Effects of polymorphisms in \textit{APOB}, \textit{APOE}, \textit{HSD11\beta1}, \textit{PLIN4}, and \textit{ADIPOQ} genes on lipid profile and anthropometric variables related to obesity in children and adolescents

Caroline C. Gasparin\textsuperscript{1}, Neiva Leite\textsuperscript{2}, Luciane V. Tureck\textsuperscript{1}, Ricardo L.R. Souza\textsuperscript{1}\textsuperscript{2}, Gerusa E. Milano-Gai\textsuperscript{2}, Larissa R. Silva\textsuperscript{2}, Wendell A. Lopes\textsuperscript{2} and Lupe Furtado-Allé\textsuperscript{2}\textsuperscript{2}

\textsuperscript{1}Laboratório de Polimorfismos e Ligação, Departamento de Genética, Universidade Federal do Paraná (UFPR) Curitiba, PR, Brazil. E-mail: lupealle@gmail.com.

\textsuperscript{2}Departamento de Educação Física, Universidade Federal do Paraná (UFPR) Curitiba, PR, Brazil.

Abstract

Genes can influence lipid profile and anthropometric variables related to obesity. The present study aimed to verify if variants of the \textit{APOE}, \textit{APOB}, \textit{ADIPOQ}, \textit{HSD11\beta1}, and \textit{PLIN4} genes are associated with lipid levels or anthropometric variables in a sample comprised of 393 Euro-Brazilian children and adolescents. DNA was genotyped by TaqMan allelic discrimination assay. The \(\varepsilon4\) and \(\varepsilon2\) alleles of the \textit{APOE} gene were associated respectively with lower high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels (\(p=0.015\) and \(p=0.012\), respectively), while the \(\varepsilon3\) allele was associated with higher abdominal circumference (\(p=0.0416\)) and excess weight (\(p=0.0001\)). The G allele (rs846910) of the \textit{HSD11\beta1} gene was also associated with excess weight (\(p=0.039\)). No other association was found. Our results indicate that the \(\varepsilon4\) and \(\varepsilon2\) alleles could contribute to lower HDL-C and LDL-C levels, respectively, furthermore, the \(\varepsilon3\) allele and the G allele (rs846910) of \textit{HSD11\beta1} gene may be risk factors for excess of weight. These findings are very important because we observed that some genetic variants influence the lipid profile and anthropometric variables early in life.

Keywords: \textit{PLIN4} gene, \textit{APOB} gene, \textit{ADIPOQ} gene, \textit{HSD11\beta1} gene, \textit{APOE} gene.

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Introduction

Dyslipidemia is closely related to the development of cardiovascular and cerebrovascular diseases, such as atherosclerosis, acute myocardial infarction, ischemic heart disease, and cerebrovascular accident, and therefore of great relevance for public health (ANVISA, 2011; Maria et al., 2011). It is estimated that 53% of American adults have lipid abnormalities (Tóth et al., 2012). In Brazil, according to Alcântara Neto et al. (2012), the prevalence of dyslipidemia among children and adolescents enrolled in the public school system was 25.5%. They also found a positive association between dyslipidemia and overweight (Alcântara Neto et al., 2012). Worldwide, in 2015, the number of overweight children under five years old had been estimated at more than 42 million (WHO, 2016).

Dyslipidemias, as well as obesity, are mainly multifactorial traits, influenced by the environment, genetic factors, and life habits. Polymorphisms of the \textit{APOB}, \textit{APOE}, \textit{ADIPOQ}, \textit{PLIN4}, and \textit{HSD11\beta1} genes are important examples of genetic causes associated with dyslipidemias and obesity. The genetic variants selected for this study seem to have functional effects, being involved in lipid metabolism and features related to obesity (Innerarity et al., 1987; Soria et al., 1989; Myant, 1993; Arita et al., 1999; Foley, 2005; Greenow et al., 2005; Heeren et al., 2006; Lara-Castro et al., 2007; Gambineri et al., 2011; Richardson et al., 2011).

The \textit{APOE} glycoprotein plays an important role in metabolism, transport, and redistribution of molecules that carry cholesterol and other lipids (Poirier, 2005). It is encoded by a gene of the same name (19q13.2) and mediates the uptake of chylomicrons, very low-density lipoprotein (VLDL) and intermediate density lipoprotein (IDL) (Mahley, 1988; Weisgraber et al., 1981). The \(\varepsilon2\), \(\varepsilon3\), and \(\varepsilon4\) alleles (rs7412: NM_000041.3:c.526C > T and rs429358: NM_000041.3:c.388T > C) are combined in two important positions (Weisgraber et al., 1981), producing therefore the three \textit{APOE} major isoforms \(E2\) (Cys 112, Cyc 158), \(E3\) (112 Cys, Arg 158), and \(E4\) (Arg 112, Arg 158) (Foley 2005; Greenow et al., 2005; Heeren et al., 2006). ApoB-100 is encoded by the \textit{APOB} gene (2p24.1) and it is present on the surface of LDLs (Blackhart et al., 1986; Innerarity et al., 1987). The R3500Q mutation (rs5742904: T/C) has been associated with increased levels of triglycerides, and therefore with dyslipidemias and cardiovascular diseases. The \(HSD11\beta1\) gene is located at 11q14.3 and expresses the CYP11B1 enzyme, which catalyzes the reduction of cholesterol to aldosterone in the adrenal gland, and to deoxycorticosterone in the zona glomerulosa of the adrenal gland (Gambineri et al., 2007). Studies have shown an association between polymorphisms of this gene and several diseases such as obesity and hypertension (Rostagno et al., 2015).

The \textit{PLIN4} gene is located at 12q24.1 and expresses lipin 4 (Lpin4), an enzyme involved in lipid metabolism. Variants of this gene have been associated with several diseases, such as obesity (Soria et al., 1989).

The \textit{ADIPOQ} gene is located at 1q25 and expresses adiponectin, a protein that is involved in lipid metabolism and glucose homeostasis. Variants of this gene have been associated with several diseases, such as obesity (Arita et al., 1999).

The \textit{APOB} and \textit{APOE} genes are located at 3q26.3 and 19q13.2, respectively, and are involved in the synthesis and transport of lipoproteins.

Send correspondence to Lupe Furtado Alle. Polymorphisms and Linkage Laboratory, Department of Genetics, Federal University of Paraná (UFPR), Curitiba, PR, Brazil. E-mail: lupealle@gmail.com.
NM_003843.2:c.10580G > A) leads to diminished affinity for its receptor (Innerarity et al., 1987; Soria et al., 1989; Myant, 1993).

**PLIN4** (19p13.3; Ensembl 2015) participates in the Perilipin/ADRP/TIP47 (PAT) family of lipid storage droplet (LSD) proteins and appears to be involved in the storage of lipids in adipocytes (Brasemae, 2007). The rs88877 (NM_001080400.1:c.*2270A > G) polymorphism is situated in the 3’UTR region of **PLIN4** gene. The less frequent allele of this site may induce a reduction of up to 20% in the PLIN4 level due to the creation of a miR-522 binding site in the 3’UTR region of the gene (Richardson et al., 2011).

The human gene encoding adiponectin, **ADIPOQ** gene (3q27), is the most expressed gene in adipose tissue (Maeda et al., 1996). Obesity, and in particular the accumulation of abdominal visceral fat, as well as type 2 diabetes mellitus, coronary disease, and arterial hypertension are accompanied by a reduction of serum adiponectin (Arita et al., 1999; Lara-Castro et al., 2007). The SNP of the **ADIPOQ** gene was rs1501299: NM_001177800.1:c.214+62G > T.

The **HSD11** gene (1q32.2; Ensembl, 2015) encodes the enzyme hydroxysteroid dehydrogenase type 1 (11β-HSD1), which is responsible for the conversion of inactive to active cortisol, in addition to regulating the interaction of cortisol with glucocorticoid receptors (Bujalska al., 1997). Transgenic rats that overexpress this enzyme in adipose tissue develop visceral obesity, insulin resistance, hyperglycemia, and hyperlipidemia (Masuzaki et al., 2001). Among its polymorphisms are rs846910 (NM_001206741.1:c.8204A > G), which corresponds to a non-coding region SNP of the **HSD11** gene, and rs12086634 (NM_001080400.1:c.332-29T > G), which occurs in an enhancer region in intron 3 (Gambineri et al., 2011).

Hence, the aim of the present study was to investigate possible influences of the **PLIN4** (rs88877), **APOB** (rs5742904), **ADIPOQ** (rs1501299), **HSD11** (rs848910 and rs12086634), and **APOE** (rs7412 and rs429358; alleles ε2, ε3, and ε4) genes on lipid and glucose levels, abdominal circumference, and obesity in a sample of children and adolescents from a population in southern Brazil.

### Subjects and Methods

#### Subjects

The sample was comprised of 393 Euro-Brazilians (13.54 ± 0.095 years old) living in Curitiba, PR, of which 143 were eutrophic and 250 overweight. Of these 393 individuals, 128 were girls (21.09% eutrophic and 78.91% overweight) and 265 were boys (43.94% eutrophic and 56.06% overweight). This study was approved by the Institutional Ethics Committee and informed consent was signed by participants and their parents or legal guardians.

Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Age- and sex-specific BMI z-score and percentiles were calculated using CDC 2000 growth charts (Kuczmarski et al., 2002). Eutrophic was defined as a < 85 percentile, overweight as a ≥85 percentile, and obesity as ≥95 percentile. The abdominal circumference (AC) was measured in centimeters (cm) at the level of the iliac crest. Thus, subjects were classified as eutrophic (percentile < 85) and overweight/obese (percentile ≥ 85) (Kuczmarski et al., 2002).

Blood samples were collected in the morning after 12 hours of fasting to perform measurements of glucose (Glu), triglycerides (TG), total cholesterol (TC), and high density lipoprotein cholesterol (HDL-C) by standard automated methods. Low density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation (Friedewald et al., 1972), for TG levels below 200 mg/dL.

#### Genotyping assays

DNA was extracted from peripheral blood by a salting-out method (Lahiri and Nurnberger, 1991) and was diluted to 20 ng/μL. All SNPs were genotyped by TaqMan allelic discrimination assay on StepOnePlus real time PCR systems (Applied Biosystems, USA). Each reaction contained 3.0 μL of Master Mix (2X), 1.7 μL of ultrapure water, 0.3 μL of primer and 3.0 μL of DNA. The reactions were performed according to the following protocol: 50 °C for 2 min, 95 °C for 10 min, and 50 cycles of 95 °C for 15 s and 62 °C for 1 min.

#### Statistical analysis

Samples were classified into two groups, eutrophic and overweight (overweight + obese), categorized into above and below the median for age, AC, Glu, TC, LDL-C, HDL-C and TG levels. Chi-square tests were performed using Clump (Jakobsson and Rosenberg, 2007) to test for Hardy-Weinberg equilibrium and to compare allele proportions between groups above and below the median and also between eutrophic and overweight. Logistic regression analyses were performed to identify variables influencing serum glucose, lipid concentrations, and AC. False discovery rate (FDR) corrections (Benjamini and Hochberg, 1995) were performed for multiple testing. The significance level adopted was 0.05 (5%).

#### Results

A descriptive analysis of the sample, displaying the variables considered in this study, is shown in Table 1. Significantly higher frequencies were found for the ε4 allele in the group below the HDL-C median (p=0.0001), and for the ε2 allele in the group below the LDL-C median (p=0.0001). Furthermore the ε3 allele was associated with higher AC and excess weight (p=0.0001). The allele frequencies are shown in Table 2. Logistic regression analysis was done using stratified TC as below and above the median as the de-
endent variable, and for the polymorphisms analyzed (dominant model for APOE gene, in which ε4 is dominant over ε2; for the other polymorphisms, dominant, recessive, and additive models were tested), gender, AG, and anthropometric classification as independent variables. The same logistic regression analysis design was performed using LDL-C, HDL-C, TG, glucose, and AC as the dependent variable and maintaining the same independent variables. We identified the APOE gene ε4 allele as a contributing factor in reducing HDL-C levels (β = -0.29 ± 0.08, p = 0.015) and the ε3 allele as a risk factor for higher AC measures (β = -0.24 ± 0.08, p = 0.041). We also found that obesity and overweight are independent risk factors for higher triglyceride levels (β = 0.30 ± 0.08, p = 0.021).

Furthermore, we observed that the A allele (rs846910) of the HSD11B1 gene was associated with excessive weight (p = 0.039, Chi-square test). It is known that there is variation in metabolic processes inherent to gender, so we conducted the same analyses separately for each gender. We observed that in girls the alleles ε2 and ε4 of the APOE gene were associated with LDL-C below the median (p = 0.001 by Chi-square test) and HDL-C below the median, independently of the other analyzed variables (β = -0.34 ± 0.08, p = 0.0039) (Table 3). Furthermore, eutrophic girls had lower mean TG levels than obese or overweight girls (β = 0.30 ± 0.08, p = 0.0039). Regarding boys, we observed that the ε2 allele is associated to lower LDL-C levels (p = 0.019 by Chi-square test) (Table 3).

Table 1 - Descriptive statistics for age, lipid profile, glucose, and abdominal circumference of the 393 individuals analyzed in this study.

| Variable* | N** | Mean ± SE | Median | Variance | SD | Boys mean ± SE | Girls mean ± SE |
|-----------|-----|-----------|--------|----------|----|----------------|----------------|
| Age       | 393 | 13.54 ± 0.095 | 13.96 | 3.56 | 1.89 | 13.54 ± 0.12 | 13.54 ± 0.17 |
| HDL-C (mg/dL) | 369 | 47.59 ± 0.89 | 46.00 | 116.203 | 10.78 | 45.44 ± 0.63 | 51.69 ± 1.02 |
| LDL-C (mg/dL) | 262 | 91.56 ± 1.85 | 87.50 | 898.187 | 29.97 | 89.93 ± 2.53 | 92.94 ± 2.72 |
| TG (mg/dL) | 376 | 99.17 ± 2.88 | 81.74 | 3055.92 | 55.28 | 96.06 ± 3.35 | 105.05 ± 5.41 |
| TC (mg/dL) | 262 | 162.67 ± 2.19 | 158.095 | 1261.96 | 35.52 | 160.42 ± 2.98 | 165.19 ± 3.24 |
| Glu (mg/dL) | 387 | 89.50 ± 0.56 | 89.00 | 120.842 | 10.99 | 90.60 ± 0.72 | 87.25 ± 0.83 |
| AC (cm) | 291 | 83.69 ± 1.07 | 81.50 | 333.001 | 18.25 | 80.77 ± 1.21 | 92.25 ± 1.94 |

* High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG), Total Cholesterol (TC), Glucose (Glu), Abdominal Circumference (AC).

**393 individuals were analyzed.

Figure 1 - Relationships between allelic variants and analyzed variables.
Table 2 - Comparisons of allele frequencies between groups below and above the median for the analyzed variables, and between eutrophic and overweight/obese individuals.

| Alleles   | Above TC (mg/dL) median | Below TC (mg/dL) median | Above LDL-C (mg/dL) median | Below LDL-C (mg/dL) median | Above TG (mg/dL) median | Below TG (mg/dL) median | Above HDL-C (mg/dL) median | Below HDL-C (mg/dL) median | Above AC (cm) median | Below AC (cm) median | Eutrophic | Overweight/Obese |
|-----------|-------------------------|-------------------------|---------------------------|----------------------------|------------------------|------------------------|---------------------------|----------------------------|----------------------|----------------------|------------|------------------|
| ε2 (APOE gene) | 3.57 ± 0.28 (6)       | 7.14 ± 0.55 (12)       | 1.83 ± 0.14 (3)           | 8.72 ± 0.66 (15)           | 4.84 ± 0.31 (12)       | 5.23 ± 0.32 (14)       | 4.92 ± 0.30 (13)           | 5.12 ± 0.32 (13)           | 6.25±0.49 (10)       | 2.31±0.15 (5)       | 3.70±0.25 (8) | 5.36±0.29 (18)   |
| ε3 (APOE gene) | 82.14 ± 6.34 (138)  | 81.55 ± 6.29 (137)    | 82.93 ± 6.16 (139)        | 80.81 ± 6.16 (139)         | 78.22 ± 4.97 (194)     | 77.10 ± 4.83 (212)     | 84.85 ± 5.22 (224)         | 5.45 ± 184               | 71.88 ± 5.68 (115) | 73.10 ± 4.85 (165) | 76.39 ± 5.20 (265) | 78.87±4.30 (265) |
| ε4 (APOE gene) | 14.29 ± 1.35 (24)    | 11.31 ± 1.31 (19)     | 15.24 ± 1.32 (25)         | 10.47 ± 1.30 (18)          | 16.94 ± 1.35 (42)      | 15.67 ± 1.24 (42)      | 22.44 ± 1.70 (27)          | 21.03 ± 0.88 (57)         | 21.87 ± 2.17 (35) | 26.39 ± 1.95 (57) | 19.91 ± 1.59 (43) | 15.77±1.12 (53) |
| G (rs846910) | 88.96 ± 2.52 (137)  | 90.85±2.25 (149)       | 88.19 ± 2.69 (127)        | 91.38 ± 2.13 (159)         | 88.75 ± 2.04 (213)     | 84.8 ± 2.27 (212)      | 87.5 ± 2.07 (224)          | 85.59 ± 2.28 (202)       | 87.86 ± 2.76 (123) | 80.58±2.76 (166)   | 80.84±2.69 (173) | 89.42±1.74 (279) |

*Only the significant findings (p < 0.05) are demonstrated in this table with p-value.
*High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG), Total Cholesterol (TC), Glucose (Glu), Abdominal Circumference (AC)
*The n of these groups are demonstrated in parentheses.

Discussion

Blood lipid levels are influenced by environmental and genetic factors (Crook, 2012). Small increments in LDL-C are the primary target for reducing cardiovascular risk (Reisch et al., 2016). In our study, as shown in Figure 1, it was observed that the APOE ε2 allele was associated with lower LDL-C levels in the total sample as well as in both girls and boys, which is consistent with the known protective effect of this allele. (Crook et al., 2012). The APOE ε2 allele appears to be protective with lower HDL-C levels, which supports the notion that the ε2 allele is an atherogenic risk factor (Frikke-Schmidt et al., 2009; Benet et al., 2007; Fuzikawa et al., 2008; Ward et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) and the protective effect of this allele (Frikke-Schmidt et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) in children and adolescents, similar to our previous findings (Frikke-Schmidt et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) in children and adolescents. Additionally, differences in allele frequencies were also found between boys and girls, which may be related to the different levels of sex hormones (Sharma et al., 2002) and other associated factors. The APOE ε2 allele appears to be associated with genetic factors (Cao et al., 2017; Crook et al., 2012), and it is known that the APOE ε2 allele is associated with BMI following the order: apo E4 > apo E3 > apo E2 (Yolk et al., 2006; Tabalban et al., 2012). Besides its association with the lipid profile, some studies have demonstrated that the APOE ε2 allele is associated with obesity (Volcik et al., 2012). According to the Atherosclerosis Risk in Communities (ARIC) study, the apo E genotypes were associated with BMI following the order: apo E4 > apo E3 > apo E2 (Tabalban et al., 2012). The APOE ε2 allele appears to be associated with lower HDL-C levels, which support the notion that the ε2 allele is an atherogenic risk factor (Frikke-Schmidt et al., 2009; Benet et al., 2007; Fuzikawa et al., 2008; Ward et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) and the protective effect of this allele (Frikke-Schmidt et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) in children and adolescents, similar to our previous findings (Frikke-Schmidt et al., 2009; Nascimento et al., 2009; Bazzaz et al., 2008; Ward et al., 2010; Ferreira et al., 2012) in children and adolescents. Additionally, differences in allele frequencies were also found between boys and girls, which may be related to the different levels of sex hormones (Sharma et al., 2002) and other associated factors. The APOE ε2 allele appears to be associated with genetic factors (Cao et al., 2017; Crook et al., 2012), and it is known that the APOE ε2 allele is associated with BMI following the order: apo E4 > apo E3 > apo E2 (Yolk et al., 2006; Tabalban et al., 2012). Besides its association with the lipid profile, some studies have demonstrated that the APOE ε2 allele is associated with obesity (Volcik et al., 2012). According to the Atherosclerosis Risk in Communities (ARIC) study, the apo E genotypes were associated with BMI following the order: apo E4 > apo E3 > apo E2 (Tabalban et al., 2012).
Table 3 - Comparisons of APOE allele frequencies between groups below and above the median for the analyzed variables, and between eutrophic and overweight/obese individuals stratified by sex.

| Alleles in | CT (mg/dl) | LDL-C (mg/dl) | TG (mg/dl) | HDL-C (mg/dl) | AC (cm) | Obesity status |
|------------|------------|---------------|------------|---------------|--------|----------------|
| Girls Group | Above the median | Below the median | Above the median | Below the median | Above the median | Below the median | Above the median | Below the median | Eutrophic | Overweight/obese |
| e2 (APOE - rs7412 and rs429358) | 2.33±0.25 (2) | 7.14±0.85 (5) | 1.22±0.14 (1) | 8.11±0.94 (6) | 2.44±0.27 (2) | 6.25±0.70 (5) | 5.21±0.53 (5) | 3.03±0.37 (2) | 0.00±0.00 (0) | 0.00±0.00 (0) | 3.12±0.55 (1) | 4.55±0.40 (6) |
| E3 (APOE - rs7412 and rs429358) | 83.72±9.03 (72) | 82.86±9.90 (58) | 84.15±9.29 (69) | 82.43±9.58 (61) | 82.93±9.16 (68) | 81.25±9.08 (65) | 87.5±8.93 (84) | 74.24±9.14 (49) | 66.67±11.11 (24) | 68.75±12.15 (22) | 84.38±14.91 (27) | 81.06±7.06 (107) | 0.0001 |
| e4 (APOE - rs7412 and rs429358) | 13.95±1.74 (12) | 10.00±1.86 (7) | 14.63±1.75 (12) | 9.46±1.81 (7) | 14.63±1.86 (12) | 12.5±1.98 (10) | 7.29±1.16 (7) | 22.73±3.15 (15) | 33.33±5.56 (12) | 31.25±5.52 (10) | 12.5±2.71 (4) | 14.39±1.60 (19) |

| Alleles in | CT | LDL-C | TG | HDL-C | AC | Eutrophic | Overweight/obese |
|------------|----|-------|----|-------|----|-----------|----------------|
| Boys Group | Above the median | Below the median | Above the median | Below the median | Above the median | Below the median | Above the median | Below the median | Eutrophic | Overweight/obese |
| e2 (APOE - rs7412 and rs429358) | 5.81±0.63 (5) | 6.38±0.66 (6) | 3.84±0.44 (3) | 7.84±0.78 (8) | 6.79±0.53 (11) | 4.17±0.30 (8) | 5.00±0.37 (9) | 5.68±0.43 (10) | 7.35±0.63 (10) | 2.91±0.22 (5) | 3.80±0.28 (7) | 5.88±0.41 (12) |
| e3 (APOE - rs7412 and rs429358) | 81.40±8.78 (70) | 79.79±8.23 (75) | 79.49±9.00 (62) | 81.37±8.06 (83) | 74.69±5.87 (121) | 79.16±5.71 (152) | 81.67±6.09 (147) | 72.73±5.48 (128) | 73.53±6.30 (100) | 71.51±5.45 (123) | 75.00±5.53 (138) | 77.45±5.42 (158) |
| e4 (APOE - rs7412 and rs429358) | 12.79±1.91 (11) | 13.83±1.98 (13) | 16.67±2.28 (13) | 10.79±1.67 (11) | 18.52±1.92 (30) | 16.67±1.47 (32) | 13.33±1.31 (24) | 21.59±2.01 (38) | 19.12±2.18 (26) | 25.58±2.16 (44) | 21.20±1.82 (39) | 16.67±1.52 (34) |

* Only the significant findings (p < 0.05) are demonstrated in this table with p-value.
* High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG), Total Cholesterol (TC), Glucose (Glu), Abdominal Circumference (AC).
* The n of these groups are demonstrated between parentheses.
levels, and according to some studies this polymorphism could be associated to metabolic syndrome (Nair et al., 2004; Duran-Gonzalez et al., 2011; Dujic et al., 2012). However, Turek et al. (2014) found that the A allele was associated with higher HDL-C levels only in women. Furthermore, it is relevant to consider that a possible linkage disequilibrium might exist with another polymorphism in the HSD11B1 gene, and another allele could be the cause of an altered lipid profile or features related to obesity (Malavasi et al., 2010).

Although our study had relevant findings, we recognize that the small sample size is a limitation, thus generalizability should be done with caution, and studies with larger samples should be done. In summary, we found that in children and adolescents, as in adults, the e4 and e3 alleles could be considered a contributing factor for dyslipidemia and traits related to obesity, respectively, while the e2 allele seems to be a protective factor, contributing to lower LDL-C and higher HDL-C levels. Furthermore, the HSD11B1 gene G allele seems to be related to obesity. Considering that effects may start early in life, a precocious intervention could be planned, therefore preventing many complications resulting from altered lipid profile and obesity.

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