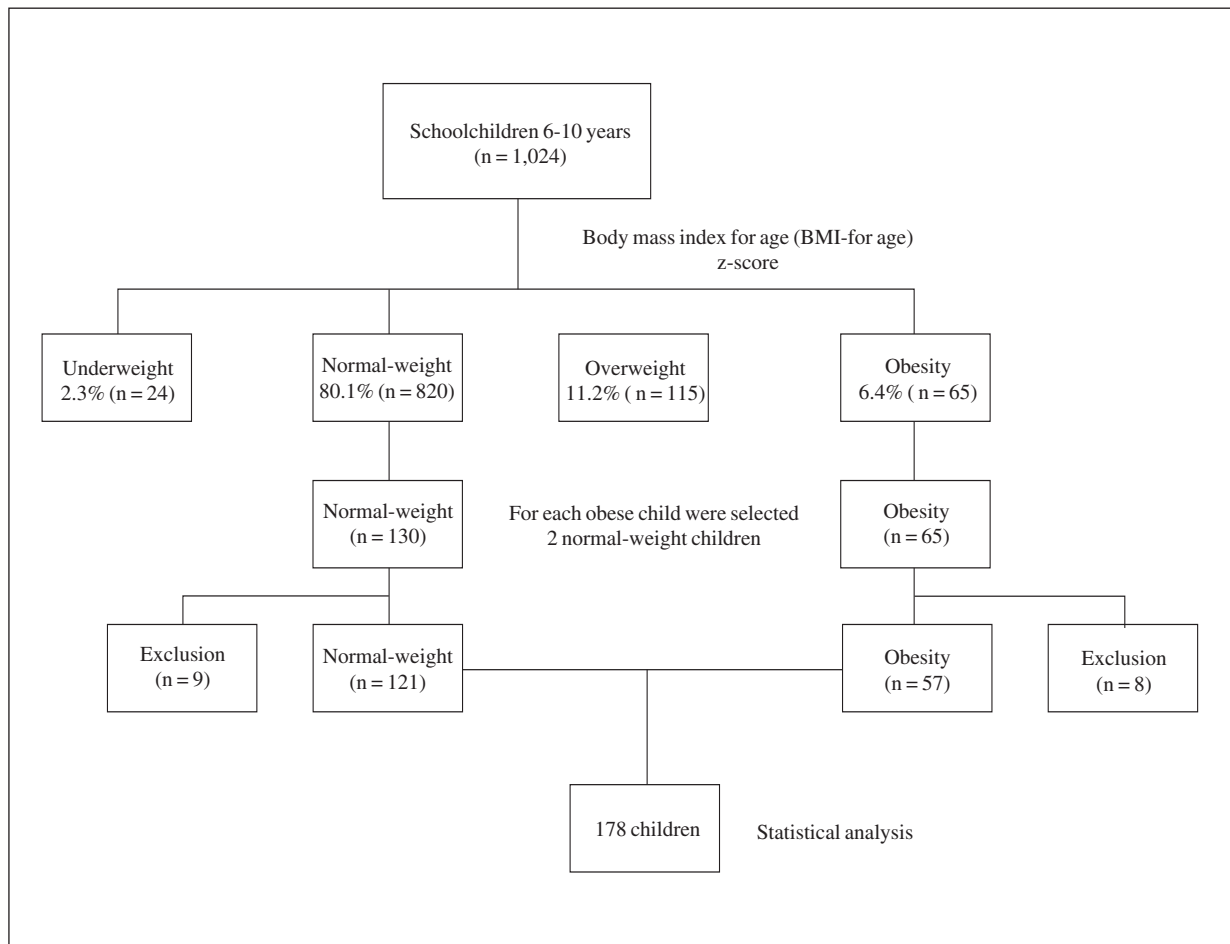
Fig. 1.—Structure of the sample selection for the study in Nova Era 2009.

We chose to use self-assessment of sexual maturation without consulting a qualified professional. However, a study by Matsudo & Matsudo has shown moderate to high concordance between the projective technique (Tanner stages) and physician assessment of sexual characteristics[34].

Finally, using BMI as a reference method for assessing child obesity at nutritional screening is also a possible limitation of this study. However, several studies have recommended this index as a good tool to predict body adiposity[35,36].

Conclusions

In conclusion, our study indicates a significant association of anthropometry, body composition, clinical and biochemical variables with adiponectin and C-reactive protein levels and insulin resistance, as assessed by HOMA-AD in obese and normal-weight children. Thus, we emphasize the importance of early identification of risk factors for cardiometabolic diseases for promoting early intervention and improved quality of life in this population.

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Association between nutritional status,
C-reactive protein, adiponectin
nd HOMA-AD in Brazilian children

Nutr Hosp. 2014;30(1):66-74

73

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