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Variants of D9N, G188A, N291S, and 93 T/G Genes in patients with Coronary Artery Diseases

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ABSTRACT

Objective: Our work aimed to study the relationship between LPL variants D9N, G188A, N291S, and 93 T/G genes and CAD in Saudi patients.

Materials and Methods: We recruited 253 CAD patients, who underwent diagnostic coronary angiography, and 207 control subjects. Several biochemical and behavioral markers were obtained, and different genotypes of LPL variants, D9N, G188E, N291S, and 93 T/G, were detected using The PCR-RFLP method.

Results: The current study found D9N genotypes, AA, AG, and GG in 71.14%, 23.72%, and 5.14% in CAD patients, respectively. the AA, AG, and GG control genotypes were found in 81.64%, 16.43%, and 1.93%, respectively. The OR of the D9N AA versus AG genotype with a 95% CI was determined to be 1.65 (1.04–2.65), (p = 0.035). The OR of the D9N AA versus AG + GG genotype with a 95% CI was 1.80 (1.16–2.81), (p = 0.009). A strong relation of the D9N AA was observed with CAD. For the G188E, N291S, 93T/G variants insignificant were observed in both CAD and control groups.

Conclusion: This study revealed the D9N variant has an association with CAD; however, no relation was detected between CAD and G188E, N291S, and 93T/G variants in the Saudi patients.

Keywords: LPL, allele, coronary artery disease, gene variant, lipid.

INTRODUCTION

Lipoprotein lipase (LPL) is an essential glycoprotein enzyme that plays a role in lipid metabolism (1). The LPL activity is an essential step in the clearance of triglyceride-rich lipoproteins. The clearance of lipoprotein is enhanced by binding LPL with chylomicrons and transported to the liver via LDL receptor-related protein (2, 3). The essential function of LPL in adipose tissue, muscle, and macrophages release the free fatty acids by the hydrolysis of triacylglycerol of chylomicrons and very low-density protein. (4, 5). It has been observed that the prevalence of atherosclerosis has increased all over the world associated with the complications of cardiovascular diseases. (6). Cardiovascular diseases (CAD) and their complications are knowing one of the major causes of death worldwide (7). Any disturbance in the level of LPL or its activity leads to diminish the level of high-density lipoprotein cholesterol (HDL-C) and elevated triacylglycerol level, which are risk factors that develop the coronary artery disease (8, 9). In an early atherogenic process, LPL expression in macrophages and other cells in vascular walls is associated with atherosclerosis (10). Genome-wide association studies have identified some loci linked to plasma lipid traits associated with altered LPL gene expression (11). A previous study described that a polymorphism of the LPL gene is linked with plasma lipid concentrations and clinical conditions in different populations (12). Furthermore, many studies have reported that the LPL gene variants are found in coding and non-coding regions (13-15). Moreover, it has been found that 80% of LPL gene variants occur in coding regions, while 20% are found in non-coding regions (16, 17). The length of the LPL gene is 30 Kb on chromosome 8p22 containing 10 exons encoding a 448 amino acid long protein. Several studies reported more than particular 100 mutations and polymorphisms in simple nucleotides of the LPL gene (18, 19). Several genetic LPL mutations and metabolic disturbances that alter the lipid and lipoprotein metabolism have been reported as CAD risk factors. (20).

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In addition to these mutations, four variants identified in the LPL gene impair the catalytic function of LPL, namely Asp9Asn (D9N, rs1801177, G280A) in exon 2, G188E (G188A) in exon 5, and Asn291Ser (N291S, rs268, A1127G) in exon 6 within the gene coding region, and 93 T/G in LPL promoter (21-24). From the transcription start site at position 93 a single nucleotide transition from T to G (93 T/G) was identified; (rs1800590, T93G) (24). The homozygous form of Asn291Ser, Gly188Glu, and Asp9Asn mutations are associated with familial chylomicronemia. In some population groups, the percentage of heterozygous mutations is (3–7%) (19). In the subjects with combined hyperlipidemia, the frequency of Asp9Asn mutations carriers was found to be approximately 4–9.8 %, while it was 3% in healthy subjects (21). In a rare mutation Gly188Glu, the glutamic acid (Glu) substituted to glycine (Gly), at position 188 in the mature enzyme and characterized with high triacylglycerol and low HDL-c plasma levels (25). This substitution represents 22% of the mutant alleles in a cohort of 56 affected subjects that appear to be a common cause of LPL deficiency (26). In hypertriglyceridemia women (16 mmol/L) the Asn291Ser mutation was associated with the high levels of plasma triacylglycerol (27). In CAD Saudi patients, the assessment of four LPL variants (Asp9Asn (D9N, rs1801177, G280A), Gly188Glu (G188A), Asn291Ser (N291S, rs268, A1127G) has not clear. So, this study evaluates the relation between four LPL gene variants and CAD in Saudi patients.

MATERIAL and METHODS

Subjects

Subjects were selected from Cardiology Department, King Khalid University Hospital at King Saud University (KSU) in Riyadh, Kingdom of Saudi Arabia (KSA). They were composed of 253 CAD (137 males and 116 females, mean age 61.73 ± 8.34 years) and 207 participants were healthy control (118 males and 89 females, mean age 58.27 ± 8.46 years). The CAD of the patients was assessed by cardiologists through the review of angiograms. The study was reviewed and approved by the ethics committee, College of Medicine, King Saud University, Riyadh, Saudi Arabia. The subjects who participate in this study Sign their written informed consent.

Blood Sampling and Biochemical Analysis.

Peripheral blood samples were collected after a 10–12 h fast into 2 tubes containing EDTA one of the tubes was centrifuged at 2000 rpm for 10 minutes. The separated plasma was collected in plain polystyrene tubes and used in measuring plasma glucose and lipid profile concentrations by using a Bayer Opera analyzer [Bayer Diagnostics, Munich, Germany]. Glucose, cholesterol, and triacylglycerol kits were purchased from Biotrol, Earth City, USA while HDL-C kit was purchased from Randox Laboratories Ltd., London, UK. The LDL-C levels were calculated (Friedewald formula). The other blood sample tube was used in DNA extraction.

DNA extraction

DNA was isolated from the blood sample using the QIAamp DNA blood Kit from QIAGEN (Germany) according to the manufacturer's instructions. The DNA purity and concentration were determined by a Nanodrop spectrophotometer.

Genotyping and variant analysis

By using the polymerase chain reaction - restriction fragment length polymorphism (PCR-RFLP) method the D9N (Asp9Asn), G188E (Gly188Glu), N291S (Asn291Ser), and 93 T/G (T93G) variants were determined from genomic DNA. The primers were designated based on previous publications (21, 23, 28). 3 µL (150 ng), of DNA sample, was added to 12.5 µL master mix (2× Promega), 2 µL each of both forward and reverse primers, and 5.5 µL distilled water (final volume of 25 µ).

In the thermal cycler instrument (My Cycler, Bio-Rad) the PCR temperature was adjusted as follows: One cycle of the first denaturation (94 ^{0}C for 5 minutes), 40 cycles of the second denaturation, annealing, and extension (94 ℃ for 20 seconds, 60 ℃ for 30 seconds, and 72 ℃ for 30 seconds, respectively) followed by one cycle of final extension (72 ℃ for 5 min).

For the product analysis, the 10 µL of PCR products were digested with 10 units (1 µL) of appropriate restriction endonuclease enzymes (New England BioLabs) in addition to10× buffer solution (2 µL). The mixture (20 µL final volume) was placed in a water bath at 65 °C for two hours for D9N variant and at 37 °C overnight for G188E, N291S, and 93 T/G variants.

The digested products alongside the 100-bp DNA Ladder (Thermo Fisher Scientific Inc.) were visualized by using UV light after separating on 3% agarose gel. The Oligonucleotide primers for DNA amplification of the studied LPL gene variants, the restriction enzymes, and fragments were described in **Table 1**.

Statistical analysis

The data were statistically analyzed using the SPSS version 24.0 (SPSS, Inc, Chicago, IL, USA). The data were summarized by the mean ± standard deviation (SD) and compared with a t-test. The enumeration data were summarized as the number (%) and compared through the chi-square test ($\chi 2$ test). Following, the allelic and genotypic frequencies calculated from the observed genotypic counts were evaluated, and the Hardy-Weinberg equilibrium expectations were estimated. A similar method was applied to study the associations between the allelic and genotypic frequencies. The relations were determined as odds ratios (ORs) and 95% confidence intervals (CIs). An odds ratio for genotype distributions $\chi 2$ analysis was performed. CAD is the odds of the allelic carriage in the diseased (CAD) group divided by the odds in the control group.

RESULTS

Baseline Characteristics of CAD and Control groups.

Table 2 shows the baseline biochemical features of the study population [253 CAD patients and 207 control subjects]. The CAD and control subjects' mean age was 61.73±8.34 and 58.27±8.46 years, respectively. The plasma level of fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), and low-density lipoprotein-cholesterol (LDL-c) were significantly increased in the CAD group compared to the control group (P=0.000 for each). There was no significant change in the high-density lipoprotein cholesterol (HDL-c) level between the two groups (p =0.07).

Clinical risk factors in CAD and Control groups

Table 3 shows some of the clinical risk factors established for CAD such as diabetes, dyslipidemia, hypertension, and smoking. There were significant changes in the previous risk factors percent between CAD and control group. Using the $\chi 2$ test, diabetes mellitus ($p < 0.0001$, OR = 55.16, 95% CI: 31.03- 98.07), dyslipidemia ($p < 0.0001$, OR = 8.97, 95% CI: 5.68 - 14.20), hypertension ($p < 0.0001$, OR = 20.12, 95% CI: 12.31-32.90), and smoking ($p = 0.0001$, OR = 2.58, 95% CI: 1.63-4.08) were determined to be independent risk factors of CAD.

Genotype and allele frequencies for the four SNPs in the LPL variants in CAD and Control groups

The genotype frequencies for D9N (Asp9Asn) (alleles described as A and G), G188E (Gly188Glu) (alleles described as G and A), N291S (Asn291Ser) (alleles described as A and G), and 93 T/G (T93G) (alleles described as T and G) lipoprotein lipase variants in CAD and control groups are represented in **Table 4**. According to the Hardy-Weinberg equilibrium model, the frequencies of the LPL polymorphism genotypes were distributed in the CAD group as the following: the AA D9N genotype in 180 patients (71.14%), 60 (23.72%) represents AG genotype, whereas 13 patients (5.14%) carried GG genotype. In the control group, AA genotype was identified in 169 subjects (81.64%), whereas 34 (16.43%) and 4 subjects (1.93%) carried the AG and GG genotypes, respectively. A significant change in genotype distribution of the D9N variant was detected between the CAD and control groups ($\chi 2 = 7.78$, $p = 0.\ 0.02$). For G188E, the frequency of GG genotype in the control subject was slightly higher than CAD patients, the GG genotype was recognized in 247 CAD groups (97.63%), however, 6 (2.37%) patients carried the GA. In the control group, the GG genotype was recognized in 206 subjects (99.5%), while only 1 (0.5%) carried the GA genotype. The AA genotype was absent in both CAD and control groups. No significant change in genotype distribution of the G188E variant was observed between both CAD and control groups ($\chi 2 = 2.71$, $p = 0.\ 0.09$). For N291S, the frequency of AA genotype in the CAD group was slightly lower in the control group, AA genotype was identified in 250 CAD patients (98.81%), whereas 2 (1.19%) patients carried the AG.

In the control group, the AA genotype was observed in 205 subjects (99.0%), however, 2 persons (1.0%) carried the AG genotype. No significant change in the genotype distribution of N291S variant was identified between CAD and control groups ($\chi 2 = 0.82$, $p = 0.\ 0.051$).

For the 93 T/G genotypes, 228 (90.10 %) CAD patients carried TT genotype, whereas 24 patients (9.50%) carried the TG genotype and 1 patient (0.40%) carried GG genotype. In the control group (n = 207), the TT genotype was identified in179 persons (86.4%) while, 26 healthy subjects (12.6%) carried the TG genotype and 2 subjects (1.0%) carried GG genotype.

For 93 T/G variant, No significant deviations in genotype frequencies between the two groups (X2 = 1.73 and p = 0.42). **Table 5** shows the significant alterations in the A and G alleles distribution of D9N genotype observed between both CAD and control groups (p = 0.003; OR = 1.81 and 95% Cl = 1.22-2.69). No significant changes in the G and A allele distribution of G188E, A and G allele distribution of N291S, and T and G allele distribution of 93 T/G genotype were detected between the CAD and the control groups (= p 0.139, 0.822, and 0.185 respectively).

CAD odds ratio associations with D9N, G188E, N291S, and 93 T/G genotypes

The odds ratios of the D9N (Asp9Asn) genotype AA vs. AG and AA vs. AG + GG genotypes (95% CI) were 1.65 (1.26-4.78), and 1.80 (1.16-2.81). Our results showed a significant association with CAD disease (p = 0.035 and 0.009, respectively). The odds ratios of the G188E (Gly188Glu) genotype GG vs. GA (95% CI) and N291S (Asn291Ser) genotypes AA vs. AG (95% CI) were 5.0 (0.59-41.90) and 1.23 (0.20-7.43), respectively, which shows insignificant association with CAD disease (p =0.137 and 0.821, respectively).

The odds ratio 93 T/G (T93G) genotypes TT vs. TG, TT vs. GG, TG vs. GG, TT vs. TG + GG and TT + TG vs. GG (95% CI) were 0.72 (0.40-1.31), 0.39 (0.04- 4.36), 0.54 (0.05-6.36), 0.70 (0.39-1.24) and 0.41 (0.04-4.52), respectively, represent no significant association between previous genotypes and CAD (p = 0.283, 0.447, 0.626, 0.224, and 0.464, respectively) (**Table 6**).

Table 1: Oligonucleotide primers for PCR amplification of the four studied polymorphisms of the LPL gene, digestion enzymes, and resulting fragments.

Primers	Enzymes	Resulting fragments
D9N (Asp9Asn) polymorphism (21). 5′-CTC CAG TTA ACC TCA TAT CC-3′ 5′-CAC CAC CCC AAT CCA CTC-3′	2U TaqI (New England Biolabs Inc., UK)	A allele: 179 bp and 52 bp G allele: 179 bp and 58 bp
G188E (Gly188Glu) polymorphism) (28). 5′-GAG CAG TGA CAT GCG AAT GT-3′ 5′-CTC CAA GTC CTC TCT CTG CA-3′	2U AvaII (New England Biolabs Inc., UK)	G allele: 131 bp, 88 bp and 86 bp A allele: 219 pb and 86 bp
N291S (Asn291Ser) polymorphism (23). 5′-GCC GAG ATA CAA TCT TGG TG-3′ 5′-CTG CTT CTT TTG GCT CTG ACT GTA-3′	2U RsaI (New England Biolabs Inc., UK)	A allele: not cleaved G allele: 215 bp and 23 bp
93 T/G (T93G) polymorphism (28). 5′-GCT GAT CCA TCT TGC CAA TGT TA-3′ 5′-CCG CGG TTT GGC GCT GAG CAA GT-3′	2U ApaI (New England Biolabs Inc., UK)	T allele: 338 bp and 286 bp G allele: 286 bp, 195 bp and 143 bp

Table 2: Baseline Characteristics of CAD patients and controls.

Characteristic	Subjects		*p*-value
	CAD n=253	Control n=207	
Age, year			
Mean±SD	61.73±8.34	58.27±8.46	0.000
Gender			
Male, %	137 (54.2%)	118 (57.0%)	0.54
Female, %	116 (45.8%)	89 (43.0 %)	
FBS, mmol/L			
Mean±SD	8.90±3.58	4.53±0.70	0.000
TC, mmol/L			
Mean±SD	4.26±1.06	3.83±0.59	0.000
TG, mmol/L			
Mean±SD	1.78±1.03	1.10±0.28	0.000
HDL-C, mmol/L			
Mean±SD	1.16±0.90	1.27±0.39	0.07
LDL-C, mmol/L			
Mean±SD	2.45±0.85	1.66±0.64	0.000

Data represent the mean ± SDs for all quantitative traits. Student's t-test and the X2test were used to compare the values of CAD patients and control subjects. FBS: fasting blood glucose, TC: total cholesterol, TG: triglyceride, HDL-c: high density lipoprotein cholesterol, LDL-c: low-density lipoprotein cholesterol.

Table 3: Clinical risk factors in the CAD patients and control subjects

Parameter	Subjects		OR	95% CI	*p*-value
	CAD n=253	Control n=207			
Diabetes					
Diabetics	218 (86.2%)	21 (10.1%)	55.16	(31.03– 98.07)	< 0.0001
Nondiabetics	35 (13.8%)	186 (89.9%)			
Dyslipidemia					
Positive	155 (61.30%)	31 (15.0%)	8.97	(5.68–14.20)	< 0.0001
Negative	98 (38.70%)	176 (85.0%)			
Hypertension					
Hypertensive	192 (75.90%)	28 (13.5%)	20.12	(12.31–32.90)	< 0.0001
Normotensive	61 (24.10%)	179 (86.5%)			
Smoking					
Smoker	81 (32.0%)	32 (15.5%)	2.58	(1.63–4.08)	0.0001
Nonsmoker	172 (68.0%)	175 (84.5%)			

CAD, coronary artery disease; OR, odds ratio; CI, confidence interval

Table 4: Genotype distributions for the four SNPs in the LPL polymorphisms in CAD Patients and control subjects

Genotype	Subjects		χ^2	*p*-value
	CAD, n (%)	Control, n (%)		
D9N (Asp9Asn)				
AA	180 (71.14%)	169(81.64%)	7.78	0.02
AG	60 (23.72%)	34 (16.43%)		
GG	13 (5.14%)	4 (1.93%)		
G188E (Gly188Glu)				
GG	247 (97.63%)	206 (99.5%)	2.71	0.09
GA	6 (2.37%)	1 (0.5%)		
AA				
N291S (Asn291Ser)				
AA	250 (98.81%)	205 (99.0%)	0.051	0.82
AG	3 (1.19%)	2 (1.0%)		
GG	-	-		
93 T/G (T93G)				
TT	228 (90.10%)	179 (86.4%)	1.73	0.42
TG	24 (9.50%)	26 (12.6%)		
GG	1(0.40%)	2 (1.0%)		

Table 5: LPL allelic frequencies in CAD patients and control subjects

Gene	Allele	CAD, n (%)	Control, n (%)	OR (95% CI)	*p*-value
D9N (Asp9Asn)	A	420 (83.0%)	372 (89.86%)	1.81 (1.22–2.69)	0.003
	G	86 (17.0%)	42 (10.14%)		
G188E (Gly188Glu)	G	500 (98.81%)	413 (99.76%)	4.96 (0.59–41.33)	0.139
	A	6 (1.19%)	1 (0.24%)		
N291S (Asn291Ser)	A	503 (99.41%)	412 (99.52%)	1.23 (0.20–7.38)	0.822
	G	3 (0.59%)	2 (0.48%)		
93 T/G (T93G)	T	480 (94.86%)	384 (92.75%)	0.69 (0.40–1.19)	0.185
	G	26 (5.14%)	30 (7.25%)		

Differences in the allelic frequencies between coronary artery disease (CAD) patients and control subjects were compared using Pearson's X2 test and without adjusting other covariates. Odds ratios with 95% confidence interval (95% CI) are presented

Table 6: CAD odds ratio associations with D9N, G188E, N291S, and 93 T/G genotypes in the LPL polymorphisms in CAD Patients and Control subjects

Genotype	OR	95%CI	*P* value
D9N (Asp9Asn) genotypes			
AA vs. AG	1.65	(1.04–2.65)	0.035*
AA vs. GG	3.05	(0.98–9.54)	0.055
AG vs. GG	1.84	(0.55–6.10)	0.317
AA vs. AG + GG	1.80	(1.16–2.81)	0.009*
AA + AG vs. GG	2.75	(0.88–8.56)	0.081
G188E (Gly188Glu) genotypes			
GG vs. GA	5.00	(0.59–41.90)	0.137
N291S (Asn291Ser) genotypes			
AA vs. AG	1.23	(0.20–7.43)	0.821
93 T/G (T93G) genotypes			
TT vs. TG	0.72	(0.40–1.31)	0.283
TT vs. GG	0.39	(0.04–4.36)	0.447
TG vs. GG	0.54	(0.05–6.36)	0.626
TT vs. TG + GG	0.70	(0.39–1.24)	0.224
TT + TG vs. GG	0.41	(0.04–4.52)	0.464

CI, confidence interval

DISCUSSION

LPL is a vital enzyme play an important role in lipoprotein metabolism that describes the lipid and lipoprotein abnormalities encountered in CAD. Various codon polymorphisms of the LPL gene have been designated, and some of them play a role in the pathogenesis of CAD (29). Therefore, in our study, we have evaluated the effect of LPL gene variations and determined the genetic frequencies in CAD and control groups in the Saudi population. CAD patients had significantly higher concentrations of fasting blood sugar (FBS), and TC, TG, and LDL-C (p = 0.000 for each) in comparison to the control subjects. There was an insignificant change in the HDL-C concentration between the CAD and control groups. Our results were consistent with those of other studies, which reported that CAD male patients had significantly higher concentrations of TC, TG, and LDL-C and low concentrations of HDL-C in comparison to the control subjects (20, 30, 31). The major clinical risk factors listed as (diabetes, dyslipidemia, hypertension, and smoking) in the CAD and control groups. There were significant differences between the CAD and the control groups concerning diabetes mellitus, dyslipidemia, hypertension, and smoking. Using the $\chi 2$ test, diabetes mellitus, dyslipidemia, hypertension, and smoking were found to be independent risk factors of CAD.

A significant effect of smoking and the D9N allele increases the risk of CAD when compared with D9N non-smokers (32). Dyslipidemia is stimulated through the interaction of N291S or D9N mutations with factors, such as pregnancy, obesity, or diabetes (33-35). The patients with CHD had significantly lower HDL-C and higher TG than the control group, whereas no difference was observed in LDL-C in both groups (32). The genotypic frequencies of D9N (Asp9Asn), G188E (Gly188Glu), N291S (Asn291Ser), and 93 T/G (T93G) LPL polymorphisms in CAD patients and control subjects. The distributions of the genotypes were according to the Hardy-Weinberg equilibrium, as expected. The significant differences in the A and G allelic distribution of the D9N genotype were observed between the CAD and the control groups (p = 0.003; OR = 1.81 and 95% Cl = 1.22–2.69). No significant differences in the G and A allele distribution of G188E, A and G allele distribution of N291S, and T and G allele distribution of 93 T/G genotype were observed between the CAD and the control groups. Various studies have reported that the N291S heterozygous carriers had an increase in plasma TG and a decrease in HDL-C (21, 23, 34). However, other studies have been reported in which no association was observed (34-39).

Van Bockxmeer et al. (2001) found a high frequency of the LPL allele in young CHD (38). The T93G, D9N, and 291S have frequencies less than 3%, with the E allele of the G188E variant having a frequency of only 0.03% (40). The higher frequencies of the 291S allele were observed in Chinese Canadians (41), French Canadians (42), and Italian (43). The D9N allele was associated with an odds ratio of 1.9 (1.2–3.0) for CHD in male subjects in Copenhagen city (44). In a meta-analysis, the frequency of D9N allele in CHD and MI Caucasians was found to be two-fold higher than the normal subjects (45). In a previous study, the D9N genotype showed a significant association with CAD, and a similar result was observed for coronary stenosis. The odds ratios of the D9N (Asp9Asn) genotype AA versus AG and AA versus AG + GG genotypes (95% CI) were 1.65 (1.26–4.78), and 1.80 (1.16 p < 2.81). These results demonstrate a significant association with CAD disease (p = 0.035 and 0.009, respectively. There was no significant association with CAD disease. (p = 0.283, 0.447, 0.626, 0.224, and 0.464, respectively) (Table 6). The OR was observed to be 0.89 (95 % CI: 0.81 –0.98) for carriers of the T allele which seems to be protective against CAD. However, the ORs for carriers of -93G, 188E, and 291S were found to be 1.22 (95 % CI: 0.98–1.52), 2.80 (95 % CI: 0.88–8.87) and 1.07 (95 % CI: 0.96–1.20), respectively 40. The D9N alleles are associated with 20% higher triglyceride and 0.08 mmol/L lower HDL cholesterol, which are well-known established risk factors for CAD. The frequencies of LPL N291S and D9N polymorphisms in Australian Caucasians were found to be 1–7% and 17–22%, respectively, similar to those reported from Europe and Scandinavia (45). Many studies have found no difference in the frequency of LPL N291S polymorphism between control and CHD subjects (46, 47). A previous study has concluded that the subjects with LPL N291S polymorphism had no risk of CAD, while subjects with D9N had a significant increase in the risk of CAD (32). The D9N mutation would decrease the activity and concentration of LPL and cause higher plasma triglyceride levels and lower HDL-C levels which would result in the formation of intermediate-density lipoprotein and chylomicrons remnants, and the development of the CAD. Therefore, the D9N mutation could decrease the concentrations of HDL by retarding the LPL activity, accelerating the cholesterol deposition, and promoting the atherosclerosis process, and eventually increased the coronary disease risk (48).

CONCLUSION

In the current study, an association between the D9N variant and CAD was observed, however, no association was observed between the G188E, N291S, 93T/G variants, and CAD. The genetic and environmental features may affect the pathogenesis of CAD, and the LPL variants have a strong role in the development of CAD. Further studies on LPL gene variants are necessary for patients with CAD to explore the effects.

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