Original Article
Association between the *MGAT1* rs634501 polymorphism and serum lipid traits in the Chinese Han and Maonan ethnic groups

Jie Wu, Rui-Xing Yin, Yong-Gang Zhou, Qing-Hui Zhang, Jin-Zhen Wu, Wu-Xian Chen

Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, People's Republic of China

Abstract: Little is known about the association of monoacylglycerol acyltransferase 1 gene (*MGAT1*) rs634501 single nucleotide polymorphism (SNP) and serum lipid profiles in the Chinese populations. The aim of this study was to detect the association of the *MGAT1* rs634501 SNP and several environmental factors with serum lipid levels in the Chinese Maonan and Han populations. Genotypes of the SNP in 2014 unrelated participants (Han, 986; Maonan, 1028) were determined by polymerase chain reaction and restriction fragment length polymorphism combined with gel electrophoresis, and confirmed by direct sequencing. The genotypic and allelic frequencies of the *MGAT1* rs634501 SNP were significantly different between the Han and Maonan populations as well as between males and females in the Maonan population. The A allele carriers had lower serum apolipoprotein (Apo) A1 levels, the ApoA1/ApoB ratio and higher ApoB levels in Maonans; and lower high-density lipoprotein cholesterol, ApoA1 levels, ApoA1/ApoB ratio, and higher triglyceride levels in Han than the A allele non-carriers. There were also different associations of the *MGAT1* rs634501 SNP and serum lipid profiles between males and females in the both ethnic groups. Serum lipid parameters in the two ethnic groups were also associated with several environmental factors. These results suggest that the association of the *MGAT1* rs634501 SNP and serum lipid parameters might have ethnic- and/or sex-specificity.

Keywords: Mannosyl (alpha-1,3-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase, single nucleotide polymorphism, lipids, environmental factors

Introduction

Coronary heart disease (CHD) is the main cause of death and disability worldwide, and it is a huge drain on public health expenditure [1-3]. CHD in the United States leads to 502,000 deaths each year [4], while the number of deaths per year in China is higher than 700,000 [5]. It is a truth universally acknowledged that dyslipidemia plays a vital role in CHD [6]. Dyslipidemia includes increased serum or plasma total cholesterol (TC) [7], triglyceride (TG) [8], low-density lipoprotein cholesterol (LDL-C) [9], and apolipoprotein (Apo) B [10] levels, together with decreased levels of ApoA1 [10], high-density lipoprotein cholesterol (HDL-C) [11] and the ratio of ApoA1 to ApoB (ApoA1/ApoB) [12].

To date, many studies have shown that dyslipidemia is a multi-factorial disease influenced by both environmental and genetic factors [13, 14]. Accumulating evidence has shown that the heritability estimates of the inter-individual variation give rise to a considerable genetic contribution [15, 16]. Recently genome-wide association studies (GWASes), which could display genetic contribution to dyslipidemia, have identified multiple lipid-related loci and provided valuable information to develop novel therapeutic interventions for dyslipidemia [17, 18].

Mannosyl (alpha-1,3-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase gene (*MGAT1*), localizes on chromosome 5, and is a key enzyme involved in glycosylation of proteins and lipids [19]. It has been found that a variant of the *MGAT1* rs12517906, rs4285184 SNPs is associated with body weight and obesity [20, 21]. Recently, GWASes have identified that genetic variant of *MGAT1* rs634501 SNP is associated with serum HDL-C level in East

Asians [22]. However, the effect of *MGAT1* rs634501 SNP on serum lipid levels is not functionally validated and the mechanism is yet unclear. Furthermore, the reproducibility of this association has not been detected in the Chinese populations to date.

China is a multi-ethnic country since ancient times. Han is the largest one and Maonan ethnic group is one of the 55 ethnic minorities with a population of 101,192 according to the sixth national census statistics of China in 2010. Maonan nationality mainly settled in the Huanjiang Maonan Autonomous County, Guangxi Zhuang Autonomous Region. In a previous study, we have shown significant association of several SNPs [23] and serum lipid levels in the Maonan population. To date, the association of rs634501 SNP and serum lipid levels has not been explored in the Chinese populations. Therefore, the aim of the present study was to assess the association of the *MGAT1* rs634501 SNP and several environmental factors with serum lipid phenotypes in the Han and Maonan populations.

Materials and methods

Study population

The present study included 2,014 unrelated subjects who were randomly selected from our previous stratified randomized samples. The sample comprised 986 Han Chinese (480 males, 48.68%; 506 females, 51.32%) and 1028 Maonan subjects (503 males, 48.93%; 525 females, 51.07%). They lived in the Huanjiang Maonan Autonomous County, Guangxi, China. Age ranged from 16 to 92 years, with a mean age of 56.25 ± 13.93 years (Han) and 57.19 ± 14.86 years (Maonan). The two ethnic groups showed similar age distribution and gender ratio. All participants were healthy and showed no evidence of diabetes, CHD, or atherosclerosis. None of the subjects was taking medications known to affect serum lipid levels, such as statins, hormones, diuretics, or beta-blockers. This study was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University (Lunshen-2014-KY-Guoji-001, 07 March 2014). Informed consent was obtained from all subjects.

Epidemiological survey

The present study was carried out using internationally standardized methods [24, 25].

Standardized questionnaire was used to collect the information on socioeconomic status, lifestyle factors, and demographics. Cigarette smoking was categorized into groups of 0 (non-smoker), ≤ 20 or > 20 cigarettes/day. Alcohol intake was quantified as the number of liang (50 g) of corn wine, rice wine, beer, rum, or liquor consumed during the preceding 12 months. Alcohol consumption was categorized based on grams consumed per day: 0 (non-drinker), ≤ 25/day or > 25/day. In the physical examination, several parameters covering body height, weight, body mass index (BMI), waist circumference, and blood pressure (BP) were measured. Height was measured, to the nearest 0.5 cm, using a stadiometer. Weight, to the nearest 50 g, was estimated by a portable weighing machine. BMI (kg/m^2) was calculated. Waist circumference was measured by a non-stretchable measuring tape. Sitting BP was measured three times with the using of a mercury sphygmomanometers. Systolic BP (SBP) was determined by the first Korotkoff sound, and diastolic BP (DBP) by the fifth Korotkoff sound.

Clinical specimen analysis

Venous blood sample (5 ml) was extracted from all subjects after at least 12 h of fasting. From the total sample, 2-ml was used to determine serum lipid levels, and the remaining 3-ml was used to extract deoxyribonucleic acid (DNA). Measurements of serum TC, TG, HDL-C, and LDL-C levels were performed enzymatically using commercially available kits (Randox Laboratories, Crumlin, UK; Daiichi Pure Chemicals, Tokyo, Japan). Serum ApoA1 and ApoB levels were assayed using a commercial turbidimetric immunoassay. All determinations were made on an auto-analyzer (Type 7170A; Hitachi, Tokyo, Japan) at the Clinical Science Experiment Center of the First Affiliated Hospital, Guangxi Medical University [26, 27].

Diagnostic criteria

The normal ranges of serum clinical values based on routine practice at our Clinical Science Experimental Center were: TC, 3.10-5.17 mmol/L; TG, 0.56-1.70 mmol/L; HDL-C, 1.16-1.42 mmol/L; LDL-C, 2.70-3.10 mmol/L; ApoA1, 1.20-1.60 g/L; ApoB, 0.80-1.05 g/L; and ApoA1/ApoB ratio, 1.00-2.50. Individuals with TC > 5.17 mmol/L and/or TG > 1.70 mmol/L were defined as hyperlipidemic. Normal

Table 1. Comparison of demographic, and lifestyle characteristics and serum lipid profiles between the Maonan and Han populations

| Characteristics	Han	Maonan	t (x^2)	P
Number (n)	986	1028		
Gender (Male/Female)	480/506	503/525	0.012	0.911
Age (years)	56.25 ± 13.93	57.19 ± 14.86	-1.465	0.143
Height (cm)	157.20 ± 8.14	156.12 ± 8.18	0.417	0.677
Weight (kg)	53.88 ± 10.60	55.16 ± 9.27	2.881	0.004
Body mass index (kg/m²)				
Underweight (BMI < 18.5)	48 (4.87)	65 (6.32)		
Normal weight (18.5 ≤ BMI < 24)	248 (25.15)	206 (20.04)	8.960	0.030
Overweight (24 ≤ BMI < 28)	608 (61.67)	660 (64.20)		
Obesity (28 ≤ BMI)	82 (8.31)	97 (9.44)		
Waist circumference (cm)	76.47 ± 8.36	76.75 ± 9.21	-0.732	0.464
Systolic blood pressure (mmHg)	130.24 ± 18.94	135.89 ± 23.93	-5.860	0.000
Diastolic blood pressure (mmHg)	81.59 ± 10.82	82.65 ± 12.16	-2.061	0.039
Pulse pressure (mmHg)	48.65 ± 14.84	53.24 ± 18.12	-6.209	0.000
Smoking status (n%)				
Nonsmoking	738 (74.85)	859 (83.56)		
≤ 20 cigarettes/day	183 (18.56)	128 (12.45)	23.463	0.000
> 20 cigarettes/day	65 (6.59)	41 (3.99)		
Alcohol consumption (n%)				
Non-drinker	783 (79.41)	818 (79.57)		
≤ 25 g/day	148 (15.01)	125 (12.16)	1.259	0.196
> 25 g/day	55 (5.58)	85 (8.27)		
Glucose (mmol/L)	6.40 ± 1.55	6.26 ± 1.44	1.541	0.215
Total cholesterol (mmol/L)	4.95 ± 1.06	4.98 ± 1.40	-0.657	0.511
Triglyceride (mmol/L)	1.66 (0.60)	1.70 (0.79)	-2.678	0.007
HDL-C (mmol/L)	1.70 ± 0.41	1.75 ± 0.46	3.806	0.002
LDL-C (mmol/L)	2.85 ± 0.66	2.82 ± 0.72	1.327	0.185
Apo A1 (g/L)	1.34 ± 0.28	1.37 ± 0.31	-2.955	0.003
ApoB (g/L)	0.89 ± 0.20	0.87 ± 0.20	1.321	0.143
ApoA1/ApoB	1.58 ± 0.49	1.64 ± 0.64	-2.014	0.044

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Apo, Apolipoprotein; ApoA1/ApoB, ratio of ApoA1 to ApoB. Triglyceride values are presented as median (interquartile range). Based on the Wilcoxon-Mann-Whitney test.

weight, overweight and obesity were defined, respectively, as a BMI < 24, 24-28 or > 28 kg/m².

DNA amplification and genotyping

Genomic DNA was extracted from peripheral blood leukocytes by the phenol-chloroform method [26, 27]. The extracted DNA was stored at 4°C until analysis. The *MGAT1* rs634501 SNP was genotyped by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. PCR amplification was performed using 5'-TTCCTGCTTAATACCCCG-CA-3' and 5'-GGTGGAGAAAGTGAGGACCA-3' as the forward and reverse primer pairs. Each amplification reaction was performed in a total volume of 25 μl, which contained 2.5 μl of 10 × PCR buffer (1.8 mM MgCl₂), 1 U of *Taq* polymerase, 2.0 μl of 2.5 mmol/L dNTPs (Tiangen, Beijing, China), 20 pmol/L of each primer and 50 ng of genomic DNA. Reactions were heated at 95°C for 5 min, followed by 33 cycles of denaturation for 30 s at 95°C, annealing for 30 s at 59°C and elongation for 35 s at 72°C. After electrophoresis on a 2.0% (w/v) agarose gel with 0.5 μg/ml ethidium bromide, the amplified products were visualized under UV light. Then
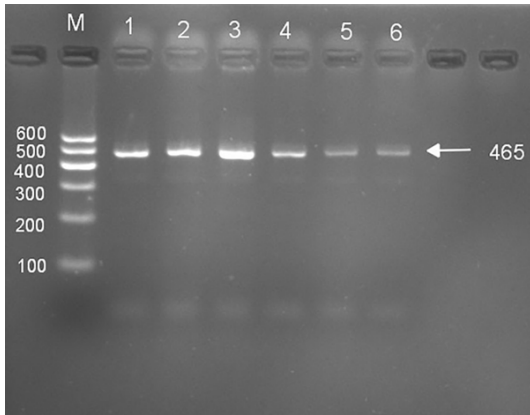
Figure 1. Electrophoresis of PCR products of the samples. Lane M, 100-bp marker ladder. Lanes 1-6, samples. The target amplicon is 465 bp long.
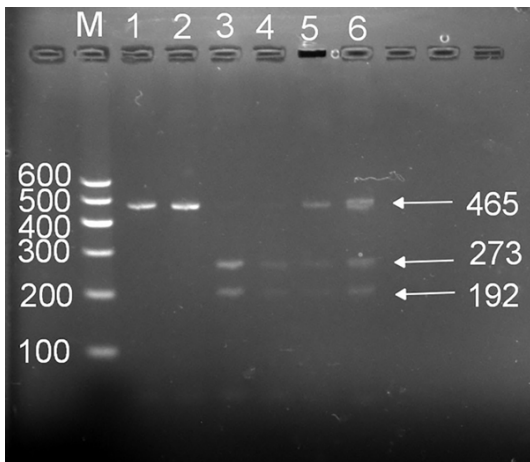
Figure 2. Genotyping of the *MGAT1* rs634501 SNP. Lane M, 100-bp marker ladder; lanes 1 and 2, GG genotype (465 bp); lanes 3 and 4, AA genotype (273- and 192-bp); and lanes 5 and 6, AG genotype (465-, 273- and 192-bp).

amplification, *TspR*I restriction enzyme was added directly to the PCR products (10 μl) at digested at 65°C for 0.5 h. Digests were run on agarose gels, stained with 2% ethidium bromide and visualized by ultraviolet illumination. Genotypes were scored by an experienced reader blinded to epidemiological and lipid results. Three samples with each rs634501 genotypes as determined by PCR-RFLP (nine samples total) were confirmed by direct sequencing. PCR products were purified on low-melting-point agarose gel, phenol-extracted, and sequenced on an ABI Prism 3100 sequencer (Applied Biosystems) by Shanghai Sango Biological Engineering Technology & Services (Shanghai, China).

Statistical analyses

Epidemiological data were recorded on a predesigned form and managed using Microsoft Excel. Statistical analyses were performed using SPSS 17.0 (IBM, Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation, and qualitative variables were expressed as percentages. Allele frequency was determined by direct counting, while accordance with predictions of Hardy-Weinberg equilibrium was assessed based on standard goodness-of-fit. Differences in general characteristics between the two ethnic groups were assessed for significance using Student's unpaired *t*-test. Differences in genotype distribution between the groups were assessed using the chi-square test. Association between genotype and serum lipid parameters was tested by analysis of covariance (ANCOVA). Data were adjusted for age, BMI, sex, BP, cigarette smoking, and alcohol consumption during statistical analyses. Multivariate linear regression analysis with stepwise modeling was performed to evaluate the association of serum lipid levels with genotypes (AA = 1, AG = 2, GG = 3) and with several environmental factors in the combined Han and Maonan populations. A $P < 0.05$ was considered significant.

Results

General characteristics and serum lipid profiles

Serum lipid levels and general characteristics of the Han and Maonan populations are summarized in **Table 1**. Maonan subjects had higher weight, BMI, SBP, DBP, pulse pressure, cigarette smoking, TG, HDL-C, ApoA1 and the ApoA1/ApoB ratio than the Han participants ($P < 0.05$ for all). There were no differences in gender ratio, age, height, waist circumference, glucose, alcohol consumption, TC, LDL-C and ApoB levels between the two ethnic groups ($P > 0.05$ for all).

Results of electrophoresis and genotyping

The expected 465-bp PCR product was identified in all subjects (**Figure 1**), and the genotype was determined based on the presence of a *TspR*I restriction site (G allele) or its absence (A allele). Subjects with a GG genotype showed only a band of 465 bp; subjects with a AG genotype showed bands of 465-, 273- and 192-bp;
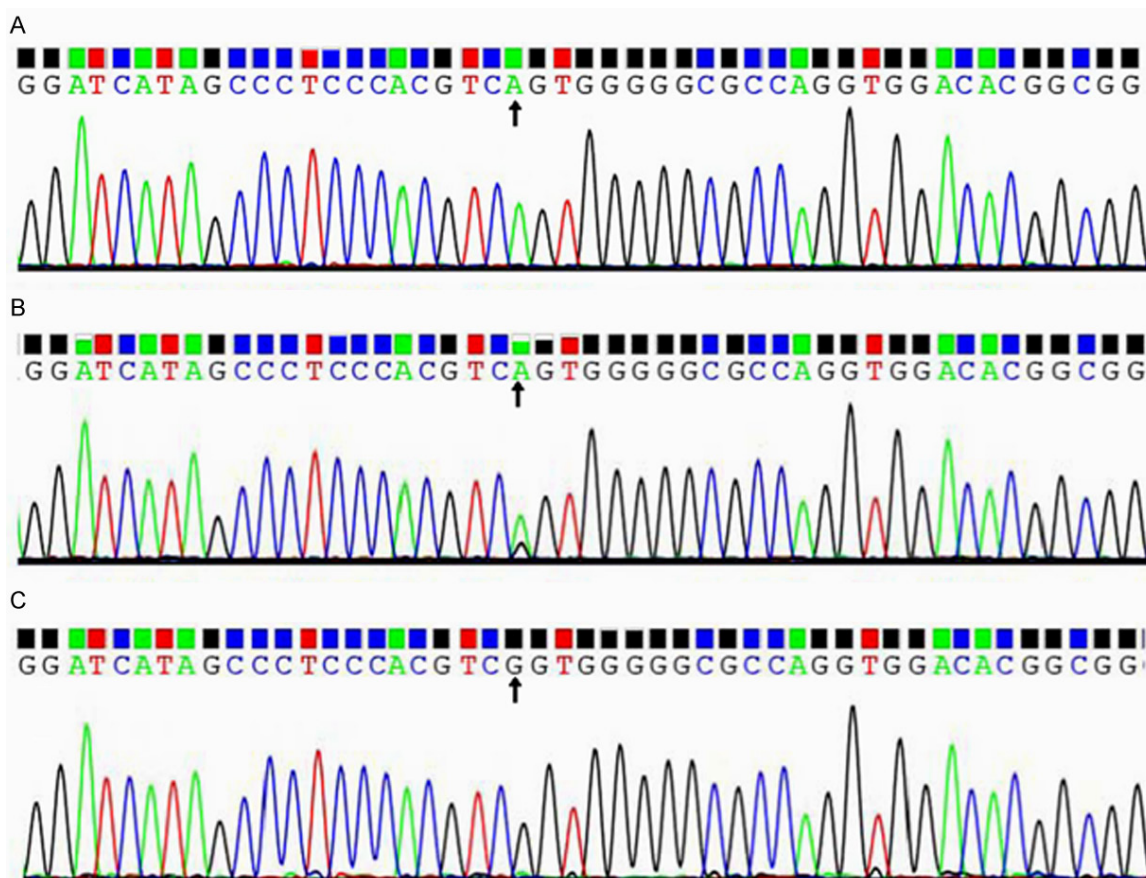
Figure 3. Partial nucleotide sequence of the *MGAT1* rs634501 SNP. (A) AA genotype, (B) AG genotype, and (C) GG genotype.

those with a AA genotype showed bands of 273- and 192-bp (**Figure 2**). The accuracy of PCR-RFLP genotyping was confirmed by direct sequencing (**Figure 3**). The genotypes of the rs634501 SNP followed the Hardy-Weinberg equilibrium.

Genotypic and allelic frequencies

The genotypic and allelic frequencies of the *MGAT1* rs634501 SNP in both ethnic groups are shown in **Table 2**. Genotypic and allelic frequencies were significantly different between the two ethnic groups, as well as between Maonan males and females ($P < 0.05$ for all), but not between Han males and females ($P > 0.05$).

Genotypes and serum lipid profiles

Table 3 summarizes the associations between genotypes and serum lipid levels in Maonan and Han ethnic groups. Serum ApoA1, ApoB

levels and the ApoA1/ApoB ratio in Maonans were different among the AA, AG and GG genotypes ($P < 0.05$). The A allele carriers had lower levels of ApoA1, the ApoA1/ApoB ratio, as well as higher level of ApoB than the A allele non-carriers. Serum TG, HDL-C, ApoA1 levels and the ApoA1/ApoB ratio in Han were different among the three genotypes ($P < 0.05$). The A allele carriers had lower HDL-C, ApoA1 levels and ApoA1/ApoB ratio, and higher TG than the A allele non-carriers. Subgroup analysis according to sex found that the three genotypes were associated with different levels of TG among Maonan males; TG, ApoA1, ApoB as well as ApoA1/ApoB ratio among Maonan females; TG among Han males; and TG and HDL-C among Han females ($P < 0.05$ for all).

Environmental factors and serum lipid traits

Tables 4, **5** describe the associations between some environmental factors and serum lipid parameters in the two ethnic groups. Several

Table 2. Comparison of genotypic and allelic frequencies at *MGAT1* rs634501 SNP between the two ethnic groups and between males and females

Group	n	Genotype			Allele	
		AA	AG	GG	A	G
Han	986	203 (20.59)	502 (50.91)	281 (28.50)	908 (46.04)	1064 (53.96)
Maonan	1028	143 (13.91)	455 (44.26)	430 (41.83)	741 (36.04)	1315 (63.96)
x^2			43.081			41.608
P			0.000			0.000
Maonan						
Male	503	62 (12.33)	211 (41.95)	230 (45.72)	335 (33.30)	671 (66.70)
Female	525	81 (15.43)	244 (46.48)	200 (38.09)	406 (38.67)	644 (61.34)
x^2			6.543			6.419
P			0.038			0.011
Han						
Male	480	105 (21.88)	253 (52.71)	122 (25.41)	463 (48.23)	497 (51.77)
Female	506	98 (19.37)	249 (49.21)	159 (31.42)	445 (43.97)	567 (56.03)
x^2			4.463			3.593
P			0.107			0.058

environmental factors such as gender, age, weight, height, waist circumference, cigarette smoking, and alcohol consumption were correlated with serum lipid parameters. Similarly, several traditional cardiovascular risk factors included BMI, blood glucose, SBP, and DBP were also correlated with serum lipid traits ($P <$ 0.05-0.001).

Multiple linear regression analysis showed that serum TG, HDL-C, LDL-C ApoB levels and the ApoA1/ApoB ratio in both ethnic groups; TC, TG, HDL-C, ApoB levels and the ApoA1/ApoB ratio in Maonans; and TG, HDL-C, LDL-C, ApoA1 levels and the ApoA1/ApoB ratio in Hans were correlated with the genotypes ($P <$ 0.05 for all; **Table 4**).

As shown in **Table 5**, when serum lipid data were analyzed according to gender, serum HDL-C levels and the ApoA1/ApoB ratio in Maonan males; ApoA1, ApoB levels and the ApoA1/ApoB ratio in Maonan females; HDL-C, ApoA1 levels and the ApoA1/ApoB ratio in Han males; and TC, TG, HDL-C, LDL-C, ApoA1 levels and the ApoA1/ApoB ratio in Han females were correlated with genotypes ($P <$ 0.05 for all).

Discussion

In the current study, we demonstrated that serum TG, HDL-C, ApoA1 levels, and the ApoA1/ApoB ratio were higher in the Maonan subjects than in Han participants. There were no significant differences in TC, LDL-C, and ApoB levels between the two ethnic groups. It is well-known that dyslipidemia is a complex trait caused by environmental and genetic factors. Family and twin studies suggest that in numerous populations, 40-60% of the variation in serum lipid profiles is genetically determined [28, 29]. Maonan is a famous mountain nationality as well as a relatively conservative minority in China. Maonan nationality has a huge different culture and life habits from the Han Chinese. To date, they still conserve the original culture and life habits and lack communication with other nationalities. Rice and corn foods are their staple diet, supplemented by sorghum, sweet potatoes, and pumpkin. Marriages arranged by their parents were common and strict intra-ethnic marriages are also popular in this minority. At the same time, the brides do not live with their husbands until the first child is born. Therefore, we considered that the hereditary characteristics and genotypes of certain lipid metabolism-related genes in this population may be different from those in the Han Chinese.

The genotypic and allelic frequencies of the *MGAT1* rs634501 SNP in diverse racial/ethnic groups are different, which can be found on the International HapMap project website (https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs = 634501). The frequency of AA, AG and GG genotypes was 5.3%, 35.4% and 59.3% in

Table 3. Comparison of *MGAT1* rs634501 genotypes and serum lipid levels in Han and Maonan populations

Gentoype	N	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ApoB
Maonan								
AA	143	5.06 ± 1.30	1.82 (0.90)	1.66 ± 0.41	2.81 ± 0.77	1.32 ± 0.24	0.89 ± 0.19	1.57 ± 0.45
AG	455	5.01 ± 1.03	1.76 (0.84)	1.67 ± 0.41	2.88 ± 0.84	1.39 ± 0.35	0.90 ± 0.21	1.63 ± 0.62
GG	430	4.99 ± 1.89	1.58 (0.72)	1.72 ± 0.40	2.78 ± 0.75	1.41 ± 0.24	0.86 ± 0.21	1.70 ± 0.52
F		0.139	4.503	2.671	1.945	4.611	3.660	6.276
P		0.870	0.105	0.070	0.143	0.010	0.026	0.002
Male								
AA	62	4.98 ± 1.00	1.87 (0.56)	1.64 ± 0.45	2.77 ± 0.81	1.33 ± 0.25	0.90 ± 0.17	1.53 ± 0.42
AG	211	4.91 ± 0.93	1.78 (0.94)	1.66 ± 0.42	2.78 ± 0.85	1.37 ± 0.45	0.90 ± 0.22	1.63 ± 0.77
GG	230	4.81 ± 1.31	1.61 (0.98)	1.74 ± 0.43	2.70 ± 0.67	1.38 ± 0.26	0.88 ± 0.21	1.67 ± 0.55
F		0.511	6.778	2.770	0.699	0.693	0.442	1.126
p		0.600	0.034	0.064	0.498	0.500	0.643	0.325
Female								
AA	81	5.13 ± 1.49	1.83 (1.22)	1.68 ± 0.38	2.85 ± 0.74	1.32 ± 0.23	0.88 ± 0.20	1.58 ± 0.46
AG	244	5.10 ± 1.10	1.70 (0.81)	1.69 ± 0.39	2.97 ± 0.83	1.40 ± 0.22	0.89 ± 0.20	1.63 ± 0.44
GG	200	5.08 ± 1.29	1.58 (0.67)	1.71 ± 0.37	2.88 ± 0.81	1.43 ± 0.20	0.84 ± 0.20	1.80 ± 0.49
F		0.043	6.117	0.362	1.174	8.078	4.832	9.7769
P		0.958	0.047	0.697	0.310	0.000	0.008	0.000
Han								
AA	203	5.06 ± 0.94	1.76 (0.57)	1.66 ± 0.41	2.89 ± 0.86	1.30 ± 0.22	0.90 ± 0.21	1.54 ± 0.49
AG	502	4.94 ± 1.09	1.66 (0.62)	1.75 ± 0.49	2.84 ± 0.66	1.35 ± 0.23	0.91 ± 0.23	1.56 ± 0.49
GG	281	4.87 ± 1.09	1.61 (0.51)	1.83 ± 0.43	2.84 ± 0.43	1.36 ± 0.19	0.89 ± 0.23	1.65 ± 0.50
F		2.056	18.236	8.587	0.522	5.061	2.021	3.597
P		0.129	0.000	0.000	0.594	0.007	0.133	0.028
Male								
AA	105	5.05 ± 0.87	1.76 (0.81)	1.61 ± 0.39	2.91 ± 0.83	1.29 ± 0.24	0.91 ± 0.20	1.50 ± 0.48
AG	253	4.91 ± 0.96	1.64 (0.69)	1.73 ± 0.55	2.87 ± 0.58	1.34 ± 0.24	0.94 ± 0.24	1.53 ± 0.54
GG	122	4.90 ± 0.67	1.63 (0.76)	1.82 ± 0.44	2.89 ± 0.46	1.37 ± 0.21	0.90 ± 0.25	1.66 ± 0.56
F		0.996	7.495	5.172	0.066	3.449	2.255	3.544
P		0.370	0.024	0.006	0.844	0.051	0.106	0.030
Female								
AA	98	5.08 ± 1.01	1.72 (0.42)	1.70 ± 0.43	2.86 ± 0.90	1.30 ± 0.20	0.89 ± 0.23	1.57 ± 0.53
AG	249	4.96 ± 1.20	1.68 (0.56)	1.77 ± 0.42	2.80 ± 0.74	1.34 ± 0.23	0.89 ± 0.21	1.58 ± 0.43
GG	159	4.84 ± 1.33	1.61 (0.36)	1.83 ± 0.42	2.79 ± 0.40	1.35 ± 0.17	0.88 ± 0.21	1.62 ± 0.44
F		1.254	17.464	3.114	0.343	2.372	0.160	0.498
P		0.286	0.000	0.045	0.710	0.094	0.852	0.608

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; ApoA1/ApoB, the ratio of Apolipoprotein A1 to Apolipoprotein B. Triglyceride values are presented as median (interquartile range). Differences among the genotypes were assessed for significance using the Kruskal-Wallis test.

Utah residents with ancestry from Northern and Western Europe (CEU); 8.1%, 45.35% and 46.55% in Japanese in Tokyo, Japan (JPT); 0, 14.16% and 85.84% in Sub-Saharan African (YRI); and 25.58%, 39.53% and 34.89% in Han Chinese in Beijing, China (CHB). The frequency of A and G alleles was 23.0% and 77.0% in CEU; 30.8% and 69.2% in JPT; 7.0% and 93.0% in YRI and 45.35% and 54.65% in CHB. In the current study, the frequency of AA, AG, GG genotypes

Table 4. Factors influencing serum lipid parameters in Han and Maonan populations

Lipid	Risk factor	B	Std.error	Beta	t	P
Han & Maonan						
TC	Gender	-0.220	0.086	-0.088	-2.542	0.011
	Cigarette smoking	0.018	0.004	0.127	4.313	0.000
	Alcohol consumption	0.003	0.001	0.068	2.420	0.016
	Waist circumference	0.028	0.006	0.201	4.887	0.000
	Systolic blood pressure	0.005	0.002	0.082	2.215	0.027
TG	Gender	-0.179	0.070	-0.090	-2.560	0.011
	Genotype	-0.125	0.035	-0.089	-3.571	0.000
	Waist circumference	0.011	0.005	0.096	2.301	0.022
	Blood glucose	0.061	0.017	0.093	3.647	0.000
HDL-C	Gender	-0.076	0.029	-0.089	-2.596	0.010
	Genotype	0.068	0.015	0.113	4.650	0.000
	Age	0.002	0.001	0.081	2.800	0.005
	Alcohol consumption	0.002	0.000	0.145	5.230	0.000
	Height	0.007	0,004	0.142	2.026	0.043
	Systolic blood pressure	-0.002	0.001	-0.080	-2.201	0.028
	Waist circumference	-0.009	0.002	-0.187	-4.608	0.000
LDL-C	Gender	0.642	0.059	0.352	10.918	0.000
	Genotype	-0.065	0.029	-0.051	-2.212	0.027
	Alcohol consumption	-0.004	0.001	-0.135	-5.135	0.000
	Blood glucose	0.061	0.014	0.101	4.294	0.000
ApoA1	Gender	0.156	0.023	0.225	6.877	0.000
	Cigarette smoking	0.004	0.001	0.087	3.144	0.002
	Alcohol consumption	0.002	0.000	0.160	5.993	0.000
ApoB	Genotype	0.045	0.016	0.066	2.855	0.004
	Age	0.002	0.001	0.056	2.038	0.042
	Height	-0.011	0.004	-0.190	-2.834	0.005
	Weight	0.013	0.005	0.277	2.598	0.009
	BMI	-0.029	0.011	-0.206	-2.688	0.007
ApoA1/ApoB	Genotype	0.096	0.022	0.124	4.417	0.000
	Age	-0.003	0.001	-0.095	-2.818	0.005
	Alcohol consumption	0.003	0.000	0.197	6.288	0.000
	Weight	-0.018	0.006	-0.311	-2.773	0.006
	Waist circumference	-0.007	0.003	-0.112	-2.190	0.029
Maonan						
TC	Gender	-0.511	0.128	-0.192	-3.984	0.000
	Genotype	0.158	0.066	0.081	2.408	0.016
	Cigarette smoking	0.021	0.006	0.149	3.671	0.000
	Alcohol consumption	0.004	0.001	0.092	2.388	0.017
	Height	-0.067	0.026	-0.427	-2.577	-0.010
	Weight	0.082	0.036	0.662	2.280	0.023
	BMI	-0.194	0.078	-0.511	-2.481	0.013
	Waist circumference	0.035	0.008	0.241	4.382	0.000
TG	Gender	-0.237	0.120	-0.113	-2.269	0.024
	Genotype	-0.134	0.062	-0.076	-2.171	0.030
	Diastolic blood pressure	0.008	0.004	0.077	2.056	0.040
	Blood glucose	0.095	0.031	0.108	3.032	0.003

HDL-C	Genotype	0.062	0.020	0.105	3.087	0.002
	Age	0.003	0.001	0.106	2.656	0.008
	Alcohol consumption	0.003	0.000	0.215	5.547	0.000
	Waist circumference	-0.009	0.002	-0.206	-3.740	0.000
	Pulse pressure	-0.002	0.001	-0.096	-2.496	0.013
LDL-C	Gender	1.325	0.054	0.758	24.427	0.000
	Age	0.003	0.001	0.056	2.161	0.031
	Cigarette smoking	0.008	0.002	0.086	3.271	0.001
	Alcohol consumption	-0.005	0.001	-0.199	-7.968	0.000
	Height	-0.029	0.011	-0.286	-2.675	0.008
	Weight	0.049	0.015	0.600	3.206	0.001
	BMI	-0.098	0.033	-0.395	-2.969	0.003
ApoA1	Gender	0.423	0.030	0.543	14.328	0.000
	Cigarette smoking	0.003	0.001	0.063	1.979	0.048
	Alcohol consumption	0.002	0.000	0.164	5.387	0.000
ApoB	Gender	-0.831	0.038	-0.742	-21.872	0.000
	Genotype	0.077	0.019	0.095	3.974	0.000
	Height	-0.029	0.008	-0.448	-3.835	0.000
	Weight	0.048	0.011	0.920	4.496	0.000
	BMI	-0,098	0.023	-0.618	-4.251	0.000
	Waist circumference	-0.009	0.002	-0.156	-4.029	0.000
	Pulse pressure	-0.003	0.001	-0.081	-2.999	0.003
ApoA1/ApoB	Genotype	0.117	0.050	0.117	2.327	0.021
	Age	-0.005	0.003	-0.123	-2.033	0.043
	Alcohol consumption	0.004	0.001	0.254	4.908	0.000
	Waist circumference	-0.019	0.006	-0.263	-2.931	0.004
	Blood glucose	-0.062	0.025	-0.127	-2.512	0.012
Han						
TC	Diastolic blood pressure	0.006	0.004	0.062	2.662	0.043
TG	Genotype	-0.077	0.036	-0.082	-2.125	0.034
	Blood glucose	0.039	0.016	0.094	2.531	0.012
HDL-C	Genotype	0.098	0.023	0.159	4.245	0.000
	Height	0.009	0.005	0.166	2.040	0.042
LDL-C	Genotype	-0.075	0.037	-0.077	-2.029	0.043
	Age	0.004	0.002	0.092	2.148	0.032
	Waist circumference	0.011	0.005	0.130	2.028	0.043
	Blood glucose	0.035	0.016	0.082	2.246	0.025
ApoA1	Genotype	0.041	0.012	0.131	2.535	0.000
	Cigarette smoking	0.004	0.001	0.118	2.853	0.004
	Alcohol consumption	0.002	0.000	0.221	5.657	0.000
ApoB	Age	0.002	0.001	0.128	3.018	0.003
	Weight	0.007	0.003	0.299	2.457	0.014
	Blood glucose	0.011	0.005	0.079	2.188	0.029
ApoA1/ApoB	Genotype	0.079	0.025	0.117	3.184	0.002
	Cigarette smoking	0.006	0.003	0086	2.101	0.036
	Alcohol consumption	0.002	0.001	0.116	3.005	0.003
	Weight	-0.021	0.006	-0.391	-3.266	0.001
	Blood glucose	-0.026	0.011	-0.086	-2.431	0.015

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; ApoA1/ApoB, the ratio of Apolipoprotein A1 to Apolipoprotein B.

Table 5. Factors influencing serum lipid parameters in the males and females of Han and Maonan populations

Lipid	Risk factor	B	Std.error	Beta	t	P
Moanan/Male						0.003
TC	Age	-0.018	0.006	-0.181	-3.025	0.003
	Cigarette smoking	0.020	0.006	0.167	3.174	0.002
	Waist circumference	0.046	0.014	0.288	3.221	0.001
TG	Blood glucose	0.105	0.059	0.150	2.781	0.006
HDL-C	Genotype	0.073	0.032	0.116	2.321	0.021
	Alcohol consumption	0.003	0.000	0.282	5.495	0.000
	Waist circumference	-0.020	0.004	-0.451	-5.052	0.000
LDL-C	Alcohol consumption	-0.005	0.001	-0.303	-5.720	0.000
	Cigarette smoking	0.008	0.003	0.129	2.382	0.018
ApoA1	Alcohol consumption	0.002	0.000	0.226	4.189	0.000
	Waist circumference	-0.012	0.004	-0.305	-3.255	0.001
ApoB	Age	0.002	0.001	0.152	2.605	0.010
	Alcohol consumption	0.000	0.000	-0.127	-2.522	0.012
	Height	-0.025	0.012	-0.780	-2.179	0.030
	Weight	0.038	0.015	1.803	2.496	0.013
	BMI	-0.080	0.040	-1.170	-1.994	0.047
	Blood glucose	0.024	0.008	0.158	3.211	0.001
ApoA1/ApoB	Genotype	0.116	0.049	0.118	2.362	0.019
	Age	-0.005	0.003	-0.121	-2.037	0.042
	Alcohol consumption	0.004	0.001	0.254	4.948	0.000
	Waist circumference	-0.019	0.006	-0.265	-2.967	0.003
	Blood glucose	-0.062	0.024	-0.013	-2.597	0.010
Maonan/female						
TC	Age	0.013	0.004	0.153	2.956	0.003
	Waist circumference	0.032	0.009	0.217	3.371	0.001
	Blood glucose	-0.123	0.040	-0.138	-3.071	0.002
TG	Waist circumference	0.017	0.006	0.170	2.611	0.009
	Diastolic blood pressure	0.007	0.003	0.099	2.105	0.036
HDL-C	Age	0.003	0.001	0.106	2.026	0.043
	Pulse pressure	-0.002	0.001	-0.106	-2.090	0.037
LDL-C	Waist circumference	0.031	0.010	0.219	3.298	0.001
ApoA1	Genotype	0.060	0.014	0.193	4.265	0.000
	Height	0.014	0.006	0.383	2.201	0.028
ApoB	Genotype	-0.042	0.012	-0.144	-3.415	0.001
	Age	0.002	0.001	0.126	2.567	0.011
	Waist circumference	0.008	0.001	0.355	5.829	0.000
	Pulse pressure	0.002	0.001	0.330	2.814	0.005
ApoA1/ApoB	Genotype	0.157	0.029	0.231	5.450	0.000
	Waist circumference	-0.016	0.003	-0.290	-4.760	0.000
	Pulse pressure	-0.004	0.001	-0.132	-2.793	0.005
Han/Male						
TC	Weight	-0.031	0.015	-0.299	-2.017	0.045
	Waist circumference	0.024	0.011	0.211	2.070	0.039
	Diastolic blood pressure	0.011	0.005	0.145	2.304	0.022
TG	Age	0.002	0.001	0.313	2.812	0.004

HDL-C	Genotype	0.160	0.044	0.235	3.685	0.000
ApoA1	Genotype	0.070	0.022	0.193	3.160	0.002
	Cigarette smoking	0.004	0.002	0.161	2.598	0.010
	Alcohol consumption	0.002	0.000	0.272	4.574	0.000
ApoB	Diastolic blood pressure	0.003	0.001	0.162	2.711	0.007
ApoA1/ApoB	Genotype	0.095	0.045	0.126	2.110	0.036
	Cigarette smoking	0.007	0.003	0.131	2.164	0.031
	Alcohol consumption	0.003	0.001	0.196	3.370	0.001
	Weight	-0.023	-.008	-0.387	-2.827	0.005
	Blood glucose	-0.045	0.019	-0.140	-2.444	0.015
Han/Female						
TC	Genotype	-0.183	0.085	-0.106	-2.162	0.031
TG	Genotype	-0.089	0.039	-0.110	-2.263	0.024
	Blood glucose	0.047	0.016	0.135	2.908	0.004
HDL-C	Genotype	0.072	0.028	0.119	2.527	0.012
LDL-C	Genotype	-0.119	0.046	-0.121	-2.617	0.009
	Age	0.013	0.003	0.273	4.940	0.000
ApoA1	Genotype	0.029	0.014	0.096	1.997	0.046
	Alcohol consumption	0.004	0.001	0.133	2.865	0.004
ApoB	Age	0.003	0.001	0.223	3.947	0.000
	Diastolic blood pressure	-0.002	0.001	-0.107	-2.222	0.027
ApoA1/ApoB	Genotype	0.065	0.031	0.100	2.100	0.036
	Age	-0.005	0.002	-0.158	-2.776	0.006
	Diastolic blood pressure	0.006	0.002	0.131	2.720	0.007

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; ApoA1/ApoB, the ratio of Apolipoprotein A1 to Apolipoprotein B.

was 20.59%, 50.91% and 28.50% in Han Chinese; and 13.91%, 44.26% and 41.83% in Maonan nationality. The frequency of A and G alleles was 46.04% and 53.96% in Han; and 36.04% and 63.96% in Maonans. The frequencies of AA genotype and A allele were lower in the Maonans than in the Han Chinese ($P < 0.05$). According to these results, we conclude that *MGAT1* rs634501 SNP may have racial/ethnic specificity in our study populations.

There were scarcely any previous studies showing a direct relationship between the rs634501 SNP and lipid levels in humans except a new GWAS which showed that the rs634501 was significantly associated with HDL-C in the population of East Asians [22]. In the present study, we showed that the A allele carriers had higher ApoB levels and lower ApoA1 levels as well as the ApoA1/ApoB ratio in Maonans; higher TG levels and lower HDL-C, ApoA1 levels as well as the ApoA1/ApoB ratio in Han Chinese; higher TG levels in Maonan males; higher TG, ApoB levels and lower ApoA1 level and the ApoA1/ApoB ratio in Maonan females; higher TG levels

in Han males; higher TG levels and lower HDL-C levels in Han females than the A allele non-carriers. These findings indicated that the association of the *MGAT1* rs634501 SNP and serum lipid levels may have racial/ethnic and /or sex specificity. As far as we know, our study is the first replication of GWAS signals about the association of the *MGAT1* rs634501 SNP with serum lipid levels in the Chinese populations. Therefore, further studies with large sample size are still needed to confirm these associations.

In addition, we also showed that several environmental factors such as age, gender, BMI, waist circumference, SBP, DBP, blood glucose, alcohol consumption and cigarette smoking were associated with serum lipid levels in both ethnic groups. Maonan nationality settles in mountainous areas and has similar eating habits. They like acidic food, such as sour meat, sour snail, and sauerkraut. Maonan people also prefer to eating vegetables, such as peas, cabbages, bittersweet vegetables, as well as pumpkin. At the same time, they consume too

many animal offals which contain abundant saturated fatty acid. Several previous studies have shown a correlation between diet and changes in blood lipid levels [30, 31] including serum ApoB, ApoA1 levels and the ApoA1/ApoB ratio which can result in the risk of CHD [32-34]. Many other previous studies have reported that diets rich in polyunsaturated fatty acids (PUFAs), high carbohydrates, or saturated fatty acid, and even stearic acid can reduce LDL-C levels [35, 36]. In the present study, we also found that different lifestyles, dietary habits, or environmental factors probably further modified the effect of genetic variation on serum lipid levels in Han Chinese and Maonan populations. These findings might be partly attributed to the difference in daily eating habits in our study populations.

There are several limitations in this study. First, the general characteristics of the both ethnic groups were different. Although these characteristics have been adjusted for statistical analysis, we could not completely eliminate the effects of these factors on serum lipid levels among different genotypes in Han Chinese and Maonan populations. Secondly, diet was not adjusted for statistical analysis. In the present study, however, the diet in this isolated population is consistent throughout the year and among individuals because of the Maonans' reliance on a limited number of locally available food items. Finally, the interactions of gene-gene, gene-environment, and environment-environment on serum lipid levels remain to be determined.

Conclusion

The present study showed that the *MGAT1* rs634501 SNP and several environmental factors were associated with some serum lipid parameters in the Chinese Han and Maonan populations, but the associated trends of the SNP and serum lipid parameters are different. There is a sex-specific association of the *MGAT1* rs634501 and serum lipid parameters in both ethnic groups.

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Disclosure of conflict of interest

None.

Abbreviations

ANCOVA, Analysis of covariance; Apo, Apolipoprotein; BMI, Body mass index; CHD, Coronary heart disease; GWAS, Genome-wide association study; HDL-C, High-density lipoprotein cholesterol; HWE, Hardy-Weinberg equilibrium; LDL-C, Low-density lipoprotein cholesterol; PCR, Polymerase chain reaction; RFLP, Restriction fragment length polymorphism; SNP, Single nucleotide polymorphism; MGAT1, Mannosyl (alpha-1, 3-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase; TC, Total cholesterol; TG, Triglyceride.

Address correspondence to: Rui-Xing Yin, Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, 22 Shuangyong Road, Nanning 530021, Guangxi, People's Republic of China. E-mail: yinruixing@163.com

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