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Original Article

Sexually dimorphic association of the B-cell CLL/lymphoma 7B gene rs2237278 and lipid-associated phenotypes

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Abstract: The biology basis for gender differences in cardiovascular diseases (CVDs) susceptibility seems ubiquitous especially for postmenopausal women, but little is known about the sexually dimorphic association of the B-cell CLL/lymphoma 7B gene (*BCL7B*) rs2237278 single nucleotide polymorphism (SNP) and environmental factors with lipid profiles in the Jing and Han populations. To study the contribution of *BCL7B* rs2237278 to both the establishment and persistence of gender differences in lipid profiles, genotyping was performed in 1148 of Jing (582 males and 566 females) and 1355 of Han (706 males and 649 females) participants using polymerase chain reaction and restriction fragment length polymorphism. Sexually dimorphic analysis showed that the genotype and allele frequencies of the *BCL7B* rs2237278 SNP were significantly different between males and females in Jing (CC, 67.87% *vs*. 61.31%; CT, 29.55% *vs*. 34.63%; TT, 2.58% *vs*. 4.06%; $P = 0.047$; T, 17.35% *vs*. 21.38%, $P = 0.015$) and Han populations (CC, 68.27% *vs*. 62.10%; CT, 29.32% *vs*. 34.36%; TT, 2.41% *vs*. 3.54%; $P = 0.046$; T, 17.07% *vs*. 20.72%; $P = 0.015$) populations. Females had higher serum triglyceride (TG) levels in Jing and lower high-density lipoprotein (HDL) cholesterol levels in Han than males. TT genotype of *BCL7B* rs2237278 SNP was a risk genotype for dyslipidemia, especially higher serum TG levels in sexually dimorphic group both of two populations and lower serum HDL-cholesterol levels in Jing females. Our findings provide evidence to support sexually dimorphic association between *BCL7B* rs2237278 SNP and serum lipid profiles may account, at least in part, for the female predominance of dyslipidemia susceptibility. Thus, although data are more limited, there is good reason to believe that cholesterol interventions for female are likely to be effective, particular in postmenopausal women.

Keywords: Sexually dimorphic association, B-cell CLL/lymphoma 7B gene (*BCL7B*), single nucleotide polymorphism, lipids, environmental factors

Introduction

Over the last decade, cardiovascular diseases have become the single largest cause of death and disability-adjusted life years (DALYs) in both men and women worldwide [1-3]. There is a growing body of recently published genetic and epidemiological evidences which demonstrated a causal role of rising triglyceride (TG) levels (alongside with reducing of high-density lipoprotein cholesterol levels) [4] and TG-rich lipoproteins in the pathogenesis of atherosclerosis and particularly coronary artery disease [5-9]. These data support the renewed interest in hypertriglyceridemia as a possible important therapeutic target for cardiovascular risk reduction [10-14]. Although several studies have shown an improvement of prognosis in women over time [15, 16], overall outcomes remain worse for women compared with men [17], providing a strong rationale for focusing on the study of sex-based differences in the outcome of hyperlipidemia [18, 19], especially hypertriglyceridemia [20]. American Heart Association (AHA) and numerous government and professional organizations [21] have jointly developed evidence-based guidelines to assist with lipid assessment and treatment in high-risk women that take into consideration the quality, quantity, and generalizability of available data to women [22-24], because of high-risk women benefit significantly and to a similar degree as

men from lipid-lowering therapy, especially postmenopausal women [25-27].

Human B-cell CLL/lymphoma 7B (BCL7) gene family [28, 29] consists of BCL7A, BCL7B, and BCL7C. A number of clinical studies have reported that BCL7 family is involved in metabolic syndrome (MetS) incidence, progression, and development [30, 31]. BCL7B (Gene ID: 9275; MIM: 605846; Cytogenetic location: 7q-11.23; Genomic coordinates (GRCh38): 7:73,536,352-73,557,734) mutants exist that influence MetS and inflammatory markers forming a predisposing MetS genetic network [32-34]. This gene encodes a member of the BCL7 family including BCL7A, BCL7B and BCL7C proteins. BCL7B contains a region that is highly similar to the N-terminal segment of BCL7A or BCL7C proteins. The BCL7A protein is encoded by the gene known to be directly involved in a three-way gene translocation in a Burkitt lymphoma cell line. This gene is located at a chromosomal region commonly deleted in Williams's syndrome. It is highly conserved from C. elegans to human. Multiple alternatively spliced transcript variants have been found for this gene. A GWAS analysis has identified the rs17145738 SNP in the intronic region of BCL7B as TG-related loci in European populations [35, 36]. However, in Chinese population, whether *BCL7B* rs2237278 SNP is associated with lipid profiles or whether it exhibits sex-specific association like the other reported *BCL7B* SNPs remains elusive.

China has a majority population of Han ethnicity and 55 officially recognized ethnic minorities [37]. The Jing ethnic group is one of several isolated minorities in the Guangxi Zhuang Autonomous Region, China. The Jing population is the only oceanic ethnic group in China, with a very small population size of 28,199 in 2010 [38]. In the early 16th century, the Jing ancestors emigrated from Vietnam to China to first settle on the three islands of Wanwei, Wutou and Shanxin in Dongxing City, where almost all of the Jing population now live [38]. We recently showed that Jing has much closer genetic relationship with the other minorities in Guangxi than with the Han nationality [39]. In addition, several previous studies have revealed that the associations of variants in several lipid-related genes and lipid profiles are significantly different between the Jing and Han populations and their gender subgroups [40, 41]. This study, therefore, was undertaken to detect the association of *BCL7B* rs2237278 SNP and several environmental factors with lipid profiles between males and females in the Jing and Han populations.

Methods and materials

Ethical approval

The study design was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University. Informed consent was taken from all participants.

Subjects

Two groups of study population including 1148 unrelated participants (582 males, 50.7% and 566 females, 49.3%) of Jing and 1355 unrelated subjects (706 males, 52.1% and 649 females, 47.9%) of Han were randomly selected from our previous stratified randomized samples [42-44]. All participants were agricultural workers from Dongxing City, Guangxi Zhuang Autonomous Region, People's Republic of China. The participants' age ranged from 15 to 80 years with the mean age of 57.14±14.21 years in Jing males, 57.36±12.49 years in Jing females, 56.41±12.95 years in Han males, 57.20±12.40 years in Han females; respectively. The age distribution and gender ratio were matched between the two groups. All participants were essentially healthy with no history of coronary artery disease, stroke, diabetes, hyper- or hypo-thyroids, and chronic renal disease. They were free from medications known to affect lipid profiles.

Epidemiological survey

The epidemiological survey was carried out using internationally standardized methods, following a common protocol [42-44]. Information on demographics, socioeconomic status, and lifestyle factors was collected with standardized questionnaires. Smoking status was categorized into groups of cigarettes per day: < 20 and ≥ 20. Alcohol consumption was categorized into groups of grams of alcohol per day: < 25 and ≥ 25. Several parameters such as blood pressure, height, weight, waist circumference were measured, and body mass index (BMI, kg/m^2) was calculated [45-47].

Biochemical measurements

A fasting venous blood sample of 5 ml was drawn from the participants. The levels of total cholesterol (TC), TG, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) in the samples were determined by enzymatic methods with commercially available kits. Serum apolipoprotein (Apo) A1 and ApoB levels were assessed by the immune-turbidimetric immunoassay [45-47].

Genotyping

Genomic DNA was isolated from peripheral blood leukocytes using the phenol-chloroform method. The *BCL7B* rs2237278 SNP was genotyped by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP). PCR amplification was performed using 5'-GAGCGTGCCTCAGGTTAC-3' as the forward and 5'-GCAGGGATGCTGGAATGA-3' as reversed primer pair. Each amplification reaction was performed in a total volume of 25 μl, 12.5 μl of 2 × *Taq* PCR MasterMix (constituent: 0.1 U *Taq* polymerase/μl, 500 μM dNTP each and PCR buffer) and nuclease-free water 8.5 μl, 20 pmol/L of each primer and 100 ng of genomic DNA, processing started with 5 min of predenaturing at 95°C and followed by 45 s of denaturing at 94°C, 30 s of annealing at 65.0°C and 1 min of elongation at 72°C for 33 cycles. The amplification was completed by a final extension at 72°C for 10 min. Then each restriction enzyme reaction was performed with 10 μl of amplified DNA, 8 μl of nuclease-free water, 1 μl of 10 × buffer solution, and 10 U of *Sty*I enzyme in a total volume of 20 μl digested at 37°C overnight. After restriction enzyme digestion of the amplified DNA, the digestive products were separated by electrophoresis on 2% agrose gel. The length of each digested DNA fragment was determined by comparing migration of a sample with that of standard DNA marker. Genotypes were scored by an experienced reader blinded to the epidemiological and lipid results. Six samples (each genotype in two; respectively) detected by the PCR-RFLP were also confirmed by direct sequencing. The PCR products were purified by low melting point gel electrophoresis and phenol extraction, and then the DNA sequences were analyzed using an ABI Prism 3100 (Applied Biosystems) in Shanghai Sangon Biological Engineering Technology & Services Co., Ltd., People's Republic of China.

Diagnostic criteria

The normal values of serum TC, TG, HDL-C, LDL-C, ApoA1 and ApoB levels, and the ratio of ApoA1 to ApoB in our Clinical Science Experiment Center were 3.10-5.17, 0.56-1.70, 1.16-1.42, 2.70-3.10 mmol/L, 1.20-1.60, 0.80-1.05 g/L, and 1.00-2.50; respectively [45-47].

Statistical analysis

The statistical analyses were performed with the statistical software package SPSS 19.0 (SPSS Inc., Chicago, Illinois). The quantitative variables were presented as mean ± standard deviation (serum TG levels were presented as medians and interquartile ranges). Allele frequency was determined via direct counting, and the Hardy-Weinberg equilibrium was verified with the standard goodness-of-fit test. The genotype distribution between the groups was analyzed by the chi-square test. General characteristics between two ethnic groups were compared by the Student's unpaired *t*-test. The association between genotypes and serum lipid parameters was tested by analysis of covariance (ANCOVA). Age, sex, BMI, smoking, and alcohol consumption were adjusted for the statistical analysis. A factorial design covariance analysis was performed to assess the interaction between genotypes and gender after controlling for potential confounders including age, BMI, smoking, and alcohol consumption. Multivariable linear regression analyses with stepwise modeling were used to determine the correlation between genotypes (CC = 1, CT = 2, TT = 3) or alleles (the T allele non-carrier = 1, the T allele carrier = 2) and several environmental factors with lipid profiles in males and females of Jing and Han populations. Two sided P value < 0.05 was considered statistically significant.

Results

General and biochemical characteristics of the subjects

Table 1 compares the general characteristics and serum lipid profiles between males and females in Jing and Han ethnic groups. The values of height, weight, waist circumference and

Table 1. Comparison of demographic, lifestyle characteristics and serum lipid levels between males and females of the Jing and Han population

Parameter	Jing (n = 1148)		Han (n = 1355)	
	Male	Female	Male	Female
Number (n (%))	582 (50.7)	566 (49.3)	706 (52.1)	649 (47.9)
Age (years)	57.14±14.21	57.36±12.49	56.41±12.95	57.20±12.40
Height (cm)	162.94±6.84	153.26±5.74[a]	162.58±5.82	152.96±6.92[a]
Weight (kg)	62.20±9.93	55.23±9.12[a]	60.07±8.77	53.78±8.99[a]
Body mass index (kg/m^2)	23.37±3.04	23.47±3.35	22.70±2.89	22.96±3.43
Waist circumference (cm)	81.58±9.72	79.22±8.70[a]	78.53±8.24	77.27±9.18[b]
Cigarette smoking (n (%))				
Nonsmoker	370 (63.6)	563 (99.4)	405 (57.3)	623 (96.0)
≤ 20 cigarettes/day	54 (9.3)	1 (0.2)	62 (8.8)	5 (0.8)
> 20 cigarettes/day	158 (27.1)	2 (0.4)[a]	239 (33.9)	21 (3.2)[a]
Alcohol consumption (n (%))				
Nondrinker	330 (56.7)	554 (97.9)	300 (42.5)	611 (94.2)
≤ 25 g/day	128 (22.0)	10 (1.8)	92 (13.0)	6 (0.9)
> 25 g/day	124 (21.3)	2 (0.4)[a]	314 (44.5)	32 (4.9)[a]
Systolic blood pressure (mmHg)	131.29±19.92	131.97±22.95	138.20±77.37	130.86±19.92[c]
Diastolic blood pressure (mmHg)	80.76±10.71	80.30±10.40	82.17±10.56	80.54±10.28[b]
Pulse pressure (mmHg)	50.53±16.26	51.67±18.12	56.03±76.15	50.32±15.90
Blood glucose (mmol/L)	6.75±1.86	6.65±1.62	6.67±1.11	6.58±1.08
Total cholesterol (mmol/L)	5.11±0.82	5.18±0.99	4.84±0.87	4.94±0.85[c]
Triglyceride (mmol/L)	1.40 (1.13)	1.50 (1.14)[b]	1.31 (1.04)	1.32 (1.10)
HDL-cholesterol (mmol/L)	1.83±0.44	1.78±0.46	1.84±0.52	1.73±0.54[a]
LDL-cholesterol (mmol/L)	2.81±0.37	2.83±0.48	2.86±0.43	2.86±0.43
Apoliprotein (Apo) A1 (g/L)	1.31±0.25	1.29±0.22	1.34±0.21	1.33±0.20
ApoB (g/L)	1.06±0.24	1.06±0.26	1.03±0.25	1.05±0.24
ApoA1/ApoB	1.31±0.36	1.29±0.42	1.35±0.36	1.34±0.40

HDL: high-density lipoprotein; LDL-C: low-density lipoprotein. [a]$P < 0.001$; [b]$P < 0.01$; [c]$P < 0.05$ in comparison with males from the same ethnic group.

Table 2. Comparison of the genotype and allele frequencies of the *BCL7B* rs2237278 mutation between males and females of the Jing and Han populations

Group	n	Genotype			Allele		HWE(P)
		CC	CT	TT	C	T	
Jing	1148	742 (64.63)	368 (32.06)	38 (3.31)	1852 (80.66)	444 (19.34)	0.351
Han	1355	885 (65.31)	430 (31.74)	40 (2.95)	2200 (81.18)	510 (18.82)	0.155
X^2			0.320		0.217		
P			0.852		0.641		
Jing	1148						
Male	582	395 (67.87)	172 (29.55)	15 (2.58)	962 (82.65)	202 (17.35)	0.465
Female	566	347 (61.31)	196 (34.63)	23 (4.06)	890 (78.62)	242 (21.38)	0.473
X^2			6.133		5.958		
P			0.047		0.015		
Han	1355						
Male	706	482 (68.27)	207 (29.32)	17 (2.41)	1171 (82.93)	241 (17.07)	0.343
Female	649	403 (62.10)	223 (34.36)	23 (3.54)	1029 (79.28)	269 (20.72)	0.244
X^2			6.160		5.918		
P			0.046		0.015		

HWE, Hardy-Wrinberg equilibrium.

Table 3. Comparison between the *BCL7B* rs2237278 C > T genotypes and serum lipid levels

Genptype	n	TC (mmol/L)	TG (mmol/L)	HDL-cholesterol (mmol/L)	LDL-cholesterol (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ ApoB
Jing	1148							
CC	742	5.11±0.87	1.38 (1.10)	1.82±0.45	2.80±0.43	1.32±0.24	1.04±0.26	1.36±0.56
CT	368	5.21±0.95	1.49 (1.20)	1.77±0.47	2.85±0.41	1.30±0.22	1.05±0.26	1.30±0.39
TT	38	5.29±1.08	1.51 (1.24)	1.68±0.37	2.95±0.46	1.29±0.22	1.06±0.24	1.30±0.38
F		1.391	16.315	2.260	2.865	0.880	0.494	0.575
P		0.249	0.000	0.105	0.057	0.415	0.610	0.563
Jing/Male	582							
CC	395	5.05±0.79	1.41 (1.10)	1.78±0.45	2.79±0.36	1.32±0.23	1.06±0.24	1.31±0.40
CT	172	5.25±0.87	1.50 (1.20)	1.77±0.50	2.85±0.38	1.30±0.22	1.06±0.24	1.30±0.41
TT	15	5.25±0.92	1.51 (1.23)	1.65±0.29	2.87±0.44	1.28±0.22	1.13±0.30	1.28±0.41
F		1.752	5.685	0.322	0.666	0.406	0.847	0.026
P		0.174	0.004	0.725	0.514	0.667	0.429	0.975
Jing/Female	566							
CC	347	5.17±0.96	1.33 (1.10)	1.86±0.44	2.81±0.50	1.33±0.27	0.97±0.21	1.40±0.45
CT	196	5.18±1.02	1.40 (1.20)	1.78±0.45	2.85±0.44	1.30±0.22	1.05±0.28	1.31±0.38
TT	23	5.31±1.19	1.42 (1.24)	1.69±0.42	2.99±0.48	1.28±0.22	1.06±0.24	1.31±0.34
F		0.032	13.667	3.062	0.975	1.646	1.592	0.692
P		0.969	0.000	0.048	0.378	0.194	0.204	0.501
Han	1355							
CC	885	4.86±0.88	1.28 (1.03)	1.82±0.29	2.85±0.44	1.35±0.20	1.04±0.23	1.35±0.39
CT	430	4.88±0.73	1.39 (1.11)	1.78±0.58	2.87±0.41	1.34±0.20	1.04±0.25	1.35±0.36
TT	40	4.92±0.83	1.47 (1.13)	1.78±0.52	2.91±0.38	1.33±0.20	1.08±0.20	1.29±0.29
F		0.673	20.580	0.331	0.714	0.393	0.370	0.400
P		0.510	0.000	0.719	0.490	0.675	0.691	0.671
Han/Male	706							
CC	482	4.82±0.92	1.27 (0.98)	1.74±0.55	2.83±0.45	1.35±0.21	1.04±0.25	1.36±0.41
CT	207	4.85±0.64	1.37 (1.06)	1.73±0.54	2.92±0.36	1.33±0.20	1.07±0.20	1.32±0.38
TT	17	4.89±0.75	1.66 (1.15)	1.72±0.64	2.92±0.37	1.32±0.13	1.10±0.20	1.24±0.31
F		0.495	13.762	0.134	2.918	0.042	0.291	0.849
P		0.610	0.000	0.874	0.055	0.959	0.747	0.428
Han/Female	649							
CC	403	4.89±0.81	1.30 (1.06)	1.88±0.35	2.83±0.44	1.32±0.20	1.02±0.25	1.38±0.34
CT	223	4.92±0.82	1.43 (1.12)	1.85±0.47	2.87±0.43	1.33±0.19	1.03±0.24	1.35±0.38
TT	23	4.95±0.90	1.47 (1.13)	1.83±0.61	2.91±0.40	1.36±0.24	1.06±0.21	1.32±0.28
F		0.040	7.537	0.308	1.629	0.736	1.901	2.887
P		0.961	0.001	0.735	0.197	0.479	0.150	0.056

the percentages of subjects smoking and consuming alcohol were different between men and women in both ethnic groups ($P < 0.05$-0.001). The values of systolic blood pressure and diastolic blood pressure were different between men and women in Han ($P < 0.001$ for each) but not in Jing. Overall, men had higher values of general characteristic parameters than women in both ethnic groups. In Jing, women had higher serum TG levels than the men ($P < 0.01$). In Han, females had lower HDL-C levels than the males ($P < 0.001$).

Results of genotyping

After the genomic DNA of the samples was amplified by PCR, the purpose gene of 331 bp nucleotide sequences could be seen in all sam-

ples. The genotypes identified were labeled according to the presence or absence of the enzyme restriction sites. Thus, CC genotype is homozygote for the presence of the site (275- and 56-bp), CT genotype is heterozygote for the presence and absence of the site (331-, 275- and 56-bp) and TT genotype is homozygote for the absence of the site (331 bp). The CC, CT and TT genotypes detected by PCR-RFLP were also confirmed by direct sequencing.

Genotypic and allelic frequencies

As shown in **Table 2**, there were no differences in the genotype and allele frequencies of the *BCL7B* rs2237278 SNP between the Jing and Han populations ($P > 0.05$ for each). The genotype frequencies of rs2237278 SNP agreed with the Hardy-Weinberg equilibrium in both populations ($P > 0.05$ for each). Gender-subgroup analysis showed that the genotype and allele frequencies of the *BCL7B* rs2237278 SNP were significantly different between males and females in Jing (CC, 67.87% *vs*. 61.31%; CT, 29.55% *vs*. 34.63%; TT, 2.58% *vs*. 4.06%; $P = 0.047$; C, 82.65% *vs*. 78.62%; T, 17.35% *vs*. 21.38%; $P = 0.015$) and Han (CC, 68.27% *vs*. 62.10%; CT, 29.32% *vs*. 34.36%; TT, 2.41% *vs*. 3.54%; $P = 0.046$; C, 82.93% *vs*. 79.28%; T, 17.07% *vs*. 20.72%; $P = 0.015$) populations.

Genotypes and lipid profiles

Table 3 describes the association between genotypes and serum lipid profiles. The levels of TG in Jing and Han populations, and gender-subgroup both in Jing and Han were different between the genotypes ($P < 0.01$), the subjects with TT genotypes had higher serum TG levels than those with CC/CT genotypes. Serum HDL-C levels in Jing females were different among the genotypes ($P < 0.05$), the TT genotype subjects had lower HDL-C levels than the CC/CT genotype subjects.

Interactions of genotypes and gender on lipid profiles

An interaction of *BCL7B* rs2237278 polymorphism and women on serum TG was noted in Jing and Han populations ($P < 0.05$-0.01; **Table 3**) but HDL-C levels just in Jing females ($P < 0.05$).

Relative factors for serum lipid parameters

Multiple linear regression analyses showed that the levels of TC, TG and LDL-C in Jing plus Han, the levels of TG and LDL-C in Jing, and TG in Han were correlated with genotypes ($P < 0.05$-0.001; **Table 4**). In gender subgroups, the levels of TC and TG in Jing males, TG and HDL-C in Jing females, TG and LDL-C in Han males and TG levels and the ratio of ApoA1 to ApoB in Han females were correlated with genotypes ($P < 0.05$-0.001; **Table 5**). Several environmental factors such as age, weight, waist circumference, cigarette smoking, alcohol consumption, BMI, fasting blood glucose, and blood pressure levels were also correlated with serum lipid parameters in males and females of both ethnic groups.

Discussion

Our study is the first to report an association between serum lipid levels and *BCL7B* rs2237278 polymorphism. We observed that serum lipid profiles were significantly different between males and females in the Jing and Han populations. And the females had higher serum levels of bad cholesterols and lower levels of good cholesterols than the males in the Jing and Han populations.

A significant difference in the genotype and allele frequencies of *BCL7B* rs2237278 SNP was also noted between the Jing and Han populations. The minor T allele frequencies in Jing and Han were 19.34% and 18.82% respectively, which were in close proximity to those of Chinese Han Beijing (17.07%) reported in international haplotype map (HapMap) project. On gender subgroup analysis, the genotype frequencies between males and females were different in Jing and Han populations. According to HapMap data, the minor allele frequency of rs2237278 was 18.02% in Japanese, and 0.88% in European. Apparently, the minor allele frequency was higher in Asian than the Western populations. These findings suggest that genotype and allele frequencies of *BCL7B* rs2237278 SNP are inconsistent among diverse ethnic groups or between males and females.

CVD definition captures clustering of cardiometabolic risk factors that predict higher risk for cardiovascular disease. Our study hypothesis is that additional to genes influencing individual cardiometabolic risk factors, genetic variants may exist that influence cardiometabolic and inflammatory markers forming a pre-

Table 4. Correlations between the relative risk factors and serum lipid levels in the Jing and Han populations

Lipid-associated phenotype	Risk factor	Unstandardized coefficient	Standard error	standardized coefficient	t	*P*
Jing plus Han						
TC	Genotype	0.065	0.031	0.040	2.096	0.036
	Ethnic group	-0.258	0.034	-0.144	-7.590	0.000
	Age	0.007	0.001	0.110	5.570	0.000
	Height	-0.010	0.002	-0.085	-4.390	0.000
	Diastolic blood pressure	0.005	0.002	0.058	3.012	0.003
	Glucose	0.127	0.012	0.205	10.647	0.000
TG	Genotype	0.266	0.031	0.154	8.489	0.000
	Gender	-0.138	0.049	-0.073	-2.802	0.005
	Age	-0.009	0.001	-0.123	-5.907	0.000
	Height	-0.026	0.003	-0.215	-7.814	0.000
	Body mass index	-0.044	0.011	-0.148	-4.052	0.000
	Waist circumference	0.042	0.004	0.402	10.589	0.000
	Cigarette smoking	0.274	0.026	0.220	10.465	0.000
	Diastolic blood pressure	0.009	0.002	0.103	5.536	0.000
	Glucose	0.109	0.012	0.166	9.087	0.000
HDL-cholesterol	Ethnic group	-0.081	0.020	-0.081	-4.147	0.000
	Gender	0.102	0.023	0.102	4.476	0.000
	Waist circumference	-0.016	0.001	-0.291	-14.559	0.000
	Cigarette smoking	-0.076	0.015	-0.115	-5.155	0.000
	Alcohol consumption	0.119	0.015	0.189	8.044	0.000
	Diastolic blood pressure	0.003	0.001	0.055	2.830	0.005
LDL-cholesterol	Genotype	0.041	0.015	0.052	2.637	0.008
	Ethnic group	0.037	0.017	0.042	2.171	0.030
	Age	0.003	0.001	0.078	3.826	0.000
	Height	-0.003	0.001	-0.057	-2.845	0.004
	Diastolic blood pressure	0.003	0.001	0.083	4.188	0.000
	Glucose	0.044	0.006	0.148	7.454	0.000
ApoA1	Gender	0.033	0.011	0.075	3.110	0.002
	Weight	-0.003	0.001	-0.116	-3.022	0.003
	Waist circumference	-0.002	0.001	-0.096	-2.621	0.009
	Alcohol consumption	0.062	0.006	0.225	10.116	0.000
	Diastolic blood pressure	0.001	0.000	0.057	2.898	0.004
	Pulse pressure	0.000	0.000	0.041	2.113	0.035
	Glucose	-0.016	0.003	-0.102	-5.243	0.000
ApoB	Age	0.002	0.000	0.104	5.248	0.000
	Height	-0.002	0.001	-0.049	-2.429	0.015
	Waist circumference	0.006	0.001	0.214	10.430	0.000
	Diastolic blood pressure	0.001	0.000	0.052	2.588	0.010
ApoA1/ApoB	Gender	0.073	0.021	0.094	3.434	0.001
	Age	-0.001	0.001	-0.044	-2.094	0.036
	Height	0.003	0.001	0.065	2.452	0.014
	Waist circumference	-0.012	0.001	-0.282	-14.228	0.000
	Alcohol consumption	0.072	0.011	0.148	6.720	0.000
	Glucose	-0.021	0.005	-0.080	-4.118	0.000
Jing						

TC	Gender	0.279	0.064	0.154	4.377	0.000
	Age	0.019	0.002	0.290	9.167	0.000
	Body mass index	0.068	0.014	0.241	4.749	0.000
	Waist circumference	-0.016	0.005	-0.166	-3.170	0.002
	Cigarette smoking	0.108	0.042	0.084	2.556	0.011
	Alcohol consumption	0.150	0.044	0.110	3.431	0.001
	Pulse pressure	-0.008	0.002	-0.151	-4.969	0.000
	Glucose	0.102	0.015	0.197	6.965	0.000
TG	Genotype	0.246	0.042	0.154	5.843	0.000
	Gender	-0.219	0.069	-0.125	-3.187	0.001
	Age	-0.006	0.002	-0.096	-3.121	0.002
	Height	-0.026	0.004	-0.236	-6.009	0.000
	Waist circumference	0.031	0.003	0.328	11.119	0.000
	Cigarette smoking	0.245	0.039	0.197	6.359	0.000
	Diastolic blood pressure	0.008	0.002	0.093	3.360	0.001
	Glucose	0.085	0.013	0.169	6.361	0.000
HDL-cholesterol	Gender	0.162	0.032	0.179	5.064	0.000
	Age	0.003	0.001	0.090	3.012	0.003
	Weight	0.006	0.003	0.126	2.147	0.032
	Waist circumference	-0.022	0.003	-0.452	-8.376	0.000
	Alcohol consumption	0.184	0.021	0.270	8.747	0.000
LDL-cholesterol	Genotype	0.059	0.023	0.075	2.587	0.010
	Age	0.004	0.001	0.133	4.556	0.000
	Diastolic blood pressure	0.003	0.001	0.063	2.140	0.033
	Glucose	0.025	0.007	0.103	3.522	0.000
ApoA1	Weight	-0.004	0.001	-0.190	-6.451	0.000
	Alcohol consumption	0.043	0.010	0.120	4.079	0.000
	Systolic blood pressure	0.001	0.000	0.071	2.436	0.015
	Glucose	-0.018	0.004	-0.132	-4.517	0.000
ApoB	Age	0.003	0.001	0.165	5.788	0.000
	Body mass index	0.016	0.002	0.204	7.138	0.000
ApoA1/ApoB	Age	-0.004	0.001	-0.148	-4.815	0.000
	Waist circumference	-0.011	0.001	-0.272	-9.500	0.000
	Alcohol consumption	0.077	0.017	0.132	4.596	0.000
	Pulse pressure	0.001	0.001	0.063	2.042	0.041
Han						
TC	Height	-0.008	0.003	-0.070	-2.485	0.013
	Cigarette smoking	-0.084	0.030	-0.078	-2.802	0.005
	Systolic blood pressure	0.001	0.000	0.079	2.951	0.003
	Diastolic blood pressure	0.004	0.002	0.053	2.004	0.045
	Glucose	0.218	0.020	0.279	10.773	0.000
TG	Genotype	0.283	0.045	0.154	6.233	0.000
	Age	-0.011	0.002	-0.147	-5.642	0.000
	Weight	-0.025	0.005	-2.236	-5.073	0.000
	Waist circumference	0.045	0.005	0.391	8.656	0.000
	Cigarette smoking	0.294	0.033	0.235	8.977	0.000
	Diastolic blood pressure	0.010	0.002	0.104	4.095	0.000
	Glucose	0.174	0.023	0.192	7.529	0.000
HDL-cholesterol	Gender	0.114	0.034	0.107	3.396	0.001

	Waist circumference	-0.014	0.002	-0.233	-8.684	0.000
	Cigarette smoking	-0.112	0.021	-0.167	-5.279	0.000
	Alcohol consumption	0.095	0.021	0.155	4.599	0.000
	Systolic blood pressure	0.001	0.000	0.056	2.072	0.038
	Diastolic blood pressure	0.004	0.001	0.080	2.918	0.004
	Glucose	-0.032	0.013	-0.066	-2.524	0.012
LDL-cholesterol	Height	-0.006	0.002	-0.120	-4.001	0.000
	Body mass index	-0.021	0.007	-0.158	-2.922	0.004
	Waist circumference	0.010	0.003	0.196	3.579	0.000
	Systolic blood pressure	0.000	0.000	0.054	1.987	0.47
	Diastolic blood pressure	0.004	0.001	0.089	3.264	0.001
	Glucose	0.087	0.010	0.223	8.484	0.000
ApoA1	Weight	-0.005	0.001	-0.225	-8.185	0.000
	Cigarette smoking	-0.015	0.008	-0.061	-1.983	0.048
	Alcohol consumption	0.069	0.007	0.293	9.355	0.000
	Diastolic blood pressure	0.001	0.001	0.072	2.714	0.007
	Glucose	-0.016	0.005	-0.085	-3.253	0.001
ApoB	Gender	-0.030	0.014	-0.063	-2.104	0.036
	Weight	-0.004	0.001	-0.152	-2.862	0.004
	Waist circumference	0.009	0.001	0.325	6.510	0.000
	Diastolic blood pressure	0.002	0.001	0.091	3.396	0.001
	Glucose	0.022	0.006	0.099	3.739	0.000
ApoA1/ApoB	Gender	0.060	0.023	0.079	2.605	0.009
	Waist circumference	-0.012	0.001	-0.285	-10.977	0.000
	Alcohol consumption	0.072	0.013	0.164	5.394	0.000
	Glucose	-0.050	0.009	-0.144	-5.599	0.000

Table 5. Correlations between the relative risk factors and serum lipid levels in the males and females of Jing and Han populations

Lipid-associated phenotype	Risk factor	Unstandardized coefficient	Standard error	standardized coefficient	*t*	*P*
Jing/Male						
TC	Genotype	0.126	0.061	0.081	2.067	0.039
	Age	0.015	0.002	0.253	5.909	0.000
	Body mass index	0.104	0.021	0.388	4.958	0.000
	Waist circumference	-0.027	0.007	-0.326	-4.063	0.000
	Alcohol consumption	0.176	0.041	0.174	4.352	0.000
	Pulse pressure	-0.013	0.002	-0.251	-5.808	0.000
	Glucose	0.082	0.018	0.186	4.614	0.000
TG	Genotype	0.082	0.018	0.186	4.614	0.000
	Age	0.186	0.003	0.091	2.388	0.017
	Height	-0.030	0.006	-0.215	-4.961	0.000
	Waist circumference	0.037	0.004	0.373	9.096	0.000
	Cigarette smoking	0.220	0.043	0.201	5.075	0.000
	Diastolic blood pressure	0.008	0.003	0.091	2.388	0.017
	Glucose	0.109	0.019	0.211	5.793	0.000
HDL-cholesterol	Age	0.004	0.001	0.123	3.163	0.002
	Body mass index	0.024	0.011	0.160	2.231	0.026

	Waist circumference	-0.024	0.003	-0.512	-7.066	0.000
	Alcohol consumption	0.201	0.021	0.352	9.406	0.000
	Systolic blood pressure	-0.003	0.001	-0.109	-2.753	0.006
LDL-cholesterol	Age	0.003	0.001	0.116	2.599	0.010
	Body mass index	0.042	0.010	0.346	4.244	0.000
	Waist circumference	-0.010	0.003	-0.264	-3.149	0.002
	Alcohol consumption	0.045	0.019	0.098	2.346	0.019
	Pulse pressure	-0.004	0.001	-0.190	-4.244	0.000
	Glucose	0.025	0.008	0.129	3.060	0.002
ApoA1	Height	-0.003	0.001	-0.091	-2.197	0.028
	Waist circumference	-0.005	0.001	-0.222	-5.277	0.000
	Alcohol consumption	0.061	0.011	0.219	5.544	0.000
	Glucose	-0.015	0.005	-0.124	-3.143	0.002
ApoB	Age	0.003	0.001	0.152	3.465	0.001
	Body mass index	0.021	0.003	0.262	6.575	0.000
	Pulse pressure	-0.002	0.001	-0.109	-2.475	0.014
ApoA1/ApoB	Age	-0.003	0.001	-0.088	-2.237	0.026
	Waist circumference	-0.014	0.002	-0.313	-7.927	0.000
	Alcohol consumption	0.096	0.020	0.185	4.691	0.000
Jing/Female						
TC	Age	0.025	0.003	0.318	7.455	0.000
	Weight	0.025	0.008	0.228	3.065	0.002
	Waist circumference	-0.019	0.008	-0.164	-2.277	0.023
	Glucose	0.135	0.024	0.222	5.620	0.000
TG	Genotype	0.279	0.053	0.205	5.293	0.000
	Height	-0.028	0.005	-0.205	-5.104	0.000
	Waist circumference	0.025	0.004	0.283	7.052	0.000
	Cigarette smoking	0.610	0.241	0.099	2.534	0.012
	Glucose	0.057	0.019	0.119	3.066	0.002
HDL-cholesterol	Genotype	-0.075	0.031	-0.097	-2.429	0.015
	Waist circumference	-0.016	0.002	-0.320	-7.791	0.000
	Diastolic blood pressure	0.005	0.002	0.111	2.698	0.007
LDL-cholesterol	Age	0.009	0.002	0.233	5.753	0.000
	Glucose	0.043	0.012	0.144	3.559	0.000
ApoA1	Body mass index	-0.008	0.003	-0.105	-2.508	0.012
	Pulse pressure	0.001	0.001	0.095	2.242	0.025
	Glucose	-0.015	0.007	-0.099	-2.323	0.021
ApoB	Age	0.005	0.001	0.230	5.675	0.000
	Body mass index	0.012	0.003	0.162	3.992	0.000
ApoA1/ApoB	Age	-0.005	0.001	-0.162	-3.977	0.000
	Body mass index	-0.023	0.004	-0.213	-5.216	0.000
Han/Male						
TC	Cigarette smoking	-0.091	0.033	-0.097	-2.755	0.006
	Diastolic blood pressure	0.011	0.003	0.130	3.732	0.000
	Pulse pressure	0.001	0.00	0.089	2.556	0.011
	Glucose	0.248	0.027	0.319	9.069	0.000
TG	Genotype	0.370	0.071	0.176	5.235	0.000
	Age	-0.020	0.003	-0.231	-5.979	0.000
	Weight	-0.037	0.008	-0.292	-4.326	0.000

	Waist circumference	0.057	0.009	0.429	6.613	0.000
	Cigarette smoking	0.242	0.042	0.203	5.694	0.000
	Diastolic blood pressure	0.014	0.004	0.135	3.966	0.000
	Glucose	0.189	0.034	0.191	5.542	0.000
HDL-cholesterol	Waist circumference	-0.018	0.002	-0.271	-7.382	0.000
	Cigarette smoking	-0.106	0.022	-0.182	-4.772	0.000
	Alcohol consumption	0.100	0.022	0.173	4.471	0.000
	Diastolic blood pressure	0.006	0.002	0.122	3.367	0.001
	Pulse pressure	0.001	0.000	0.078	2.175	0.030
LDL-cholesterol	Genotype	0.063	0.029	0.077	2.158	0.031
	Diastolic blood pressure	0.005	0.001	0.131	3.652	0.000
	Glucose	0.110	0.014	0.288	8.077	0.000
ApoA1	Waist circumference	-0.006	0.001	-0.260	-7.351	0.000
	Cigarette smoking	-0.018	0.008	-0.083	-2.248	0.025
	Alcohol consumption	0.081	0.008	0.368	9.846	0.000
ApoB	Waist circumference	0.006	0.001	0.219	6.083	0.000
	Diastolic blood pressure	0.003	0.001	0.154	4.284	0.000
	Glucose	0.037	0.008	0.173	4.869	0.000
ApoA1/ApoB	Age	0.003	0.001	0.094	2.567	0.010
	Waist circumference	-0.014	0.002	-0.291	-8.112	0.000
	Alcohol consumption	0.079	0.015	0.186	5.208	0.000
	Diastolic blood pressure	-0.003	0.001	-0.083	-2.339	0.020
	Glucose	-0.062	0.013	-0.173	-4.761	0.000
Han/Female						
TC	Height	-0.012	0.005	-0.095	-2.499	0.013
	Glucose	0.201	0.030	0.257	6.776	0.000
TG	Genotype	0.178	0.057	0.115	3.137	0.002
	Weight	-0.021	0.007	-0.222	-3.094	0.002
	Waist circumference	0.041	0.007	0.436	6.120	0.000
	Cigarette smoking	0.412	0.089	0.174	4.647	0.000
	Pulse pressure	-0.006	0.002	-0.103	-2.703	0.007
	Glucose	0.176	0.030	0.220	5.916	0.000
HDL-cholesterol	Waist circumference	-0.010	0.002	-0.178	-4.600	0.000
	Glucose	-0.038	0.019	-0.078	-2.014	0.044
LDL-cholesterol	Age	0.004	0.001	0.101	2.448	0.015
	Height	-0.005	0.003	-0.083	-2.080	0.038
	Glucose	0.064	0.016	0.160	4.054	0.000
ApoA1	Body mass index	-0.010	0.002	-0.163	-4.164	0.000
	Alcohol consumption	0.042	0.017	0.092	2.378	0.018
	Diastolic blood pressure	0.002	0.001	0.080	2.007	0.045
	Glucose	-0.021	0.007	-0.114	-2.918	0.004
ApoB	Age	0.003	0.001	0.130	3.306	0.001
	Weight	-0.007	0.002	-0.247	-3.316	0.001
	Waist circumference	0.011	0.002	0.413	5.625	0.000
ApoA1/ApoB	Genotype	0.048	0.024	0.075	1.978	0.048
	Height	0.009	0.002	0.178	4.688	0.000
	Waist circumference	-0.012	0.002	-0.292	-7.605	0.000
	Glucose	-0.044	0.013	-0.130	-3.492	0.001

disposing cardiometabolic genetic network. BCL7B is a member of BCL7 family, located on chromosome 7q11.23, is one of the pleiotropic genetic variants independently effects on cardiometabolic phenotypes. A genome-wide analysis identified the share genetic background including *BCL7B* mutations of inflammation and cardiometabolic phenotypes in European ancestry [34]. It shown that for *BCL7B*, lipid appeared to be the most important mediators. And BCL7B rs13233571 can increase serum TG levels and decrease serum HDL-C levels [48]. In our present study, the minor allele of *BCL7B* rs2237278 was significantly associated with pleiotropic (one SNP influence many traits) effects on increased serum TG levels and decrease serum HDL-C traits in sexually dimorphic subgroups. The *BCL7B* rs2237278 SNP was correlated with TG in the combined population of Jing and Han. The reason for this discrepancy is not fully understood. It might be due to the differences in genetic backgrounds, estrogen, ethnic populations and/or simply due to the low power of this study.

Among women who carry BCL7B rs2237278 SNP, additional factors-including exposure to estrogen change when postmenopausal-may shape the risk of dyslipidemia and CVD. Understanding the interplay between gene and the endocrine could illuminate the ultimate origins of hyperlipidemia in women, possibly leading the way to new strategies for prevention and treatment [49]. Some of the disparity in the risk from gene is generational. One repeated finding is that, by age 50, gene mutations carriers born in the early twentieth century seem to have a lower risk of CVD than those born later [50]. The pattern suggests that outside influences interact with genes, and that something in the endocrine has change in an unfavorable way. If research can figure out what those influences are, and why they have increased disease prevalence, maybe in the future they will gain new, maybe in the future they will gain new, less invasive tools to delay disease onset-and possibly prevent hereditary CVD together. Gillian Bentley [51], an anthropologist at Durham University in the UK who studies Bangladeshi immigrants, thinks that society-wide shifts could partly explain the increase of disease during the past century both in related mutations carriers and non-carriers. One line of evidence is that the reproductive hormone levels of Bangladeshi immigrants very according to when the women arrived in the United Kingdom. For those who came before puberty, adult hormone levels are similar to native-born Britons'. But if they arrived after puberty, their hormone levels remain suppressed relative to native Britons, but similar to levels of women in Bangladesh. Accordingly, South Asian immigrants who arrived as adults tend to develop disease less often native Britons. But their British-born children have a risk closer to native Britons. "They're all from the same genetic background. We match them in terms of region of origin. And they move environments, and they look completely different", she says. "What does that say about genes" [52]? In my opinion, there are lots of things you cannot change about your genetics, but there are lots you can change about your interaction including therapeutically targeting the estrogen. This study is the first attempt to report the gender specific association of *BCL7B* rs2237278 SNP. Therefore, further studies with larger sample size are still needed to confirm this association.

Several environmental factors were also correlated with lipid profiles in males and females of both Jing and Han populations. Fishery is the major source of income for Jing population and fish is appeared most frequently dish on their tables. Fish rich in omrga-3 polyunsaturated fatty acids (N-3PUFA) have been suggested to have a favorable effect on serum concentrations of pleiotropic lipid traits. Previous researches demonstrated the effects of N-3PUFA on key metabolic functions, including significant rise in total cholesterol, triglyceride and LDL-C levels and decrease in HDL-C levels [53, 54].

There are some potential limitations in our study. First, it is undeniable that this study has insufficient power to produce a robust conclusion; therefore, such a small-scale study needs to replicate in independent cohorts. Second, the impact of diet was not evaluated in this study. Third, there are not subgroups between premenopausal and postmenopausal because of the number of female cases is not enough.

Conclusion

Our findings provide evidence to support sexually dimorphic association between *BCL7B* rs2237278 SNP and serum lipid profiles may

account, at least in part, for the female predominance of dyslipidemia susceptibility. Thus, although data are more limited, there is good reason to believe that cholesterol interventions for female are likely to be effective, particular in postmenopausal women.

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Disclosure of conflict of interest

None.

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