British Journal of Medicine & Medical Research
16(5): 1-10, 2016, Article no.BJMMR.24670
ISSN: 2231-0614, NLM ID: 101570965

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Association of the Lipoprotein Lipase S447X and Neuropeptide Y Leu7Pro Genetic Polymorphisms with the Lipid Profiles of Individuals with and without Evidence of Coronary Artery Disease

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Authors' contributions

This work was carried out in collaboration between all authors. Authors MDBF, DBS, GDP and FRS designed the study and wrote the protocol. Authors WOP, AG and DCF managed the field work with the individuals participating in the study. Authors WOP, SOTK and CRM managed the experimental process in the laboratory. Authors WOP, MDBF, DBS and FRS managed the analyses of the study results. Authors WOP, SOTK and FSO managed the literature searches and wrote the first draft of the manuscript. Author MDBF coordinated the project and the Grants. Authors GDP and JYP interpreted data, reviewed the manuscript and edited. All authors contributed to the writing, read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/24670
Editor(s):
(1) Vijay K. Yadav, Metabolic Research Laboratory, National Institute of Immunology, Aruna Asaf Ali Marg, New Delhi, India.
Reviewers:
(1) Volodymyr Chernyshenko, Palladin Institute of Biochemistry NAS of Ukraine, Ukraine.
(2) Eman Ali Toraih, Suez Canal University, Egypt.
Complete Peer review History: http://sciencedomain.org/review-history/15028

Original Research Article

Received 28th January 2016
Accepted 3rd June 2016
Published 15th June 2016

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ABSTRACT

Background: Coronary artery disease (CAD) is a multifactorial disease whose etiogenesis involves a number of environmental, genetic and lifestyle-related factors. Genetic polymorphisms are noteworthy among these factors because they alter gene expression and, thus, the functions of the respective products.
Methods: A case-control study was conducted in the Cardiology Institute, with 79 subjects classified as cases with CAD, and 96 subjects as controls without CAD or other disease. In this study, we evaluated the association between the single-nucleotide polymorphisms (SNPs) of S447X and Leu7Pro of the lipoprotein lipase (LPL) and neuropeptide Y (*NPY*) genes, respectively.
Results: No differences were found in the frequencies of *LPL* SNP between the cases and controls. However, the *LPL* 447X allele carriers exhibited a near-significant difference in the triglycerides (*p=0.086*) and higher mean in the HDL-c (*p=0.018*). *NPY* polymorphisms proved to be infrequent in this study population, and no significant difference was observed between the groups.
Conclusions: Our findings provide further support of the genetic polymorphisms effect on the lipid metabolism control. So, further studies are needed to assess the functional effect of this and other polymorphisms, on *LPL* and in the *NPY* activity, and their impact on CAD risk.

Keywords: Coronary artery disease; lipoprotein lipase; neuropeptide Y; single-nucleotide polymorphisms.

ABBREVIATIONS

AAs : Autoantibodies;
AT1-AAs: Autoantibodies against angiotensin AT1 receptors;
CAD : Coronary artery disease;
HDL-C : High-density lipoprotein cholesterol;
HLA : Leukocyte antigen;
LDL-C : Low-density lipoprotein cholesterol;
Leu7Pro : NPY genes;
LPL : Lipoprotein lipase;
NPY : Neuropeptide Y;
PCR : Polymerase chain reaction;
S447X : LPL gene;
SNPs : Single-nucleotide polymorphisms;
TG : Triglyceride;
VLDL : Very low-density lipoprotein.

1. INTRODUCTION

Coronary artery disease (CAD) stands out among cardiovascular diseases as the leading cause of death worldwide, it's responsible for approximately 17.3 million deaths per year, and 7 million because CAD. These figures are predicted to be even higher in the future, primarily in developing countries. In Brazil, cardiovascular diseases, especially CAD, are the leading cause of natural deaths, accounting for 286 deaths *per* 100,000 inhabitants [1].

Many genetic risk markers have been associated with cardiovascular diseases, such as HLA-DRB1 or HLA-DQB1 polymorphism that are related to an increased frequency of autoantibodies (AAs) against angiotensin AT1 receptors (AT1-AAs) found in patients with essential hypertension, [2] others provides some genetic and environmental influences in the cardiometabolic disorders [3] Indeed, mutations may promote changes in gene products in key pathways involving lipid metabolism, eating behaviors, the response to the inflammatory process or blood coagulation [4].

The genes encoding the lipoprotein lipase (LPL) enzyme and the neuropeptide Y (NPY) neurotransmitter stand out among candidate genes for CAD susceptibility, because they are involved in circulatory homeostasis [5]. LPL plays a key role in triglyceride (TG) metabolism, as it is able to hydrolyze the TG contained in lipoproteins, including chylomicrons and very low-density lipoprotein (VLDL), when adhered to the endothelial surface of blood capillaries [6].

NPY has been shown to be a key neurotransmitter that is able to regulate satiety, and have been associated with high serum lipid levels and cardiovascular disease [7] Findings reported by Kaipio et al. [8], showed that NPY is associated with appetite control and mutations in this gene affect food intake and obesity, risk factors for CAD.

The present study assessed whether polymorphisms in the lipoprotein lipase (*S447X*) and neuropeptide Y (*Leu7Pro*) genes affect the onset of CAD and the lipid profiles of cases and controls.

2. MATERIALS AND METHODS

2.1 Subjects

A case-control study was conducted with 175 participants; 79 (45.14%) classified as cases with CAD, and 96 (54.86%) as controls without CAD or other disease. Were included in the case group, CAD carriers with documented disease or an episode of myocardial infarction and the presence of electrocardiographic characteristic alterations. Each group was paired according to gender and age group (5-year intervals). Individuals without CAD history were evaluated by clinical and cardiac exams and only those who had exhibited normal resting and stress test electrocardiograms were enrolled in control group. Carriers of rheumatic, hepatic, renal, endocrine and neurological diseases were excluded. The study was approved by the Research Ethics Committee of Santa Cruz State University (Protocol 324/09). All study participants were volunteers and willingly signed an Informed Consent Form.

2.2 Anthropometric Data

Weight and height were measured with the subjects standing barefoot and wearing light clothing, using a Plenna® portable scale with 100-g accuracy and a 150-kg capacity and a portable stadiometer with a 0.1 cm accuracy. Circumference measurements were performed at the waist, hip and abdomen using a measuring tape made of non-expandable synthetic material, graduated in millimeters.

2.3 Biochemical Assessment

Blood samples were collected in vacuum tubes by puncture of the median cubital vein and were used for assessing TG, total cholesterol and high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and VLDL cholesterol, according to protocols described by the manufacturers of the applied diagnostic kits (Liquiform: Labtest Diagnóstica S.A. Lagoa Santa-MG, Brazil).

2.4 DNA Extraction and Amplification

Genomic DNA extraction was performed in the Laboratory of Immunopathology and Genetics of the Federal University of Recôncavo da Bahia according to the manufacturer's recommendations (KiagenFlexigene 250®). The extracted DNA was spectrophotometrically quantified (Smart SpecTM Plus, BioRad) by reading the absorbance at 260 nm.

2.5 Polymorphism Analysis of the *LPL* and *NPY* Genes via Polymerase Chain Reaction

The *LPL* and *NPY* genes were amplified via polymerase chain reaction (PCR), based on previous studies (Munshi et al. 2012 and Masoudi-Kazemabad et al. 2012), using 50 ng of genomic DNA in a 25-µl reaction, with 10 mM Tris-HCl, pH 8.3, 50 mM KCl, 1.5 mM MgCL2, dNTPs and 0.5 µg of each primer. The primers used for the *LPL* gene were LPL1 – forward, 5'-TAC-ACT-AGC-AAT-GTC-TAG-CTG-A-3' and LPL2 – reverse, 5'-TCA-GCT-TTA-GCC-CAG-AAT-GC-3' (DNA Express Biotecnologia LTDA), together with 1.25 U of Taq DNA-polymerase (QIAGEN). The reaction mixture was subjected to pre-treatment at 90℃/5 min, followed by 35 cycles at 94℃/1 min, 60℃/30 sec and 72℃/45 sec, with a final step at 72℃/2 min, generating a 488-bp PCR product. The primers for the NPY gene were NPY1- forward, 5'-CCC-GTC-CGT-TGA-GCC-TTC-TG-3' and NPY2-reverse, 5'-CGG-TCC-CGC-GGT-CCC-3' (DNA Express Biotecnologia). The reaction mixture was subjected to pretreatment at 94℃/5 min, followed by 30 cycles at 94℃/1 min, 69℃/1 min and 72℃/1 min, with a final step at 72℃/10 min, in a thermocycler (Amplitherm), generating a 238-bp PCR product.

2.6 Restriction Fragment Length Polymorphism (PCR-RFLP) Analysis

Following amplification, 20 µl of LPL DNA was digested using 1.25 U of MnLI at 37ºC for 18 h, and the resulting fragments were separated via electrophoresis in a 2% agarose gel (Pronadisa), which was stained using GELRED dye (Bitium). The presence of 288- and 200-bp fragments indicates a homozygous wild-type allele (CC), while the presence of 250-, 200- and 38-bp fragments indicates a homozygous mutant allele (GG), and 288-, 250-, 200- and 38-bp fragments indicate a heterozygous allele (CG genotype; rs:328 - http://www.ncbi.nlm.nih.gov/). The wild-type and mutant alleles were expressed as S447 and X447, respectively. For the NPY gene, 20 µl of amplified DNA was digested using 1.25 U of BsiEI at 37℃ for 18 h, and the resulting fragments were separated using electrophoresis in a 2% agarose gel stained with GELRED. The

presence of the 238-bp fragment indicates a homozygous wild-type allele (Leu7/Leu7), while the presence of 190- and 48-bp fragments indicates a homozygous mutant allele (Pro7/Pro7), and the presence of 238-, 190- and 48-bp fragments indicates heterozygous alleles (Leu7/Pro7; rs:16139 - http://www.ncbi.nlm.nih.gov/). The results were recorded by taking photos and using a digital storage system (EDAS 290, Kodak: cat. No. 8486045).

2.7 Statistical Analysis

The data were entered into EpiData 3.0, and analyses were performed in STATA 9.0. The description of cases and controls was conducted according to the presence of lipoprotein lipase and neuropeptide Y polymorphisms, gender, age and socio-economic status, beyond the lipid profile. Continuous variables were compared using Student's t test and categorical variables using the chi-squared test. A *p-value* of less than 0.05 was considered statistically significant. The frequencies of all of the identified alleles, genotypes and phenotypes were represented as percentages. The genotype frequencies observed for LPL and NPY SNPs were tested for Hardy-Weinberg equilibrium (HWE) between cases and controls.

3. RESULTS AND DISCUSSION

In order to correlate the *LPL* and *Leu7Pro* gene polymorphism with the development of CAD, were evaluated 175 individuals, 79 (45.14%) classified as cases with CAD, and 96 (54.86%) as controls without CAD or other disease. The mean age of case group was 64.8±8.8 years, including 54 men and 25 women. The mean age of the control group was 63.0±9.2 years, including 62 men and 34 women. No statistic difference in age was found between the groups (Table 1).

Similarly, no significant difference was found between the ethnic groups, consisting of 11 men and twelve white women patients and eight men and fourteen white women controls; four men and twelve black women patients and six men and eighteen black women controls; ten men and twenty admixed women patients and thirty men and twenty admixed women controls (Table 1).

The S447X polymorphism is one of the most frequent among the various proteins involved in the intravascular lipid metabolism, showing frequencies ranging from 17 to 22% in Caucasian populations [9]. Similar values were found in Brazil when assessing carriers and non-carriers of this polymorphism [5]. In our study we found 16% of carriers for the LPL S447X polymorphism in groups, case and control.

More specifically, according to the work of Pena et al. 2010 [10] and the self-declaration of the participants with regard to ethnicity, 14% white, 13% black, 17% admixed and one native people carry the *LPL* heterozygous genotype in the control group. And in the case group, 18% white, 11% black, 18% admixed carries the *LPL* heterozygous genotype, showing no significant differences between than (*p=0.807*). We also found in the control group, a black man and a admixed woman homozygous mutant (G/G) (Table 2).

Others studies with different populations have shown different frequencies, as in Sudan, where the allele frequency *LPL* heterozygous genotype was 7.1% [11]. Similarly, the *LPL* heterozygous genotype variant in the Venezuela population was 9.4%, and the homozygous mutant was not identified [12] Minor frequencies of *LPL* 447X allele were 11.1% and 6.2% among subjects without CAD compared with CAD subjects in the Turkey population [13].

Statistically significant differences were observed between the cases and controls in relation to total cholesterol and LDL-c concentrations in the blood plasma, with the concentrations being lower in the cases than in the controls (*p<0.001*; Table 1). These results were probably because the cases used hypocholesterolemic medication, such as statins. On the other hand, the abdominal circumference measurements were significantly larger in the cases than controls (*p=0.034*; Table 1), evidenced by the higher BMI in case group, demonstrating greater amount of overweight or obese individuals, although there was no statistical difference between groups (Table 1). As can be seen, there is a prevalence of overweight and obesity in the Northeast Brazilian population, in this age group, confirmed in other study carrying out in the same country region [14].

The distribution of the lipid and anthropometric profiles was assessed among the carries and no-carries *LPL* heterozygous genotype variant individuals (Table 2). Higher mean concentrations of TG and total cholesterol and lower mean HDL-c concentrations occurred in the non-carrier group, although there was a lack of statistical significance between the groups.

When we comparative the lipid profiles just in the case group, *LPL* heterozygous genotype carriers variant showed lower mean TG levels compared with non-carriers. In addition, a statistically significant difference was observed in the mean HDL-c concentrations between carriers and non-carriers polymorphism, with higher levels being found among carriers (*p=0.018*) (Table 3).

In another study with an Iranian population, the *LPL* S447X (rs328-GG-GC) genotype was significantly related to a higher concentration of TG, compared to the CC wild-type [15] Likewise, triglycerides were significantly lower in African American women with the -93GG compared to the -93TT *LPL* genotype [16].

Table 1. Characteristics of the study participants regarding their lipid and anthropometric profiles

Variable	Cases (n = 79)	Controls (n = 96)	Significance (*p*)
Age (years)	64.8±8.8	63.0±9.2	0.177
Gender M/F	25/54	34/62	0.599
Withe M/F	11/12	8/14	0.817
Blacks M/F	4/12	6/18	1.000
Admixed M/F	10/20	20/30	0.551
TC (mg/dl)	161.3±44.4	190.7±44.8	<0.001
HDL-c (mg/dl)	43.1±8.9	41.6±9.0	0.280
LDL-c (mg/dl)	89.8±33.1	115.4±39.6	<0.001
TG (mg/dl)	146.1±102.5	175.6±103	0.063
VLDL-c (mg/dl)	30.7±20.9	34.9±20.6	0.191
BMI (kg/m^2)	27.1±3.9	26.1±4.4	0.117
HC (cm)	97.8±7.8	95.1±8.7	0.034
AC (cm)	97.3±10.2	94.5±11.8	0.111

Differences between groups were assessed using Student's t-test; Gender M/F: male / female; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; VLDL-c: very low density lipoprotein cholesterol; BMI: body mass index; HC: hip circumference; AC: abdominal circumference

Table 2. Distribution of the lipid and anthropometric profiles of carriers and non-carriers of the S447X polymorphism

Variable	S447X+447X (n = 30); Carriers	S447 (n = 142); Non-carriers	Significance (*p*)
Age (years)	64.5±9.6	63.7±9.0	0.653
Gender M/F	6/24	53/89	0.069
TC (mg/dl)	175.2±46.1	178.9±47.4	0.697
HDL-C (mg/dl)	43.5±7.3	42.2±9.8	0.500
LDL-C (mg/dl)	102.9±38.1	104.7±39.2	0.818
TG (mg/dl)	145.6±96.2	166.8±106.4	0.315
VLDL (mg/dl)	31.74±20.1	33.5±21.2	0.678
BMI (kg/m2)	26.6±4.2	26.5±4.2	0.880
HC (cm)	95.4±9.3	96.5±8.2	0.536
AC (cm)	97.3±13.1	95.4±10.8	0.405

Differences between groups were assessed using Mann-Whitney; TC - total cholesterol; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; VLDL-C - very low-density lipoprotein cholesterol; BMI - body mass index; HC - hip circumference; AC - abdominal circumference

Table 3. Distribution of lipid profile in the CASES between carriers and non-carriers of the S447X polymorphism

Lipid (mg /dl)	S447X + 447X (n = 13); Carriers	S447 (n = 65) non-carriers	Significance (*p*)
HDL	49.0±4.1	42.7±8.3	0.018
TG	103.2±48.4	165.8±116.2	0.086
CT	176.2±28.5	167.5±45.8	0.549
LDL	106.9±25.9	91.7±33.6	0.164

Differences between groups were assessed using Student's t-test; HDL-C - high-density lipoprotein cholesterol; TC - total cholesterol; LDL-C - low-density lipoprotein cholesterol;

The 447X allele had favorable effects on lipid levels among Turkey CAD patients. Homozygotes and heterozygotes displayed lower total cholesterol, lower TG, and lower LDL-c [13]. The S447X was significantly different between the Iranian patients with CAD and the healthy subjects ($p<0.001$), and the presence of S447X G allele polymorphism increases the TG level and decrease HDL-c level [17]. Besides, the S447X and *APO E* polymorphisms may have a synergetic effect and alter plasma triglyceride concentration in overweight Greek men [18].

On the basis of genome wide association data and HDL-c and TG concentrations, in other study with men and women Koreans, the polymorphism, was in high linkage disequilibrium with the serine 447 stop (S447X) LPL mutation. The authors found that T allele carrying reflecting the *LPL* S447 allele was positively associated with follow-up measurement of HDL-c concentrations, suggesting that carriers of the *LPL* S447 allele have the benefit from moderate alcohol consumption and a diet high in unsaturated fat to minimize reduction of blood HDL-c concentrations and that obese persons who do not carry the *LPL* S447 allele need to control body weight to prevent hypertriglyceridemia [19].

In addition to the direct correlation of *LPL* polymorphism with lipid levels in the blood and consequently a higher risk for CAD, these mutations have been implicated in other diseases. A meta-analysis compared with 447SS homogeneous carriers, those with 447X variant had a lower risk of hypertension. Similarly, compared with 447S allele carriers, those with 447X allele carriers also had a lower risk of hypertension [17]. The genotype CC of S447X was associated with high systolic blood pressure, high diastolic blood pressure, and with increase of total cholesterol in Mexican families [18]. It was shown that, diabetes mellitus led to loss of the protective lipid profile in patients with CC genotype in Egyptians. In addition, rs328 is associated with a favorable lipid profile in diabetic Egyptian patients [19]. Genetic variants of LPP, including rs328 also showed significant correlations with incident ischemic stroke in Chinese diabetic population [20].

The results of the present study suggest a trend of the rs328 has a protective effect against CAD by increasing the LPL enzymatic activity. These findings highlight lower mean lipid levels among carriers of rs328 compared with non-carriers. Our findings corroborate with what were reported by other authors, [13] although just few studies had been published associating the *LPL* polymorphism with CAD. Research on the association of the rs328 with lipid concentrations and the risk of CAD indicate significant differences, with lower levels of TG and higher HDL-c levels found in carriers, suggesting that this polymorphism provides protection against CAD and is associated with a significant reduction in disease severity [13,21]. High HDL-c levels and lower TG concentrations help to prevent early CAD, [22] and reducing the risk of developing cardiovascular disorders related to lipid metabolism [23].

Plasma levels of NPY become elevated due to the increased sympathetic activation present in stress-related cardiac conditions. Also, *NPY* and Y receptor polymorphisms have been identified that may predispose individuals to increased risk of hypertension and cardiac complications [24] The *Leu7Pro* polymorphism originally has been reported to be associated with high levels of plasma lipids, which are associated, in turn, with an increased risk for cardiovascular disease [25,26,27], and more recently with myocardial infarction, ischemic stroke and accelerated progression of atherosclerosis, [28,29] and hypertension [30].

The allele frequency of the *NPY* rs16139 was investigated in 6,626 subjects from Europe, North-America, South-America, Asia and the Middle-East, and shows significant differences between some populations with different genetic backgrounds, ranging from 0.5 to 10% [31,32]. The *NPY* rs16139 was observed in all populations of European descent and the Israeli population, with a mean frequency of about 4%. The highest frequencies of this polymorphism have been observed in Nordic countries, providing a geographic pattern of its distribution with a decreasing gradient from north to south. [31] On the other hand, the frequency of rs16139 of *NPY* was 5.9% in the Iranian population [33].

A previous Brazilian study showed a 0.03 minor allele frequency of rs16139 allele frequency [34]. The occurrence of rs16139 of *NPY* proved to be infrequent too in our study population. Only 6 of the 175 (3.4%) individuals showed a heterozygous genotype (A/C) and homozygous polymorphisms were not found; which indicate that it is expected based on known minor allele frequency (Table 4).

Nevertheless, a significantly higher frequency of the Leu7Pro genotype it was observed in Iranian CAD patients, where the Pro7 had significantly

higher values for weight, BMI, hip circumference and prevalence of diabetes mellitus [33]. Furthermore, there was a significant difference in Pro7 frequency between diabetics versus nondiabetics, dyslipidemic versus nondyslipidemic, and obese versus nonobese Iranian CAD patients [28]. A logistic regression analysis indicated that the *NPY* polymorphism rs16147 was nominally associated with an increased risk of CAD. In stratified analyses, the C allele was significantly associated with a reduced risk of CAD in Iranian males and subjects who were <50 years of age [35]. On the other hand, the frequency of the variant G allele of the *NPY* gene was significantly higher in CAD patients without metabolic syndrome. Compared to the AA genotype of the *NPY* gene, where Iranian individuals carrying the GG genotype had a reduced risk of metabolic syndrome [35].

In a multicentric study, the functional *NPY* variant rs16147, C allele was associated with a greater reduction in waist circumference. In addition, the authors found statistically significant genotype-dietary fat interaction on the change in total abdominal adipose tissue, visceral adipose tissue, and subcutaneous adipose tissue at 24 months, where the rs16147 T allele appeared to associate with more adverse change in the abdominal fat deposition in the high-fat diet group than in the low-fat diet group [36]. A study with Caucasian women found the CT-genotype of the SNP rs16147 to be significantly associated with lower waist-to-hip ratio, compared to homozygote gene carriers. However, no association between rs16147, waist-to-hip ratio and serum leptin levels was found in Caucasian men in the same study [37].

The NPY polymorphism distribution in our study population was analyzed in relation to carriers (Leu7Pro) and non-carriers of *NPY* Leu7Leu, and no significant difference (*p=0.151*) were observed between the groups (Table 4), although higher concentrations of total cholesterol and LDL-c were found among carriers than non-carriers individuals. Additionally, lower levels of TG and VLDL and a lower BMI and hip circumference were observed in carriers versus non-carriers of the *NPY* Leu7Pro polymorphism in the analysis of the lipid and anthropometric profile in this study.

Both rs16147 and *NPY* alleles (rs16131) were associated with the risk of obesity, and the latter was also associated with insulin resistance, triacylglycerol's leptin, and HDL-c in Spanish children, confirming the association of these *NPY* alleles with obesity, and its possible impact on the early onset of metabolic syndrome features, mainly triacylglycerol [38]. Another study, conducted with children, adolescence, and young adults in a German community, homozygote carriers of the *NPY* alleles exhibited significantly lower BMI scores when compared with individuals carrying the T allele. In addition, a significant genotype by age interaction emerged, indicating that the genotype effect increased during the course of development [39]. Two SNPs (rs17149106 (G>T) and *NPY* alleles (T>C), with minor allele frequencies of 4%, were associated with elevated risks of obesity. TTCC carriers had an increased risk of obesity compared with those carrying the common haplotype GCTT. Carriers of the *NPY* alleles had greater BMI than non-carriers. The *NPY* alleles were associated with weight gain since adolescence/early adulthood, but were not associated with abdominal adiposity as measured by waist circumference and waist to hip ratio in that study [40].

Table 4. Distribution of the lipid and anthropometric profiles of carriers and non-carriers of the Leu7Pro polymorphism

Variable	Leu7Pro (n = 6) carriers;	Leu7Leu (n = 116) non-carriers	Significance (*p*)
Age (years)	61.5±7.4	63.9±9.2	0.517
Gender M/F	2/4	57/109	0.959
TC (mg/dl)	182.8±26.0	178.1±47.7	0.810
HDL-C (mg/dl)	47.6±10.9	42.3±9.3	0.173
LDL-C (mg/dl)	106.8±25.0	104.3±39.6	0.877
TG (mg/dl)	141.8±38.9	163.8±106.0	0.613
VLDL (mg/dl)	28.3±7.9	33.3±21.3	0.566
BMI (kg/m2)	24.6±4.5	26.6±4.2	0.209
HC (cm)	95.1±7.3	96.4±8.4	0.519

Differences between groups were assessed using Student's t-test; TC - total cholesterol; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; VLDL-C - very low-density lipoprotein cholesterol; BMI - body mass index; HC - hip circumference;

4. CONCLUSION

The results obtained in this study corroborate with others studies, where S447X polymorphism can be associated with decreased TG and increased HDL-c concentrations, especially in individuals with CAD. Although there was a low frequency of the NPY polymorphism in the study population, the mean HDL-c levels were higher and TG lower among Leu7Pro carriers. Further studies should be conducted to better assess the trends found in this study.

FUNDING

This study was funded by the Bahia State Research Foundation (*Fundação de Amparo à Pesquisa do Estado da Bahia*, FAPESB), Grant Agreement (*Termo de Outorga*) 074/2010, and the Federal University of Recôncavo da Bahia (Universidade Federal do Recôncavo da Bahia, UFRB).

ACKNOWLEDGEMENTS

We are thankful for help from UFRB technicians José Mario Ferreira dos Santos, Glauber Andrade dos Santos and Taiana de Araújo Conceição for the valuable work conducted in the development of this research.

COMPETING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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