Original Article

The Association of the APOC3 and APOA5 Gene Polymorphisms with Dyslipidemia in Thais

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Background: Although the association between the apolipoprotein A5 (APOA5), and apolipoprotein C3 (APOC3) genetic variants with dyslipidemia have been extensively studied in various populations. However, the association between the apolipoprotein A5 (APOA5), and apolipoprotein C3 (APOC3) genetic variants with dyslipidemia was limited in Thai population.

Objective: The present study was to examine whether APOA5 and APOC3 gene polymorphisms associated with increased risk of developing dyslipidemia in Thais.

Materials and Methods: Two hundred participants were recruited in case-control studies, Four SNPs in APOC3 (rs2854116 T/C, rs2854117 C/T, rs5128 G/C) and APOA5 (rs651821 T/C) genes were genotyped by PCR-RFLP methods.

Results: The results showed that polymorphism in rs651821 of APOA5 gene was significantly associated with high triglyceride levels (p=0.017). The risk of dyslipidemia increased for carrying T/C+C/C genotypes and C allele of rs651821 in APOA5 gene were 2.02 (OR: 2.02, 95% CI: 1.07 to 3.79, p=0.028) and 2.27 (OR: 2.27, 95% CI: 1.10 to 4.69, p=0.025), respectively. The haplotype analysis of variants in APOC3 (rs2854116, rs2854117, rs5128) and APOA5 (rs651821) genes, carrying with CTCC haplotype was significantly higher the risk of dyslipidemia (OR: 3.42, 95% CI: 1.23 to 9.49, p=0.019), compared with the common haplotype (TCGT).

Conclusion: The risk allele (C allele) in rs651821 of APOA5 gene was associated with increasing risk of dyslipidemia by 2 times, and also haplotype carriers of APOC3 (rs2854116 (C), rs2854117 (T), rs5128 (C)) and APOA5 (rs651821 (C)) genes have higher risk of developing dyslipidemia by 3 times in Thai population. However, the association between SNPs in APOC3 gene and dyslipidemia was not observed in the present study.

Keywords: Gene; Single nucleotide polymorphism (SNP); Dyslipidemia; Haplotype

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Dyslipidemia is characterized by abnormally increased triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C) levels in plasma[1]. Dyslipidemia is well-established as a risk factor for cardiovascular diseases (CVD) and atherosclerosis[2,3] and promotes to develop metabolic syndrome (MetS), stroke and metabolic-related diseases[4-6]. The prevalence of dyslipidemia has been rising in many countries including Thailand[7]. There are many factors contributing to development of dyslipidemia such as diet, lifestyle, exercise, and genetic background[1,3]. The apolipoprotein A5 (APOA5) and the apolipoprotein C3 (APOC3) genes located on chromosome 11. APOA5 and APOC3 genes are crucial genes that involved with regulating lipid[8,9]. Many previous studies showed that rs2854116, rs2854117, rs5128 in APOC3 and rs651821 in APOA5 gene were associated with lipid profiles, coronary heart disease (CHD) and dyslipidemia in various ethnic groups, namely Chinese, Indian, Taiwanese[10-20]. The meta-analysis reported that rs2854116, rs2854117, and rs5128 polymorphisms were strong associated with plasma triglyceride levels[21,22]. But the molecular mechanisms remain unclear. The possible one of the explanations is that variants enhance the transcription activity of APOC3 but its effect may be due to linkage disequilibrium with other functional variants. However, the association of these four SNPs have reported apparently conflicting finding and limited in Thais. The purpose of this study was to investigate the association of single nucleotide polymorphisms (SNPs) in APOA5, APOC3 genes with dyslipidemia in Thai population.

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Materials and Methods

Participants

A total of 200 unrelated adult participants were

recruited from the Department of Internal Medicine, Faculty of Medicine, Srinakharinwirot University (Thailand), and aged 35 to 65 years old. The classification of participants divided into 2 groups, according to The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines[23,24]. The characteristics of the dyslipidemia group were TG ≥200 mg/dL, TC ≥240 mg/dL, LDL-C ≥160 mg/dL, HDL-C <40 mg/dL; and the control group were TG <150 mg/dL, TC <200 mg/dL, LDL-C <100 mg/dL, HDL-C ≥40 mg/dL. Individuals who had cardiovascular diseases (CVD), thyroid disease, malignant tumor, psychological disease, multiple organ failure, chronic liver disease, smoking, pregnant women, or heavy alcohol consumption (>12 oz. per week) were excluded from the present study. All participants provided written informed consent to participate in the present study, according to the Declaration of Helsinki. The present study was approved by the Research Ethics Committee of the University of Srinakharinwirot (approved number SWUEC/E-146/2559).

Anthropometric and biochemical analysis

Body weight was measured in light clothes and without shoes using a body composition monitor (Omron HBF-375, body composition monitor, Japan). Height was measured with a stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Waist circumferences were measured at the between of the lower lib and the superior iliac crest using a flexible anthropometric tape. Blood pressure was measured in the sitting position with automatic sphygmomanometer (Omron VP-100, Japan) on the left arm after 10 minutes rest.

A fasting venous blood samples were drawn from each participant for measuring total cholesterol, HDL-C, LDL-C, triglyceride levels and DNA analysis. Biochemical analysis was conducted with using automatic analyzer (Abbott CI 8200, United State).

DNA extraction and genotyping

Three single nucleotide polymorphisms (SNPs) of APOC3 gene and one SNP of APOA5 gene, namely rs2854116, rs2854117, rs5128 and rs651821, respectively were genotyped in all participants. Genomic DNA was extracted from peripheral blood leukocytes using a DNA extraction kit (FlexiGene® DNA kit, Qiagen). The DNA quantity and purity were measured for each DNA samples using a Nanodrop ND-1000 spectrophotometer (version 3.3). The DNA samples were stored at -20°C until use. Genotyping was performed using the Polymerase Chain Reaction followed by Restriction Fragment Length Polymorphism (PCR-RFLP) technique to investigate polymorphisms in the gene fragments. PCR was done using 3 pairs of primer that designed using the Primer 3 plus program as following: (F) 5' GTT GAA GTC AGG GTC GGA GA 3' and (R) 5' CCT AGG TCA GTC CTC TTG AGC 3' for rs651821 (APOA5); (F) 5' CCA GAC ACA GAT GGC ACA CT 3' and (R) 5' GGA GCA CCG TTA AGG ACA AG 3' for rs5128 (APOC3); (F) 5' TCC TTC CTA GCT GAC TGG CT 3' and (R) 5' CCT GCC TGG ATT GAA ACC CA 3' for rs2854116 and rs2854117 (APOC3). PCR cycling was performed using a ProFlex™ PCR system (Thermo Fisher Scientific Inc., United State) under the following conditions: 5 min at 94°C for DNA denaturation followed by 30 cycles of PCR (45 sec denaturation at 94°C, 30 sec annealing at 55 to 62°C, 30 sec extension at 72°C) followed by 72°C for final step. The amplicons were digested with MseI, SacI, FokI and MspI (FastDigest restriction enzyme, Thermo Scientific) for rs651821 (APOA5), rs5128, rs2854116, rs2854117 (APOC3), respectively. The DNA fragments were separated and visualized by agarose gel electrophoresis 3% and gel documentation (Syngene G:BOX HR, United Kingdom), respectively (Figure 1). Five percent of PCR samples were confirmed the PCR-RFLP results by using the commercial DNA sequencing service (Macrogen Inc., Seoul, South Korea).

Statistical analysis

Descriptive analysis was presented as mean±SD, median, interquartile range (IQR), frequencies and percentage to describe the general characteristics of participants, biochemical parameter, genotypes, and allele frequencies. The Mann-Whitney U test was used to test a nonparametric statistical of parameters between dyslipidemia and control groups. Statistical analyses were conducted using SPSS (version 16, Chicago, IL). The association between APOC3, APOA5 polymorphisms and dyslipidemia were assessed

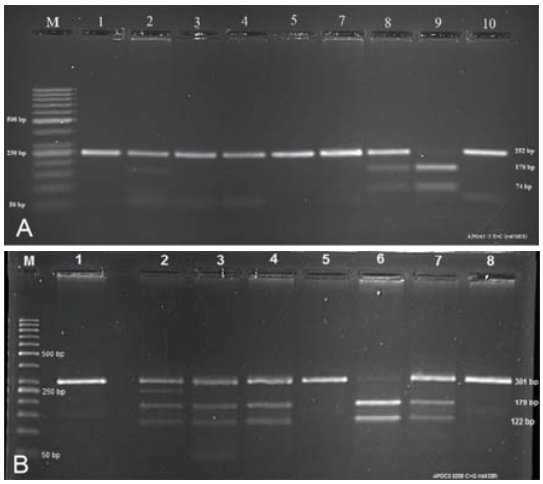

Figure 1. Genotyping of the APOC3 and APOCA5 gene polymorphisms: A) Genotyping of APOA5 -3 T>C (rs651821) using PCR-RFLP: T/T: 252 bp; T/C: 252, 178, 74 bp; C/C: 178, 74 bp. B). Genotyping of APOC3 3238 G>C (rs5128) using PCR-RFLP: G/G: 301 bp; G/C: 301, 179, 122 bp; C/C: 179, 122 bp.

with logistic regression, assuming dominant and co-dominant models, linkage disequilibrium (LD), and haplotype frequencies were carried out using the SNPStats web tool[25]. Chi-square test was used to test the Hardy-Weinberg Equilibrium (HWE) for the four SNPs. The association between lipid profiles and SNPs in the study population were tested using Kruskal-Wallis test. A two-side p-value <0.05 was considered as statistical significance.

In the present study, we computed the effective sample size and statistical power to detect a SNP in case-control study that under assumption of 5% disease prevalence, 5% α, 80% power, and 1:1 case to control ratio. The minimum number of cases required 24 cases and 24 controls. Sample size was calculated by PS Power and Sample Size (version 3.1.2, USA).

Results

Characteristics of study participants

Two hundred participants were divided into 100 dyslipidemia cases and 100 controls. The mean (SD.) age of study participants was 50 (13) and 45 (10) years in cases and control groups, respectively. The general and biochemical characteristics of study participants are shown in Table 1. Statistically significant differences were observed between study groups, such as BMI, waist circumferences, blood pressure, visceral fat, TC, HDL-C, LDL-C, TG ($p<0.05$). Genotype frequencies of the four SNPs in the present study participants did not derived from HWE.

The association among biochemical parameters, genotype, and dyslipidemia phenotype

The result showed that carrying with heterozygous or homozygous variants in rs651821 of APOA5 gene were related higher triglyceride level (p=0.017) (Table 2). The carriers of minor allele (C allele) of APOA5 in rs651821 gene was significantly associated with increased risk of dyslipidemia by 2.02 (95% CI, 1.07 to 3.79, p=0.028) (Table 3). The result of dominant model showed that no significant differences among SNPs in APOC3 gene with increased risk of being dyslipidemia in study participants. However, the result presented that who carry heterozygous/homozygous variants in rs651821, APOA5 gene was higher risk of being dyslipidemia by 2.27 (95% CI, 1.10 to 4.69, p=0.025) (Table 3).

Linkage disequilibrium and haplotype analysis

Disequilibrium (D') and r^2 were performed using the linkage disequilibrium (LD) test. The pairwise D' were showed strong LD among three SNPS in APOC3 gene (D' >0.80, Table 4). The haplotype analysis was conducted to examine the effect of the four SNPs (in order of rs2854116 (T>C), rs2854117 (C>T), rs5128 (G>C), rs651821 (T>C)) with dyslipidemia. The result showed 8 possible haplotype patterns in Table 5. The common haplotype was TCGT (39.54%). Carriers of CTCC haplotype showed further increase dyslipidemia risk (OR: 3.41, 95% CI: 1.23 to 9.49, p=0.019), compared to the wild-type haplotype (TCGT).

Discussion

In the present study, there were no association of variants in rs2854116, rs2854117, rs5128 of APOC3 gene with TC, TG, LDL-C, and HDL-C. The study of Federica S. et al, showed that no association between rs2854116, rs2854117 polymorphisms and lipid profiles in obese Italian[26]. The plasma lipid levels of participants with rs5128 genotypes (C/C, C/G, G/G) were did not significant difference in North Chinese Han population[14]. The result from Niculescu LS. et al, revealed that no association between the presence of minor allele in rs2854116 of APOC3 gene and

Table 1. General characteristic of study participants

Variables	Dyslipidemia group (n=100)	Control group (n=100)	p-value
Gender (male/female)	37/63	11/89	0.04
Age (years)	50±13	45±10	<0.001
Body mass index (kg/m^2)	25.6±4.7	22.2±3.5	<0.001
Systolic blood pressure (mmHg)	121.7±15.3	110.2±12.4	<0.001
Diastolic blood pressure (mmHg)	73.4±12.7	67.8±12.9	0.001
Waist circumferences (cm)	86.4±12.0	74.5±9.2	<0.001
Visceral fat (%)	10.5±6.5	5.2±3.2	<0.001
Total cholesterol (mg/dL)	237.6±42.9	174.3±17.6	<0.001
LDL-cholesterol (mg/dL)	164.6±42.5	102.7±19.5	<0.001
HDL-cholesterol (mg/dL)	52.3±14.6	65.8±14.2	<0.001
Triglyceride (mg/dL)	190.0±17.4	76.6±26.7	<0.001

Data was presented as mean±SD; statistical analysis was the Mann-Whitney U test; statistically significance at p-value <0.05.

Table 2. Single association of between lipid profiles and APOC3/APOA5 genetic variants in study group

SNPs	Genotypes	TC (mg/dL)	TG (mg/dL)	LDL-C (mg/ dL)	HDL-C (mg/ dL)
APOC3 -455 T>C (rs2854116)	T/T (n=53)	195.0 (177.5 to 242.0)	95.0 (72.0 to 137.5)	126.0 (107.5 to 167.5)	57.0 (47.5 to 72.0)
	T/C (n=94)	189.5 (172.7 to 240.0)	101.0 (62.2 to 169.2)	117.0 (98.5 to 169.5)	59.0 (47.7 to 69.0)
	C/C (n=42)	196.5 (178.5 to 247.0)	98.0 (68.2 to 157.5)	127.5 (103.0 to 165.7)	62.0 (55.0 to 68.0)
	p-value	0.539	0.988	0.686	0.559
APOC3 -482 C>T (rs2854117)	C/C (n=43)	190.5 (174.5 to 231.75)	88.5 (70.5 to 153.5)	123.0 (108.0 to 164.0)	58.0 (47.0 to 68.5)
	C/T (n=104)	191.0 (171.2 to 240.0)	103.5 (64.2 to 168.2)	119.0 (100.0 to 172.0)	59.0 (48.0 to 69.7)
	T/T (n=42)	198.0 (178.0 to 247.0)	99.0 (65.0 to 156.0)	127.0 (101.0 to 166.0)	62.0 (51.2 to 98.7)
	p-value	0.772	0.859	0.973	0.859
APOC3 3238 G>C (rs5128)	G/G (n=94)	194.0 (177.0 to 247.0)	97.5 (70.5 to 147.0)	123.0 (106.0 to 170.0)	58.5 (50.7 to 68.0)
	G/C (n=84)	191.5 (170.0 to 240.0)	100.0 (63.0 to 159.5)	123.5 (99.7 to 169.5)	59.5 (46.2 to 69.7)
	C/C (n=20)	187.0 (170.2 to 250.2)	106.0 (69.0 to 217.7)	104.5 (93.5 to 167.5)	59.0 (44.0 to 71.0)
	p-value	0.644	0.736	0.434	0.961
APOA5 -3 T>C (rs651821)	T/T (n=113)	188.0 (170.0 to 234.0)	86.0 (62.5 to 139.0)	117.0 (101.5 to 164.0)	61.0 (520 to 71.0)
	T/C (n=79)	214.0 (175.0 to 246.0)	107.0 (79.0 to 218.0)	147.0 (102.0 to 174.0)	56.5 (44.5 to 64.5)
	C/C (n=8)	211.5 (165.7 to 247.0)	121.5 (56.2 to 266.5)	144.5 (88.0 to 175.2)	61.5 (42.5 to 72.7)
	p-value	0.150	0.017	0.290	0.066

Data was presented as median (Interquartile range); statistical analysis was the Kruskal-Wallis test, statistical significance at p-value <0.05. The p-value was compared between each genotype of SNP and each parameter of lipid profile.

Table 3. Comparison of genotypes, allele frequency of APOC3/APOA5 variants in study group

Gene/SNPs	Genotypes	Dyslipidemia n (%)	Controls n (%)	OR (95% CI)	p-value
APOC3 -455 T>C (rs2854116)	T/T	26 (29.2)	27 (27.6)	1.00	
	T/C	44 (49.4)	50 (51.0)	0.92 (0.40 to 2.15)	
	C/C	21 (21.4)	21 (21.4)	1.09 (0.39 to 3.06)	0.940
	Total (n)	91	98		
	T/C + C/C	65 (70.8)	71 (72.5)	0.97 (0.44 to 2.14)	0.940
	T allele	0.54	0.53	1.00	
	C allele	0.46	0.47	1.04 (0.62 to 1.73)	0.890
APOC3 -482 C>T (rs2854117)	C/C	24 (25.8)	19 (19.8)	1.00	
	C/T	51 (54.8)	53 (55.2)	0.71 (0.29 to 1.78)	
	T/T	18 (19.4)	24 (25.0)	0.55 (0.19 to 1.65)	0.560
	Total (n)	93	96		
	C/T + T/T	69 (74.2)	77 (80.2)	0.67 (0.28 to 1.57)	0.350
	C allele	0.53	0.53	1.00	
	T allele	0.47	0.47	0.74 (0.43 to 1.28)	0.290
APOC3 3238 G>C (rs5128)	G/G	46 (46.9)	48 (48.0)	1.00	
	G/C	40 (40.8)	44 (44.0)	0.88 (0.41 to 1.86)	
	C/C	12 (12.3)	8 (8.0)	1.09 (0.32 to 3.67)	0.800
	Total (n)	98	100		
	G/C + C/C	52 (53.1)	52 (52.0)	0.91 (0.45 to 1.87)	0.800
	G allele	0.33	0.30	1.00	
	C allele	0.67	0.70	0.98 (0.57 to 1.68)	0.940
APOA5 -3 T>C (rs651821)	T/T	46 (46.0)	67 (67.0)	1.00	
	T/C	49 (49.0)	30 (30.0)	2.23 (1.06 to 4.69)	
	C/C	5 (5.0)	3 (3.0)	2.79 (0.40 to 19.21)	0.078
	Total (n)	100	100		
	T/C + C/C	54 (54.0)	33 (33.0)	2.27 (1.10 to 4.69)	0.025
	T allele	0.70	0.82	1.00	
	C allele	0.30	0.18	2.02 (1.07 to 3.79)	0.028

Data was presented as co-dominant (wild type vs. heterozygous variant vs. homozygous variant), dominant (wild type vs. variants) and log additive model (normal allele vs. risk allele). Statistical analysis was carried out by SNPStats web tool. Statistical significance at p-value <0.05. OR was adjusted for age and sex as covariate.
OR = Odds ratio; CI = confidence interval; SNP = single nucleotide polymorphism.
Total (n) were not the same in each SNP due to there were some missing data.

Table 4. Pairwise linkage disequilibrium (LD) of SNPs in APOC3 and APOA5 genes

SNP (D')	APOC3 -455 T>C (rs2854116)	APOC3 -482 C>T (rs2854117)	APOC3 3238 G>C (rs5128)	APOA5 -3 T>C (rs651821)
APOC3 -455 T>C (rs2854116)	-			
APOC3 -482 C>T (rs2854117)	0.8856	-		
APOC3 3238 G>C (rs5128)	0.8023	0.8139	-	
APOA5 -3 T>C (rs651821)	0.3307	0.3581	0.4457	-

Data was presented as D', D' represented how often of these two SNPs are coinherited, D'>0.8 is high linkage disequilibrium. LD analysis was conducted using SNPStats web tool

Table 5. Haplotype frequencies of study group with haplotype pattern of rs2854116 T>C[1], rs2854117 C>T[1], rs5128 G>C[1], rs651821 T>C[1] in APOC3 and APOA5 genes.

Haplotype patterns	Dyslipidemia (Frequencies)	Control (Frequencies)	Crude OR (95% CI)	Adjusted OR (95% CI)[2]	p-value
T C G T	0.3709	0.4188	Reference	Reference	-
C T G T	0.1862	0.1288	1.90 (0.94 to 3.80)	2.09 (0.94 to 4.67)	0.074
C T C T	0.0882	0.1976	0.46 (0.21 to 0.99)	0.46 (0.18 to 1.22)	0.120
C T C C	0.1745	0.0791	3.21 (1.38 to 7.47)	3.42 (1.23 to 9.49)	0.019
T C G C	0.0549	0.0611	1.30 (0.44 to 6.89)	1.62 (0.46 to 5.75)	0.460
T T G T	0.0093	0.0432	0.44 (0.07 to 2.85)	0.41 (0.05 to 3.14)	0.390
C T G C	0.0171	0.0209	0.67 (0.07 to 6.74)	1.54 (0.22 to 10.99)	0.670
C C G T	0.0083	0.0257	0.47 (0.06 to 3.56)	0.15 (0.01 to 1.80)	0.140

Haplotype analysis was conducted using SNPStats web tool. Statistical significance at p-value <0.05. The p-value compute for adjusted OR.
[1] Underline on allele (C) was risk allele, [2] Adjusted OR: adjustment for age and sex.
OR = Odds ratio; CI = confidence interval

the lipid profiles[17]. The association between APOC3 polymorphisms and dyslipidemia was not observed in the present study. The finding was controversy result in many populations. The results from multi-ethnic populations revealed that the carrying with variants in rs2854116 was associated with increasing risk of metabolic syndrome (Mets) than non-carriers (OR: 1.73, 95% CI: 1.40 to 2.14)[19].

The study in Taiwan showed that rs2854116, rs2854117, and rs5128 of APOC3 were significant differences in genotype frequencies between hypertriglyceridemia and control groups ($p<0.05$)[18]. A study in India demonstrated that rs2854116 variants was associated with dyslipidemia ($p<0.05$)[13]. The carriers of variants genotypes (G/C+C/C) and minor allele (G allele) in rs5128, APOC3 gene increased risk of being dyslipidemia by 1.749 (95% CI: 1.221 to 2.506) and 1.477 (95% CI: 1.127 to 1.936), respectively in Han Chinese[15]. The distribution of genotypes in rs2854116 and rs2854117 of APOC3 gene was significant differences between MetS case and control groups ($p<0.05$)[17,20]. The CC genotype (homozygous variants) in rs2854116 was associated with increased risk of coronary artery disease (CAD) and ischemic stroke, compared to T/C and T/T genotypes[12,27].

However, the carriers of minor allele of rs2854117 in APOC3 gene were having the high TG, high fasting blood glucose, and low HDL-C levels in Romania population[17]. Nevertheless, the association between lipid profiles and APOC3 gene polymorphisms were observed in multi-ethnic participants[19], Taiwanese[18], Indians[13,28], and Chinese population[29] in previous studies.

Moreover, the result in the present study found that the carrying of heterozygous or homozygous variants in rs651821 of APOA5 gene was related with higher triglycerides level in study participants. This finding was similar with the previous studies that demonstrated a significantly associated with increased triglyceride level in Chinese and Indian[10,11,16,28,30]. The carriers of C/C+T/C genotypes in rs651821, APOA5 gene were associated with increased triglyceride level, compared to T/T genotype in Chinese children and adolescents[16]. The result from Aparna A, et al study[28] revealed that APOA5 variants (rs651821 T>C) related with increased TG levels and not associated with TC, HDL-C and LDL-C in Indians.

The result of this study presented that the carrying with T/C and C/C genotypes in rs651821 APOA5 gene was higher risk of being dyslipidemia by 2.27 (95% CI, 1.10 to 4.69, p=0.025). The carriers of minor allele (C allele) rs651821 in APOA5 gene was significantly associated with increased risk of dyslipidemia by 2.02 (95% CI, 1.07 to 3.79, p=0.028). The findings in this study were similar with prior studies that found the association between rs651821 variants with dyslipidemia and metabolic diseases. The study in China demonstrated that more increasing risk of dyslipidemia for the carrying of the homozygous variant (C/C) or heterozygous + homozygous variants (C/T+C/C) were 9.912 (95% CI: 3.766 to 26.715) or 1.859 (95% CI: 1.298 to 2.665) than of wild type (T/T). The carrying of C allele (risk allele) versus T allele was increased risk to develop dyslipidemia by 2.027 (95% CI: 1.524 to 2.695)[15]. The carrying with variant genotypes (C/T+C/C) and risk allele (C allele) in rs651821, APOA5 gene were related with increasing risk of obesity development[16].

The carriers of CTCC haplotype showed further increase dyslipidemia risk (OR: 3.41, 95% CI: 1.23 to 9.49, p=0.019), compared to the wild-type haplotype (TCGT). There were no previous studies investigated the interaction effects of four SNPs (rs2854116 T/C, rs2854117 C/T, rs5128 G/C, rs651821 T/C). However, haplotype analysis from previous studies reported that carrying at least one risk allele of these four SNPs in the haplotype pattern

associated with hypertriglyceridemia[18,28], dyslipidemia[15], MetS[20] and ischemic stroke[12].

Conclusion

This study found that the carriers of variants in rs651821 of APOA5 gene associated with increased risk of dyslipidemia, possible via the elevation of TG level. However, there were no association between SNPs in APOC3 gene with dyslipidemia. The CTCC haplotype was correlated with increasing risk of dyslipidemia than the carrying of TCGT of haplotype (common haplotype). Further research should be performed in the larger size of study population.

What is already known on this topic?

High linkage disequilibrium (D' >0.8) among SNPs in APOC3 gene.

Major genetic risk factors for dyslipidemia in Thai population.

The interaction of SNPs in APOC3 and APOA5 genes contribute to the development of dyslipidemia.

What this study adds?

There were few studies that investigate the association between genetic factors and dyslipidemia in Thai population. Our study reveals that genetic factors have been confirmed as important factor for the development of dyslipidemia in Thai. In addition, the future studies are needed to examine interaction between environmental factors (such as dietary consumption, exercise, and alcohol consumption, etc.) and genetic factors in larger sample size in Thai population.

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Authors' contributions

Principle investigator, experimental performing, data analysis, and manuscript writhing: Dr. Wanida Chuenta. Corresponding author, study concept and design, and data collection: Dr. Sivaporn Wannaiampikul. Data collection, analysis and interpretation: Brian Lee. Contributed reagents, laboratory machines, and project management: Miss Apinya Cheewaphan. All authors had read and approved the final manuscript.

Potential conflicts of interest

The authors declare no conflict of interest.

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