IMPACTS OF CYP7A1 AND SLCO1B1 POLYMORPHISMS ON SERUM LIPID LEVELS IN HEALTHY TURKISH POPULATION

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ABSTRACT

Introduction: *Serum lipid levels can be affected by certain genes. CYP7A1 and SLCO1B1 genes may have a part in lipid metabolism. The distinctions in CYP7A1 and SLCO1B1 genotypes may be related to serum levels of lipid. The goals of this pilot study were to detect the frequencies of CYP7A1 g.-203A>C (rs3808607) and SLCO1B1 c.388 A>G (rs2306283) polymorphisms in a healthy Turkish population and to explore the relationship between these polymorphisms and serum levels of lipid.*

Materials and methods: *Genomic DNA was obtained from 120 healthy Turkish participants, who fasted for 10-12 hours. CYP7A1 and SLCO1B1 polymorphisms were detected based on polymerase chain reaction-restriction fragment length polymorphism techniques. The serum lipid levels were determined by standard methods.*

Results: *The frequencies were determined as 57.9% A allele and 42.1% C allele for CYP7A1 gene, 56.2% A allele and 43.8% G allele for SLCO1B1 gene. The serum lipid levels were affected by gender and also the gene-by-gender interaction for CYP7A1 genotypes, but this was not observed for SLCO1B1 genotypes.*

Conclusion: *This study is the first to document the frequencies of CYP7A1 g.-203A>C in the Turkish population and to reveal the relationship between CYP7A1 g.-203A>C or SLCO1B1 c.388 A>G polymorphism and serum levels of lipid.*

Keywords: *CYP7A1, SLCO1B1, polymorphism, serum lipid levels, Turkish population.*

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Introduction

Dyslipidemia is a very significant and alterable risk cause in the development of atherosclerosis and cardiovascular disease (CVD), which is the most frequent reason of mortality and morbidity in not only developing but also developed countries[(1)]. Dyslipidemia includes low levels of high-density lipoprotein cholesterol (HDL-C), and high levels of serum or plasma low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC) [(2)]. Twin and family reports have demonstrated that genetic polymorphism may be responsible for 40 to 80% of inter-individual changes in lipid concentrations[(3)]. Variations in certain genes can affect serum lipid levels. Cholesterol 7α-hydroxylase enzyme (CYP7A1, EC 1.14.13.17) is one of the cytochrome P450 enzymes included in the metabolism of endogenous substances. CYP7A1 is a rate-limiting enzyme involved in the synthesis of bile acid from cholesterol, which is the first way of cholesterol elimination from the body and is defined as classic conversion (or neutral) pathway, and ensures cholesterol homeostasis[(4)]. The CYP7A1 gene that encodes CYP7A1 enzyme is expressed only in the liver of humans[(5)]. The CYP7A1 gene is

localized to chromosome 8q12.1, spans nearly 10 kb, and consists of one 5'-untranslated region, five introns, six exons, one 3'-untranslated region[4-6]. The CYP7A1 enzyme has a key part in cholesterol conversion and therefore the CYP7A1 gene polymorphisms can influence the activity of CYP7A1 and cholesterol metabolism[7]. Several surveys have been performed to assess the relationship between the CYP7A1 gene variations and metabolic disorders of bile acids and cholesterol[6, 8]. Most studies concerning the CYP7A1 gene variations focused on a common single-nucleotide polymorphism (SNP) A>C in the promoter region of CYP7A1, which is at position -203 from the transcriptional start site or position -278 from the translation initiation codon[9]. However, to our knowledge, no investigations have been performed on the CYP7A1 g.-203A>C polymorphism in the Turkish population.

The organic anion transporter protein (OATP1B1) is one of the major hepatic uptake transporters and is mostly expressed in the basolateral membrane of hepatocytes[10]. OATP1B1 allows the transport of a large range of endogenous compounds like sulfate, bile acids, bilirubin, thyroid hormones, and exogenous substrates like HMG-CoA reductase inhibitors (statins), methotrexate and irinotecan[10, 11]. OATP1B1 is encoded by the solute carrier organic anion transporter family member 1B1 (SLCO1B1) gene. This gene is localized to chromosome 12p12.1 and has 15 exons and 190 prevalent variants with a minor allele frequency above 5%[12]. Many SNPs are defined for the human SLCO1B1 gene. One of the most prevalent polymorphisms in the SLCO1B1 gene is SLCO1B1 c.388A>G (rs2306283), which has been related to the prominently elevated activity of OATP1B1[13]. OATP1B1 have been notified to play a significant part in the hepatocellular uptake and thus the elimination of many chemicals and endogenous compounds[10]. Therefore, this SLCO1B1 gene polymorphism affects the hepatocellular uptake and elimination of substrates compounds. Many studies have been carried out to explore the impacts of SLCO1B1 polymorphism on exogenous compounds, particularly on lipid-lowering effectiveness of statins. On the other hand, there are limited studies examining the impacts of the SLCO1B1 c.388A>G polymorphism on endogenous compounds like TC, bile acids[14, 15].

Also, there are no studies that have examined the impacts of the SLCO1B1 c.388 A>G polymorphism on the levels of the serum lipid parameters in the Turkish population. CYP7A1 and SLCO1B1 genes may have a part in lipid metabolism. The distributions of polymorphisms in these genes can vary greatly between diverse populations and may lead to inter-and intra-population distinctions in serum lipid levels. The objectives of this pilot study were to investigate the allele and genotype frequencies of CYP7A1 g.-203A>C (rs3808607) and SLCO1B1 c.388 A>G (rs2306283) in a healthy Turkish population and to examine the relationship between CYP7A1 and SLCO1B1 polymorphisms and serum lipid levels, including TC, TG, HDL-C, LDL-C, very-low-density lipoprotein (VLDL).

Materials and methods

Study population and blood sampling

The current study was carried out with 120 unrelated healthy Turkish individuals at Mersin University and the Mersin City Training and Research Hospital, Turkey.

The inclusion criteria were as follows:

• To be unrelated healthy volunteers;

• To be between the ages of 18 and 65 and to have fasted for 10-12 hours.

The exclusion criteria were as follows:

• Pregnancy;

• Having any chronic diseases (diabetes, stroke, hepatic and renal failures);

• History of cardiac disorders;

• High fasting blood glucose (>140 mg/dL);

• Taking drugs affecting serum lipid levels (statins, diuretics, beta-blockers, etc.);

• Consuming alcohol.

The current study was performed after receiving the approval of the Ethics Committee of Mersin University (22/10/2015, protocol no: 2015/317) according to the Good Clinical Practices and the Helsinki declaration. The study was explained to the participants in detail and informed consent was acquired from the whole participants.

The blood samples of the participants were received by venipuncture in tubes containing heparin. Collection was carried out between 08:00 a.m. and 10:30 a.m. after the participants had fasted for 10-12 hours.

Molecular analysis

Genomic DNA isolations was done using the Thermo Scientific Genomic DNA Purification Kit (GeneJET Whole Blood Genomic DNA Purification Mini Kit, catalog no K0782, Thermo Scientific™) as per the manufacturer's directions. DNA yield

was calculated via absorbance measured at 260 nm. The samples were maintained at -80°C till further analyses.

The CYP7A1 rs3808607 and SLCO1B1 rs2306283 polymorphisms were identified through the polymerase chain reaction-restriction fragment length polymorphism techniques (PCR-RFLP) on the Thermal Cycler (Thermo, UK). The CYP7A1 g.-203A>C (rs3808607) polymorphism was performed in accordance with the method defined by Han et al.[16] with slight changes. PCR amplification of CYP7A1 was performed using the sequences 5'-AATGTTTTTCCCAGTTCTCTTTC-3' for forward primer and 5'- AATTAGCCATTTGTTCATTC-TATTAG-3' for reverse primer.

The primers were used to amplify the 393 bp fragment of the gene. PCR products were digested at 50°C overnight with Bsa I restriction enzyme (Thermo Fisher Scientific). The genotypes of the wild type (300, 93 bp), mutant (261, 93 and 39 bp) and heterozygous (300, 261, 93 and 39 bp) were determined using 2% agarose gel with ethidium bromide. SLCO1B1 c.388A>G (rs2306283) polymorphism was identified according to Liu et al[17] with slight modifications. Analysis of the SLCO1B1 c.388A>G SNP was performed using primers set; F: 5'-ATAATGGTGCAAATAAAGGGG -3' and R: 5'-ACTATCTCAGGTGATGCTCT -3'. The PCR products of 214 bp were digested in 15 minutes at 65°C using Fast Digest Taq I restriction enzyme (Thermo Fisher Scientific). The genotypes of the wild type (151, 63 bp), mutant (128, 63 and 23 bp) and heterozygous (151, 128, 63 and 23 bp) were detected using 3% agarose gel with ethidium bromide.

For quality assurance, 10% of the samples at random were reanalyzed, which provided 100% concordance.

Biochemical analysis

Serum lipids (VLDL, HDL-C, LDL-C, TC, TG), fasting blood glucose, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were evaluated using ADVIA Chemistry XPT System (Siemens, Germany).

Statistical analysis

The allele and genotype frequencies were obtained using the genotype counting method. The comparison of the observed genotype frequencies of CYP7A1 with their expected frequencies was performed in accordance with the Hardy-Weinberg equilibrium. The comparison of CYP7A1 or SLCO1B1 gene frequencies and baseline characteristics between the genders was detected by chi-square and Mann-Whitney U test, respectively. The comparison of the effects of genotypes, gender, and gene-by-gender interactions on serum lipid levels were performed with one-way analysis of variance (ANOVA) followed by Duncan multiple comparison test and Mann-Whitney U test, where deemed necessary. The statistical analysis was conducted with IBM SPSS computer software for Windows 25.0. P values less than 0.05 were admitted as statistical significant.

Results

Baseline characteristics

Out of the 120 Turkish participants, 63 (52.5% of subjects) were female and 57 (47.5% of them) were male. In Table 1, statistically significant distinctions were observed between the genders in the matter of baseline characteristics.

Baseline characteristics	Total (all subjects)	Female	Male	P-value*
	120 (100)	63 (52.5)	57 (47.5)	
Age, years	28.54±9.62	25.59±8.11	31.81±10.16	<0.001
BMI, kg/m^2	24.29±3.70	22.76±3.30	25.87±3.43	<0.001
Weight, kg	70.48±13.66	61.94±9.95	79.17±11.25	<0.001
Height, cm	169.67±8.25	164.55±5.99	174.89±6.87	<0.001

Table 1: Baseline characteristics of the subjects in the study.
*BMI; Body mass index. Data are expressed as mean ± SD. Based on Mann–Whitney U test, significant difference at *P<0.001.*

Genotype and allele frequencies

The genotypes and alleles frequencies of CYP7A1 g.-203A>C and SLCO1B1 c.388 A>G in both the combination of all participants regardless of gender and in the separation of them by gender are presented in Table 2. The frequencies are in accordance with the Hardy-Weinberg equilibrium (P>0.05).

Polymorphism, gender, and serum lipid levels

The associations between the CYP7A1 g.-203A>C gene polymorphisms and serum levels of lipid in the Turkish participants were examined both by combining all participants regardless of gender and by separating them by gender (Table 3). In all participants, no significant difference was determined among the CC, AC and AA genotypes for lipid parameters (P>0.05).

			% Frequency (number)				
			All subjects (120)	Female (63)	Male (57)	X^2	p-value
CYP7A1	Genotype	*AA*	37.50 (45)	33.33 (21)	42.11 (24)	X^2=1.056 df=2	0.589
		AC	40.83 (49)	44.45 (28)	36.84 (21)		
		CC	21.67 (26)	22.22 (14)	21.05 (12)		
	Allele	*A*	57.9 (139)	55.6 (70)	60.5 (69)	X^2=0.607 df=1	0.436
		C	42.1 (101)	44.4 (56)	39.5 (45)		
SLCO1B1	Genotype	*AA*	32.5 (39)	25.40 (16)	40.35 (23)	X^2=3.324 df=2	0.19
		AG	47.5 (57)	50.79 (32)	43.86 (25)		
		GG	20.0 (24)	23.81 (15)	15.79 (9)		
	Allele	*A*	56.2 (135)	50.8 (64)	62.3 (71)	X^2=3.209 df=1	0.073
		G	43.8 (105)	49.2 (62)	37.7 (43)		

Table 2: The frequencies of CYP7A1 g.-203A>C and SLCO1B1 c.388 A>G polymorphisms in Turkish population.

	Genotype			P value*			
Lipid parameters, mg/dL	AA	AC	CC	ANOVA	AA vs AC	AA vs CC	AC vs CC
All subjects, n	45	49	26				
TC	179.13±34.87	186.61±34.55	175.15±38.52	0.367	0.569	0.893	0.385
TG	102.91±38.32	123.61±64.93	114.00±50.21	0.173	0.147	0.674	0.737
HDL-C	49.63±9.61	53.49±12.96	48.08±10.43	0.097	0.231	0.843	0.122
LDL-C	108.65±31.0	108.24±31.89	101.89±37.01	0.682	0.998	0.694	0.718
VLDL	20.58±7.66	24.64±13.38	27.30±22.69	0.142	0.363	0.143	0. 737
Female, n	21	28	14				
TC	170.09±15.09	194.07±33.98	161.71±33.78	0.000	**0.010**	0.587	**0.000**
TG	95.14±34.66	109.18±56.86	77.5±23.11	0.039	0.483	0.367	**0.029**
HDL-C	55.22±7.85	59.66±12.45	54.3±8.26	0.189	0.311	0.964	0.257
LDL-C	94.89±13.06	112.76±31.55	91.88±30.05	0.009	**0.047**	0.923	**0.015**
VLDL	19.03±6.93	21.84±11.37	15.5±4.62	0.039	0.483	0.367	**0.029**
Male, n	24	21	12				
TC	187.04±44.59	176.67±34.39	190.83±39.06	0.553	0.662	0.961	0.593
TG	109.71±40.76	142.86±71.22	156.58±37.73	0.021	0.111	**0.002**	0.494
HDL-C	44.98±8.47	45.26±8.35	40.82±7.72	0.287	0.993	0.338	0.307
LDL-C	120.12±36.81	101.91±32.07	115.9±42.68	0.249	0.231	0.949	0.583
VLDL	21.94±8.15	28.57±15.20	41.06±27.58	0.018	0.172	**0.002**	0.224

Table 3: Relation between CYP7A1 g.-203A>C polymorphism and serum lipid levels in the healthy Turkish subjects.

*Values were mean±SD. *bold values show statistically significant P values (P<0.05). Comparisons were performed using ANOVA followed by Duncan multiple comparison test. TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL: very-low-density lipoprotein, ANOVA: one-way analysis of variance.*

The females that have CC genotype possessed lower levels of TC, TG, LDL, VLDL compared to those with AC genotypes (P<0.05). In addition, the females with AA genotype possessed lower levels of TC and LDL as opposed to subjects with AC genotype (P<0.05). Nevertheless, there was not an important distinction in the serum levels of HDL-C among the genotypes in the women. In the males, no association was found between the serum levels of TC, HDL-C and LDL-C and the CYP7A1 genotypes (P>0.05). However, the serum TG and VLDL levels were found to be significantly more elevated in the CC genotypes as opposed to the AA genotypes (P<0.05). The relationship between the SLCO1B1 c.388A>G gene polymorphism and serum lipid levels was also investigated both by combining all participants regardless of gender and by separating them by gender (Table 4). It was determined that this polymorphism and serum levels of lipid were not significantly related.

	Genotype			P value*			
Lipid parameters, mg/dL	AA	AG	GG	ANOVA	AA vs AG	AA vs GG	AG vs GG
All subjects, n	39	57	24				
TC	189.00±34.59	176.39±34.50	179.65±39.59	0.223	0.200	0.572	0.927
TG	116.29±59.32	112.29±50.81	112.87±50.84	0.933	0.930	0.968	0.999
HDL-C	50.24±13.00	51.19±11.50	51.28±7.95	0.907	0.915	0.935	0.999
LDL-C	114.75±32.31	102.37±30.88	105.13±35.44	0.184	0.166	0.496	0.937
VLDL	24.19±16.34	23.50±14.31	23.21±11.65	0.961	0.973	0.964	0.996
Female, n	16	32	15				
TC	184.19±25.31	178.47±34.37	174.13±33.54	0.683	0.831	0.661	0.903
TG	96.63±55.62	95.97±42.65	101.53±41.98	0.925	0.999	0.953	0.921
HDL-C	60.01±10.83	57.49±10.67	52.84±8.54	0.150	0.706	0.135	0.326
LDL-C	105.16±19.26	101.43±30.03	100.96±32.43	0.893	0.904	0.911	0.998
VLDL	19.33±11.12	19.19±8.53	20.31±8.39	0.925	0.999	0.953	0.921
Male, n	23	25	9				
TC	192.08±39.60	173.63±35.22	190.00±49.89	0.242	0.237	0.991	0.593
TG	128.88±59.23	134.04±53.46	134.13±61.71	0.944	0.947	0.972	0.494
HDL-C	43.98±10.20	43.05±6.39	48.36±6.15	0.295	0.918	0.401	0.307
LDL-C	121.42±37.91	103.63±32.64	112.97±41.66	0.260	0.230	0.838	0.583
VLDL	27.44±18.56	29.29±18.18	28.65±15.29	0.938	0.933	0.985	0.224

Table 4: Relation between SLCO1B1 c.388 A>G polymorphism and serum lipid levels in the healthy Turkish subjects.

Values were expressed as mean±SD. Comparisons were performed ANOVA followed by Duncan multiple comparison test. TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL: very-low-density lipoprotein, ANOVA: one-way analysis of variance.

Furthermore, the impacts of gender on serum levels of lipid were examined irrespective of the genotypes (Table 5). It was observed that there were statistically significant distinctions between in the serum TG, HDL-C and VLDL levels of the male and female participants (P<0.001), but not in the TC and serum LDL-C levels. It was observed that the serum levels of VLDL and TG were considerably more elevated in the males as opposed to the females (P<0.05), while the serum levels of HDL were importantly more elevated in the females as opposed to the males (P<0.05).

		Gender		
Lipid parameters, mg/dL	Total	Female	Male	P-value*
TC	181.33±35.69	178.89±31.82	184.02±39.66	0.511
TG	113.77±53.45	97.46±45.40	131.79±56.21	< 0.001
HDL-C	50.88±11.41	57.02±10.41	44.21±8.32	< 0.001
LDL-C	107.08±32.50	102.28±27.91	112.59±36.56	0.227
VLDL	23.69±14.46	19.49±9.08	28.41±17.69	< 0.001

Table 5: The effects of gender on serum lipid levels irrespective of genotypes.
*Values were expressed as mean ± SD. Based on Mann–Whitney U test, significant difference at *P<0.001. TC: Total cholesterol, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL: very-low-density lipoprotein.*

Discussion

This study is the first to document the frequencies of CYP7A1 g.-203A>C in a healthy Turkish population and to reveal the relationship between CYP7A1 g.-203A>C or SLCO1B1 c.388 A>G polymorphism and serum levels of lipid in the healthy Turkish population.

To date, several investigations have been carried out to examine the potential relationship between CYP7A1 g.-203A>C polymorphism and plasma or serum levels of lipid in Caucasian and Asian populations. However, the results on the relationship of CYP7A1 polymorphism with the alterations in plasma or serum lipid levels were incoherent. In this study, no relationship was determined between serum levels of TC, LDL-C and HDL-C and the AA, AC and CC genotypes in the males (P>0.05). These results were in agreement with those reported by Abrahamsson et al.[18] and Barcelos et al.[19]. Abrahamsson et al.[18] declared that there was not connection between CYP7A1 g.-203A>C polymorphism and plasma LDL-C concentration in middle-aged Swedish males. Barcelos et al.[19] also reported no relationship between CYP7A1 g.-203A>C polymorphism and the concentrations of LDL-C, HDL-C or TC in dyslipidemic male population. However, some studies have shown that the C allele or CC genotype are associated with elevated serum lipid levels. Couture et al.[20] revealed that the existence of at least one C allele was related with more elevated plasma concentrations of LDL-C and a rising TC/HDL rate in males. In the study conducted with 11 healthy males, Kovar et al.[21] found that the participants with the CC genotype responded to a high-fat diet with an increment in TC and LDL-C. Wang et al.[22] declared that the CC genotype was related with elevated LDL-C levels in normolipidemic females and males. Hofman et al.[23] investigated the TC levels of 104 subjects who participated in dietary cholesterol trials and 112 subjects who participated in cafestol trials. They found that the participants who had the CC genotype had a higher response of plasma HDL-C and TC after an increment in dietary cholesterol and cafestol. In the current study, it was also defined that serum levels of TG and VLDL were increased in the male participants with the CC genotypes compared to the male subjects with the AA genotype.

In contrast, Hubacek et al.[24] reported the CC genotype had an important decrement in plasma TC after conducting a study on 131 males from the Czech MONICA, who received the sufficient dietary fat intake and were observed for eight years. In the study conducted with a Netherlands population, Hofman et al.[25] reported that the AA genotype was related with an important increment in serum TG levels in a healthy normolipidemic male population and with significantly higher serum levels of cholesterol in hypertriglyceridaemia patients. Barcelos et al.[19] reported that subjects carrying the C allele possessed considerably lower concentrations of TG (P=0.02) when compared to the AA homozygotes after the modification of diet and adjustment of covariates. They also determined that the CC and AC genotypes indicated a larger decrease in TG concentrations compared to the AA genotype in a dyslipidemic male population. Couture et al.[20] found that female participants with the CC genotype had importantly lower TG levels compared to those with the AC genotype. Consistent with the above results, but unlike the TG and VLDL results regarding males, in the present study, serum TG and VLDL levels were determined to be lower in the female participants that have the CC genotype as opposed to those with

the AC genotype. This showed that there can be a gene-by-gender interactions. In addition to all these results, Hegele et al.[26] declared that the CYP7A1 promoter polymorphism was inconsequently related with serum levels of lipid in three normolipidemic Canadian populations. They determined that the CYP7A1 polymorphism was related to reduced plasma HDL-C concentration in the Hutterites, increased plasma TC and LDL-C in the Inuit, and was not importantly related with any plasma lipoprotein trait in the Oji-Cree. The plasma concentrations of lipid showed variation in the populations because of ethnicity, genetic factors, diet habits etc. This may clarify why the results of the studies were different.

There are limited studies examining the impacts of the SLCO1B1 c.388 A>G polymorphism on endogenous compounds such as total cholesterol, bile acids[14,15]. Xiang et al.[14] reported that bile acids and 7α-hydroxy-4-cholesterin-3-one/cholesterol ratio were significantly more elevated in the participants with the 388AA-521TT genotypes compared to the subjects with the 388GG-521TT genotypes in a healthy Finnish population. However, the SLCO1B1 polymorphism was found to have no impact on plasma TC concentration. Xiang et al.[15] also reported that there was only an association between the SLCO1B1 genotype and plasma TC concentration, however this relationship was not important after correction for multiple testing. Additionally, they declared that the gender contributed considerably more to alteration in fasting plasma bile acid concentrations as opposed to the CYP7A1 or SLCO1B1 polymorphisms. In both studies it was reported that the SLCO1B1 polymorphism did not affect TC concentration. These findings are in compliance with the outcomes of this study. In the current research, it was explored that the impact of the SLCO1B1 c.388A>G polymorphism on the serum levels of lipid, including HDL, LDL, TG, TC, VLDL. It was not found statistically significant in the examination of all participants regardless of gender and separately in terms of gender. Accordingly, it can be concluded that gene or gene-by-gender interactions have no impact on serum levels of lipid in healthy individuals with SLCO1B1 polymorphism.

Several studies have been conducted on the influence of the SLCO1B1 c.388A>G polymorphism on the lipid-lowering effectiveness of statin as exogenous substances. Rodrigues et al.[27] documented that the c.388GG genotype was related to more elevated LDL-C reduction in atorvastatin therapy. Sortica et al.[28] stated that the subjects with the SLCO1B1 388G allele showed a considerable decline of TC and LDL-C with simvastatin therapy. Additionally, Shabana et al.[29] revealed that the SLCO1B1 A388G polymorphism indicated gender-associated impacts on TG alteration. However, some studies reported that the SLCO1B1 c.388A>G polymorphism was not related with lipid-lowering response to pravastatin, lovastatin, fluvastatin[30], atorvastatin and simvastatin[30-32]. In a meta-analysis report conducted by Dai et al.[33], it was determined that a total of 13 studies reported that the SLCO1B1 c.388 A>G polymorphism did not influence the lipid-lowering effectiveness of statin.

Premenopausal women have been reported to have more favorable lipid profiles compared to men, with more elevated HDL-C, and lower levels of LDL-C, TC, TG [34]. Partially consistent with these findings, the present study determined that the serum levels of TG and VLDL were 35% and 47% higher, respectively, in the males compared to the females and that also the serum levels of HDL-C were 30% more elevated in the females compared to the males. These differences between gender can be due to baseline characteristics.

In conclusion, this study provides information about the frequencies of CYP7A1 and SLCO1B1 polymorphisms in a healthy Turkish population and suggests that serum levels of lipid are affected by gender and also by gene-gender interaction for CYP7A1 genotypes, but not for SLCO1B1 genotypes.

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