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Association of *IL-6* and *CRP* gene polymorphisms with obesity and metabolic disorders in children and adolescents

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ABSTRACT

Activation of adipose tissue inflammation is associated with obesity caused by lipid accumulation in adipocytes. Through this activation, proinflammatory cytokines, such as Interleukin-6 (IL-6) and C-reactive protein (CRP) seem to influence metabolic disorders. The present study evaluated whether polymorphisms in the *CRP* (rs1205) and *IL-6* (rs1800795, rs2069845) genes are associated with the development of metabolic disorders in children and adolescents. A cross-sectional study was performed, consisting of 470 students from the municipality of Santa Cruz do Sul, Brazil, aged 7-17 years. Body mass index (BMI) was classified according to overweight and obesity. Genotyping was performed by real-time *Polymerase Chain Reaction* (PCR). Anthropometric characteristics, biochemical markers, immunological markers and blood pressure were assessed. Descriptive statistics, chi-square and logistic regression were used for the analyses. No association was detected between the rs1800795 polymorphism and the assessed variables. Individuals with the risk genotype in the rs1205 gene were associated with the risk of developing hypercholesterolemia (OR 2.79; CI 1.40, 5.57; $p = 0.003$). Carriers of the risk genotype in the rs2069845 gene are associated with the risk of developing obesity (OR 3.07; CI 1.08, 8.72; $p = 0.03$). The polymorphism rs2069845 was associated with obesity and rs1205 was associated with the risk of developing hypercholesterolemia in Brazilian schoolchildren.

Key words: Inflammation, obesity, polymorphisms, risk, schoolchildren.

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INTRODUCTION

The increase in size and number of adipose cells is associated with obesity, which leads to metabolic disorders (Greenberg and Obin 2006). Childhood obesity that persists into adolescence results in physiological and pathological effects that increase morbidity and mortality in adulthood (Bastien et al. 2014, Nickelson et al. 2014, Raj 2012, Rodrigues et al. 2011) and is considered an early risk factor associated with hypertension, type 2 diabetes mellitus (DM2) (Alderete et al. 2014, Kaneko et al. 2011), heart disease, atherosclerosis (Baker et al. 2007), osteoarthritis, some types of cancer (Abrantes et al. 2002), non-alcoholic fatty liver disease, infertility and psychiatric diseases (Kelsey et al. 2014). Considering that the risk factors of obesity are multifactorial, the identification of these risks is crucial to prevent the epidemic of childhood obesity (Dev et al. 2013).

Obesity has been associated with chronic low-grade inflammation (Carolan et al. 2014), triggered by white adipose tissue (WAT), which was previously considered as a passive fat depot (Roth et al. 2011). However, recent data has shown that the WAT is an active factor in the metabolism linked to the production of proinflammatory cytokines, such as tumor necrosis factor alpha (TNF- α), interleukins (IL-1 and IL-6) and C-reactive Protein (CRP) (Petersen and Pedersen 2005, Genest 2010, Roth et al. 2011, Shi et al. 2014). Together with adipocytes, endothelial cells, fibroblasts and immune cells located in adipose tissue, can all contribute to inflammatory cytokine secretion (Roth et al. 2011). Studies on genes encoding different cytokines have shown the presence of several single-nucleotide polymorphisms (SNPs), which may be useful in studies of allele and genotype frequencies in different populations (Mendoza-Carrera et al. 2010, Corpeleijn et al. 2010, Franceschi et al. 2009, Tabassum et al. 2012).

The available evidence suggests that variations in the metabolic modulation of *CRP* and *IL-6* genes may play a relevant role in the etiology of metabolic disorders related to obesity. Based on this assumption, the present study evaluated whether the gene polymorphisms *IL-6* rs1800795, *IL-6* rs2069845 and *CRP* rs1205 are related to the development of metabolic abnormalities and obesity in children and adolescents in southern Brazil.

MATERIALS AND METHODS

Study Subjects and Design

A retrospective, cross-sectional study consisting of 470 children (aged 7-9 years) and adolescents (aged 10-17 years), 54% girls, from five schools in the municipality of Santa Cruz do Sul, state of Rio Grande do Sul, Brazil. This study is part of a larger project, whose sample size was calculated according to the formula of the Division of Research Nea (Christensen 1980) of which a population of 20,540 from the public and private education system in Santa Cruz do Sul-RS, were considered. 470 students were selected as a convenience sample in this preliminary sampling. The population of this research is predominantly of Germanic origin (Filho and Monasterio 2012). All study participants reported their free participation in the study by having the free and informed consent form signed by their parents or guardians. This study was reviewed by the Research Ethics Committee of the Universidade Santa Cruz do Sul, under protocol number 120.090/2012.

Anthropometric measurements were performed using the Body Mass Index (BMI), based on the curves of percentiles from the Centers for Disease Control and Prevention/National Center for Health Statistics (CDC/NCHS 2000), according to gender and age, considering underweight ($< p5$), normal weight ($\geq p5$ and $< p85$), overweight ($p \geq 85$ and $< p95$) and obesity ($\geq p95$). Waist Circumference (WC) was measured with an inelastic tape, using as reference the narrowest part of the trunk between the ribs and the iliac crest and hip at the greater trochanter level and, subsequently, classified

according to the criteria established by Taylor et al. (2000) according to gender and age, which considers as a normal circumference a percentile ≤ 80 and obesity a percentile > 80. The percentage of body fat (%BF) was calculated using the equation of Slaughter et al. (1988) and subsequently classified according to Lonman's data (1987), cited by Heyward and Stolarczyk (2000), into two categories: 1) very low, low and optimal; and 2) moderately high, high and very high.

Blood pressure (BP) was assessed according to the parameters established at the VI Brazilian Guidelines on Hypertension (SBC 2010), using the auscultatory method and previously calibrated aneroid devices consisting of three cuffs of different sizes, making it possible to consider the width/length ratio of 1:2 for each arm circumference. Values below the 90th percentile were considered normotensive, as long as they were < 120/80 mmHg; between percentiles 90-95th, they were considered borderline; and ≥ 95th percentile, as arterial hypertension; it is noteworthy that any value ≥ 120/80 mmHg in adolescents, even if below the 95th percentile, was considered borderline.

Laboratory Analyses

Blood was collected after at least 12 hours of fasting by venipuncture. Blood samples (10 mL) were separated into aliquots and then stored in a freezer at -20°C.

Measurements of total cholesterol (TC), HDL-C cholesterol, triglycerides (TG) and glucose were performed using Kovalent commercial kits (Kovalent do Brazil Ltda) and CRP was measured using DiaSys kits (DiaSys Diagnostic Systems, Germany), in Miura One equipment (ISE, Rome, Italy). For TC, LDL-C cholesterol and TG, values were classified as: acceptable, borderline and high; for HDL-C, as acceptable, borderline and low (NHLBI 2012). LDL-C cholesterol was calculated using the Friedewald et al. equation (1972). Glucose was considered normal at < 100 mg/dL and as pre-diabetes with levels from 100 mg/dL to 125 mg/dL (ADA 2011). CRP levels were considered as low, medium and high, with values corresponding to < 1.0; 1.0 to 3.0 and > 3.0 mg/L, respectively (Shine et al. 1981, Pearson et al. 2003) and subsequently reclassified as normal and high.

Serum CRP levels were measured using a high-sensitivity assay. Students with CRP levels > 10 mg/L were excluded from the study, as they suggested an acute inflammatory process (Pearson et al. 2003).

Genotyping

DNA extraction was carried out in whole blood anticoagulated with EDTA, using the Salting out method described by Miller et al. (1988). DNA quantification was carried out in the NanoDrop 2000c Spestrophotometer equipment (ThermoScientific, Wilmington, USA).

IL-6 rs1800795, *IL-6* rs2069845 and *CRP* rs1205 polymorphisms were genotyped and the choice of these genes occurred after searching the literature and evaluating allele frequency in the National Institutes of Health: International HapMap Project (http://www.ncbi.nlm.nih.gov), considering that the study population is predominantly of German origin (Filho and Monasterio 2012). The technique used for genotyping was real-time PCR in StepOne Plus® equipment (Applied Biosystems, Foster City, CA, USA) according to the manufacturer's instructions, using allelic discrimination assays. Probes TaqMan™ rs1205, rs2069845, rs1800795 (customized assay) and Master Mix PCR Universal were purchased from Applied Biosystems (Foster City, CA, USA). Genotyping was performed in duplicate, with an accuracy of 100%.

Statistical Analyses

Descriptive analysis based on the mean and standard deviation was used to specify the subjects' characteristics. Bivariate and multivariate logistic regression analyses were performed to estimate odds ratios between polymorphisms rs1800795,

rs2069845 and rs1205 and anthropometric characteristics, biochemical markers and blood pressure levels of the subjects. The Hardy-Weinberg equilibrium (HWE) was analyzed for all polymorphisms and the p value was calculated by the chi-square test. The statistical analysis of the data was carried out using SPSS 20.0 software (IBM, Chicago, USA). P values < 0.05 were considered significant.

RESULTS

Patients Characteristics

Descriptive characteristics of the 470 students, as well as the allele and genotype frequencies for the *IL-6* and *CRP* genes can be seen on Table I. Among the selected sample subjects, it was observed that the overall mean age was 13.13 (± 2.99 years), 15.3% were overweight and 9.8% were classified as obese.

TABLE I
Descriptive characteristics of the subjects.

	N = 470 (%)	Mean (SD)
Gender[a]		
Female	254 (54)	
Age range [a,b]		13.13 (2.99)
Adolescent	397 (84.5)	
BMI (Kg/m^2)[a,b]		20.44 (4.01)
Overweight	72 (15.3)	
Obesity	46 (9.8)	
WC (cm)[a,b]		66.52 (9.14)
Elevated	62 (13.2)	
%BF[a,b]		20.77 (7.57)
Moderately high, high and very high	175 (37.2)	
SBP (mmHg)[a,b]		104.30 (12.67)
Risk	18 (3.8)	
DBP (mmHg)[a,b]		64.76 (12.29)
Risk	37 (7.9)	
Total Cholesterol (TC) (mg/dL)[a,b]		176.76 (35.39)
Elevated	99 (21.1)	
LDL Cholesterol (mg/dL)[a,b]		122.56 (33.36)
Elevated	165 (35.1)	
HDL Cholesterol (mg/dL)[a,b]		54.20 (10.44)
Low	30 (6.4)	
Triglycerides (TG) (mg/dL)[a,b]		73.33 (32.13)
Elevated	33 (7.0)	
Glucose (mg/dL)[a,b]		91.41 (11.33)
Pre-diabetes	95 (20.2)	
CRP (mg/L)[a,b]		1.39 (0.69)
Elevated	58 (12.3)	

[a]Values expressed as mean ± standard deviation (SD). [b]Age range: child, 7-9 years; adolescent, 10-17 years. [b]BMI: overweight p≥85 and <p95; obesity ≥p95; [b]elevated Waist Circumference (WC) p>80; [b]Percentage of Body Fat (%BF): altered, moderately high, high and very high; [b]Systolic Blood Pressure (SBP) and [b]Diastolic Blood Pressure (DBP) considered at risk ≥p95; [b]elevated Total Cholesterol (TC) >199.9 mg/dL; [b]elevated LDL Cholesterol >129.9 mg/dL; [b]Low HDL Cholesterol <39.9 mg/dL; [b]elevated Triglycerides (TG) >99.9 mg/dL (<9 years) and >129.9 mg/dL (>10 years); [b]Glucose: pre-diabetes 99.9 to 125.9 mg/dL; [b]elevated C-Reactive Protein (CRP) >3.0 mg/L.

Visceral fat, measured by WC was elevated in 13.2% of the students and 37% were classified as having moderately high, high and very high %BF. Laboratory analysis showed that 21% had elevated TC, 35% had altered LDL-C, 20% were classified as having pre-diabetes or altered glucose levels and 12% had high CRP levels. The genotypic proportions observed were in Hardy-Weinberg equilibrium (data not shown) for the three analyzed polymorphisms. The observed allelic frequencies for the polymorphisms were 32.8% for rs1800795/C, 36.8% for rs2069845/G and 39% for rs1205/T (Table II).

TABLE II
Descriptive allele and genotype frequencies.

Polymorphisms	Genotypes/Alleles	N=470 (%)
IL-6 rs1800795 G/C*	GG	213 (45.3)
	GC	206 (43.8)
	CC	51 (10.9)
	G	632 (67.2)
	C	308 (32.8)
IL-6 rs2069845 A/G*	AA	180 (38.3)
	AG	234 (49.8)
	GG	56 (11.9)
	A	594 (63.2)
	G	346 (36.8)
CRP rs1205 C/T*	CC	174 (37.0)
	CT	226 (48.1)
	TT	70 (14.9)
	C	574 (61)
	T	366 (39)

*risk allele.

Association Among Clinical Factors and Genotypes

The bivariate logistic regression analysis (Table III) showed that individuals with the risk genotype rs1205 *CRP* gene have a greater association with the risk of developing hypercholesterolemia (OR = 2.12; 95% CI: 1.28, 3.51, p = 0.003), after performing multivariate logistic regression analysis it was noted that subjects with the risk genotype rs1205 in the *CRP* gene had a risk factor for developing hypercholesterolemia (OR = 2.79; 95% CI: 1.40, 5.57; p = 0.003) and the risk genotype rs2069845 in the *IL-6* gene showed an association with the risk of developing obesity (OR = 3.07; 95% CI: 1.08, 8.72; p = 0.03) in Brazilian children and adolescents. The rs1800795 polymorphism indicated no significant association in the analyzed model.

DISCUSSION

According to the inflammatory markers related to the risk of developing metabolic disorders in healthy individuals, we assessed the effect of polymorphisms rs2069845 (*IL-6*), rs1800795 (*IL-6*) and rs1205 (*CRP*) as they are associated with obesity and metabolic disorders in children and adolescents (Feng et al. 2003, Kolz et al. 2008, Tabassum et al. 2012). Increasing evidence suggests that polymorphisms associated with low-grade inflammation may be a determining factor for metabolic complications commonly associated with obesity (Roth et al. 2011, Shoelson et al. 2006, Wexler et al. 2005, Yudkin et al. 2004, Tabassum et al. 2012).

The study observed that carriers of the risk genotype rs1205 in the *CRP* gene were associated with hypercholesterolemia (Table III). Hu et al. (2010) also showed associations between the rs1205 polymorphism and waist circumference, diabetes, TG and HDL-C in Chinese adult individuals; however, there was no association between this polymorphism and the parameters established for obesity. A study carried out in six European cities (Athens, Rome, Barcelona, Augsburg, Stockholm and Helsinki) with adult subjects showed that rs1205 was associated with lower serum concentrations of *CRP*. Regarding the clinical covariates, BMI and total cholesterol were associated with higher CRP values.

A dose-dependent effect is suggested for rs1205, which is located in the 3'UTR flanking region, considered a region possibly controlled by RNA cleavage and intracellular stability, export and localization (Kolz et al. 2008). In a study with 448 Mexican adolescents, the analysis of metabolic

traits was performed, in which the rs1205 *CRP* gene showed no significant association with TG, but was associated with HOMA and fasting glucose; however the statistical significance did not persist after correction for multiple tests (Duran-Gonzalez et al. 2011).

In Table III, comparisons showed that being a carrier of the rs2069845 risk variant increased by 3.07-fold the chance of developing obesity (p <0.05). IL-6 is a physiological regulator that has several functions in different organs, including the central nervous system, cardiovascular, immune and hepatic systems, among others; its dysregulation affects several pathological conditions (Hong et al. 2007, Guimarães et al. 2007).

The presence of high concentrations of IL-6 is related to inflammation, whereas polymorphisms such as rs1800795 and rs2069845 are associated with obesity and other diseases such as insulin resistance, metabolic syndrome and type 2 diabetes mellitus (Mendoza-Carrera et al. 2010, Corpeleijn et al. 2010, Steemburgo et al. 2009, Tabassum et al. 2012). In a study carried out in India with children and adolescents aged 11 to 17 years, the *IL-6* polymorphism rs2069845 had its risk allele associated with overweight/obesity, whereas in this same study *IL-6* polymorphism rs1800795 was not associated with overweight/obesity (Tabassum et al. 2012). In recent years, the results of genetic variation between diet and chronic diseases have been studied and the presence of several *IL-6* polymorphisms constitutes a major role in the obesity phenotypes (Steemburgo et al. 2009).

Associations between the *IL-6* rs1800795 gene and biochemical markers, blood pressure and anthropometric characteristics were not significant in our study. However, some studies show that carriers of the C allele for the *IL-6* polymorphism rs1800795 have higher BMI, IL-6, CRP, insulin resistance and lipoprotein levels, identified in children, adolescents and adults (Eklund et al. 2006, Goyenechea et al. 2006, Jones et al. 2001).

A study carried out in London with 571 Caucasian adults found that 76% of CC carriers had metabolic syndrome (MS), when compared to 56% of individuals with GG genotype; consonant with that, the C allele frequency was significantly higher in individuals with MS, when compared to those without the syndrome (Stephens et al. 2007). In disagreement with these observations, other studies indicate that the G allele has been associated with increased IL-6 secretion, lipid disorders (Fernández-Real et al. 2000), insulin resistance and diabetes (Hamid et al. 2005). The present study did not evaluate insulin.

The allelic frequencies of SNPs analyzed in this study (Table II) are mostly similar to those found in previous publications with Caucasian populations (Dedoussis et al. 2004, Duran-Gonzalez et al. 2011, Ljungman et al. 2009, Goyenechea et al. 2007, Sousa et al. 2012), showing a frequency distribution similar to the one of this present study.

Regarding the anthropometric and clinical characteristics of the subjects evaluated in the study, it was observed that 25.3% of the study subjects were overweight or obese and 13.2% had elevated WC (Table I). In a previous study of this population, the prevalence of overweight and obesity was 25.3% among boys and 25.6% among girls, whereas 19% had elevated WC (Reuter et al. 2013).

In this study, obese individuals showed significant values when compared with *IL-6* risk genotypes rs2069845, whereas in relation to other *CRP* (rs1205) and *IL-6* (rs1800795) polymorphisms, this association was not significant. An explanation for this fact might be the sample size, even though they are representative for the studied population. The analysis also showed that having the risk genotype for the *CRP* rs1205 gene is associated with hypercholesterolemia and thus, we suggest further studies of *CRP* polymorphisms in our population, as it is believed that CRP levels add prognostic value to the lipid parameters, being able to identify subjects at risk for future cardiovascular events.

TABLE III
Association of *IL-6* polymorphisms and *CRP* with anthropometric measurements, biochemical markers and blood pressure in individuals with altered variables.

Variables		*CRP* rs1205 (CT+TT[c])		*IL-6* rs1800795 (GC+CC[c])		*IL-6* rs2069845 (AG+GG[c])	
		Bivariate analysis: OR (95% CI)	**Multivariate analysis: OR (95% CI)**	**Bivariate analysis: OR (95% CI)**	**Multivariate analysis: OR (95% CI)**	**Bivariate analysis: OR (95% CI)**	**Multivariate analysis: OR (95% CI)**
BMI[a]	Overweight	1.29 (0.75, 2.22)	1.46 (0.79, 2.67)	0.68 (0.41, 1.13)	0.87 (0.49, 1.53)	0.70 (0.42, 1.18)	0.66 (0.37, 1.20)
	Obese	0.94 (0.50, 1.77)	1.55 (0.57, 4.18)	1.37 (0.72, 2.59)	2.32 (0.85, 6.31)	1.24 (0.64, 2.38)	3.07* (1.08, 8.72)
CRP >3.0 mg/L[b]		0.95 (0.54, 1.68)	1.03 (0.56, 1.88)	0.80 (0.46, 1.39)	0.66 (0.37, 1.20)	0.93 (0.53, 1.64)	0.65 (0.28, 1.51)
WC (cm)[b]		0.85 (0.49, 1.47)	0.64 (0.27, 1.48)	1.00 (0.58, 1.72)	0.65 (0.28, 1.51)	0.77 (0.45, 1.33)	0.78 (0.50, 1.21)
%BF (%)[b]		0.85 (0.57, 1.24)	0.74 (0.47, 1.17)	0.78 (0.53, 1.13)	0.78 (0.50, 1.21)	0.70 (0.48, 1.04)	2.23 (0.92, 5.37)
HDL-C (mg/dL)[b]		1.18 (0.54, 2.60)	1.41 (0.61, 3.29)	2.01 (0.90, 4.50)	2.23 (0.92, 5.37)	2.12 (0.89, 5.06)	0.99 (0.57, 1.73)
LDL-C (mg/dL)[b]		1.28 (0.86, 1.90)	0.68 (0.39, 1.18)	0.99 (0.67, 1.45)	0.99 (0.57, 1.73)	0.93 (0.63, 1.37)	1.23 (0.64, 2.38)
TC (mg/dL)[b]		2.12* (1.28, 3.51)	2.79* (1.40, 5.57)	0.99 (0.63, 1.55)	1.23 (0.64, 2.38)	0.99 (0.63, 1.57)	0.57 (0.26, 1.27)
TG (mg/dL)[b]		1.91 (0.84, 4.34)	1.54 (0.63, 3.74)	0.67 (0.33, 1.36)	0.57 (0.26, 1.27)	0.72 (0.35, 1.48)	0.57 (0.35, 0.92)
Glucose (mg/dL)[b]		1.13 (0.70, 1.81)	1.11 (0.67, 1.82)	0.60 (0.37, 0.92)	0.57 (0.35, 0.92)	0.59 (0.37, 0.93)	1.22 (0.33, 4.43)
SBP (mmHg)[b]		1.18 (0.43, 3.21)	1.92 (0.51, 7.20)	1.03 (0.40, 2.67)	1.22 (0.33, 4.43)	0.97 (0.37, 2.56)	1.18 (0.47, 2.96)
DBP (mmHg)[b]		0.85 (0.43, 1.68)	0.70 (0.28, 1.77)	1.09 (0.55, 2.15)	1.18 (0.47, 2.96)	1.02 (0.51, 2.04)	1.12 (0.43, 2.86)

Abbreviations: OR, Odds ratio; CI, Confidence interval; CRP, C-Reactive Protein; WC, Waist Circumference; %BF, Percentage of Body Fat; HDL Cholesterol; LDL Cholesterol; TC, Total Cholesterol; TG, Triglycerides; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure. Bivariate and Multivariate Logistic Regression – [a]BMI-overweight ($p \geq 85$ and $<p95$) and obesity ($\geq p95$), [b]This table used the parameters of individuals whose variables were altered, [c]risk allele, **p* Value <0.05.

The results suggest that the risk genotype of *CRP* rs1205 gene is associated with the development of hypercholesterolemia and the risk genotype of *IL-6* rs2069845 gene is associated with the development of obesity in Brazilian children and adolescents. No association was found between *IL-6* rs1800795 polymorphism and the anthropometric parameters, blood pressure levels and biochemical markers assessed in the study.

We emphasize the importance of studies capable of identifying the influence of a particular gene on a phenotype in a certain population with different eating habits and lifestyles that can supposedly affect this phenotype. All students received their biochemical profile analysis after their participation in the study and those with abnormal results were referred for appropriate treatment.

We also suggest future studies to demonstrate the association of inflammatory markers and comorbidities related to obesity in childhood and adolescence, as well as investigate other variations in the studied genes and other polymorphisms associated with metabolic disorders in the Brazilian population, aiming at clarifying issues that may lead to an inflammatory-metabolic imbalance and possibly, to future health complications.

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RESUMO

A ativação da inflamação do tecido adiposo está relacionada com a obesidade, causada pelo acúmulo de lipídios nos adipócitos. Através dessa ativação, citocinas pró-inflamatórias como Interleucina-6 (IL-6) e Proteína C-Reativa (CRP) parecem influenciar as desordens metabólicas. O presente estudo avaliou se polimorfismos nos genes da *CRP* (rs1205) e da *IL-6* (rs1800795 rs2069845) estão relacionados com o desenvolvimento de alterações metabólicas em crianças e adolescentes. Estudo transversal, foi feito com 470 escolares do município de Santa Cruz do Sul, Brasil, com idades entre 7 a 17 anos. O índice de massa corporal (IMC) foi classificado de acordo com sobrepeso e obesidade. A genotipagem foi realizada através da *Reação em Cadeia de Polimerase (PCR)* em tempo real. Características antropométricas, indicadores bioquímicos, marcadores imunológicos e a pressão arterial foram avaliados. Estatísticas descritivas, qui-quadrado e regressão logística foram utilizadas para as análises. Nenhuma associação foi detectada entre o polimorfismo rs1800795 e as variáveis avaliadas. Indivíduos com o genótipo de risco no gene rs1205 foram associados ao risco de desenvolver hipercolesterolemia (OR = 2,79; IC: 1,40, 5,57; $p = 0,003$). Portadores do genótipo de risco no gene rs2069845 estão associados com o risco de desenvolver obesidade (OR = 3,07; IC: 1,08, 8,72; $p = 0,03$). O polimorfismo rs2069845 foi relacionado com obesidade e o rs1205 associado ao risco de desenvolver hipercolesterolemia em escolares brasileiros.

Palavras-chave: Inflamação, obesidade, polimorfismos, risco, escolares.

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