

Serum Lipids are Novel Predictors for Thyroid Autoimmunity in the General Population with Normal TSH Levels From A Cross-Sectional Study

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Abstract

Objective

Serum lipids have been shown to regulate inflammatory and immune processes, but little is known about their association with thyroid autoimmunity. This study aimed to investigate the association of serum lipids with thyroid autoantibody positivity in the general population with normal thyroid-stimulating hormone (TSH) levels.

Methods

Data regarding the 7,688 subjects' baseline characteristics were retrospectively collected. All subjects were categorized into four groups according to thyroid autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb) positivity and serum lipid levels were compared. Binary logistic regression models were used to evaluate the risk of TgAb or TPOAb positivity with increasing serum lipid levels.

Results

In 6,456 included subjects, after adjusting for confounders, the risk of TgAb positivity was positively associated with increasing low-density lipoprotein cholesterol (LDL-C) levels (OR 1.10, 95%CI 1.02–1.19, $P=0.014$) and negatively correlated with the increasing high-density lipoprotein cholesterol (HDL-C) levels (OR 0.80, 95%CI 0.67–0.96, $P=0.014$). In female subjects, the association between increasing LDL-C (OR 1.15, 95%CI 1.05–1.26, $P=0.004$) or HDL-C levels (OR 0.74, 95%CI 0.60–0.91, $P=0.005$) and TgAb positivity become more pronounced. Moreover, there was a positive correlation between LDL-C levels and TPOAb positivity (OR 1.14, 95%CI 1.02–1.26, $P=0.016$).

Conclusion

We have shown the associations of HDL-C and LDL-C with thyroid autoantibody positivity in the general population with normal TSH levels in a gender-dependent manner. This study highlights that serum lipids may be new predictors of thyroid autoimmunity even when TSH is within the reference range.

Introduction

Thyroid autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb) are key markers of thyroid autoimmunity. These antibodies are of great value for the diagnosis and management of autoimmune thyroid disease (AITD), which predominately consists of Hashimoto thyroiditis (HT or chronic lymphocytic thyroiditis). According to a 2020 epidemiological survey by our group [1], the overall prevalence of positive thyroid autoantibodies was 14.19% in the Chinese population. TgAb positive and TPOAb negative (TPOAb⁻TgAb⁺) status along with TPOAb positive and TgAb negative (TPOAb⁺TgAb⁻)

status were detected in 9.70% and 10.19%, respectively. The prevalence of TgAb or TPOAb positivity (TPOAb⁺/TgAb⁺) was significantly higher in women than in men and increased with age.

In the 1960s, the relationship between thyroid autoimmunity and hyperlipidemia was suggested [2], and dyslipidemia was conventionally thought to be a consequence of AITD. For example, Tamer et al. [3] indicated that thyroid autoimmunity may be a risk factor for hyperlipidemia independent of the thyroid function in patients with HT. On comparison with TPOAb-negative subjects, Mazaheri et al. [4] reported that hypothyroid patients with TPOAb levels > 1000 IU/mL may have lower high-density lipoprotein cholesterol (HDL-C) levels. This is further supported by Kang et al. [5] who concluded that high TPOAb levels above the normal range can lead to dyslipidemia in euthyroid population. In AITD patients, Chen et al. [6] showed that the risk of hyperlipidemia also increased even when thyroid-stimulating hormone (TSH) levels were within the normal range. Moreover, a prospective observational study conducted by Srivastava et al. demonstrated that dyslipidemia was found in 100% of subclinical hypothyroidism patients with positive TPOAb [7].

Alternatively, recent evidence emerges that serum lipids may be involved in the development of AITD [8-10]. Stein et al. [11] and Gullu et al. [12] contend that statins or 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors could produce anti-inflammatory and immune-suppressing effects at the level of the thyroid gland. Wu et al. [13] showed that simvastatin and atorvastatin were able to inhibit the human leukocyte antigen D-related (HLA-DR) expression on thyrocytes of patients with AITD. In addition, Krysiaket al. [14] affirmed that fenofibrate, a peroxisome proliferator-activated receptor- α (PPAR- α) activator (i.e., fibrates class of drugs), could decrease serum titers of TgAb and TPOAb in HT patients.

Regardless of the direction of causality between dyslipidemia and AITD, the inflammatory and immune pathways have central roles in the pathogenesis of both dyslipidemia and AITD. We submit that there may be common pathways between these two diseases through the action of thyroid autoantibodies TgAb and TPOAb. This study aimed at investigating the associations of increasing serum lipid levels with thyroid autoantibody positivity in the general population with normal TSH levels.

Materials And Methods

Study participants and design

A total of 7,688 individuals were enrolled in a study as part of a routine health check-up at the Health Medical Center of the First Hospital of China Medical University from January 2017 to December 2018. The inclusion criteria of the participants were: (1) aged 14 years or older and (2) received thyroid function and antithyroid antibodies testing. Exclusion criteria included: under 14 years old (n = 0), missing serum lipids (n = 108), abnormal TSH levels (n = 459), had a history of thyroid surgery (n = 199) or incomplete data (n = 466). The database lacked information on medication (including thyroid medication and lipid medication), smoking, alcohol consumption, and other concomitant autoimmune diseases. Finally, 6,456 subjects were included in this retrospective cross-sectional study.

Data Collection

All data were retrospectively collected from the hospital information system. During the routine health check-up, weight and height were measured having participants wear light clothing and no shoes. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Waist circumference (WC) was measured at the umbilicus level in a standing position. Systolic blood pressure (SBP) were measured twice consecutively in the same arm at 2-minute interval between the measurements with the subjects in a seated position after at least 5 minutes of rest. The average of the two SBP measurements were used in subsequent statistical analysis.

Biochemical measurements

Venous blood samples were collected in the morning between 7:00 am to 10:00 am after an 8-12 hour fast, and then promptly centrifuged and analyzed. The concentrations of fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and HDL-C were determined by enzymatic methods on the Automatic Biochemical Analyzer.

Thyroid indexes measurements

The levels of serum TSH, TgAb, and TPOAb were determined in all subjects on the same day of blood sampling, using the automated immunochemiluminescent assay (ICMA) kits (Abbott, IL, USA). The reference ranges of TSH, TgAb, TPOAb were 0.35-4.94 mIU/L, < 4.11 IU/ml, < 5.61 IU/ml, respectively, and the intra- and inter-assay coefficient of variation for these serum parameters were < 8%. TSH abnormality was defined as greater than 4.94 mIU/L or less than 0.35 mIU/L according to the ICMA kit. TgAb and TPOAb positivity were considered at ≥ 4.11 IU/ml and ≥ 5.61 IU/ml, respectively.

Statistical Analysis

Continuous variables were shown as mean \pm standard deviation (SD) for those with normal distribution and were described as median (first quartile-third quartile) for those with skewed distribution. One-way ANOVA and the Kruskal-Wallis test were used for intergroup comparisons. All categorical variables were presented as count (percentage) and the Pearson χ^2 test was used to compare variables across different groups. The associations between serum lipid levels (continuous variable) and TgAb or TPOAb positivity (categorical variable) were assessed by binary logistic regression models. Model 1 adjusted for age and/or gender, and Model 2 further adjusted for BMI, WC, SBP and FPG. Results were expressed as odds ratios (OR) with 95% confidence interval (CI). All statistical analyses were performed with SPSS Statistics, Version 22.0 (IBM Corporation, NY, USA). A two-tailed P value of less than 0.05 was deemed to be statistically significant.

Results

Baseline characteristics of subjects

A total of 6,456 subjects (3,298 women and 3,158 men) with normal TSH levels were evaluated. The mean age was 47.64 ± 11.17 years. The overall thyroid antibody positivity was 29.8% (1921/6456) with higher prevalence in females than in males (42.4% versus 16.5%). The most common thyroid antibody positivity status was TPOAb⁺TgAb⁺ at 14.5% prevalence, followed by TgAb⁺ alone at 12.4% and TPOAb⁺ alone at 2.9%.

Table 1 summarizes the baseline characteristics of subjects grouped according to thyroid antibody status. There were significant differences between the four groups for age, gender, BMI, WC, SBP, FPG, TSH, TgAb, TPOAb, TG and HDL-C (all $P < 0.001$). TC and LDL-C levels were not significantly different between the groups ($P = 0.427$ and $P = 0.646$, respectively). Subjects with TPOAb⁺TgAb⁻ were significantly older and had higher TgAb levels than control group subjects with negative antibodies (TPOAb⁻TgAb⁻) ($P < 0.001$). In the TPOAb⁻TgAb⁺ group, BMI, WC, SBP, FPG and TG were found to be significantly lower than the control group ($P < 0.001$), while the percentage of women, TSH, TPOAb and HDL-C were significantly higher than the control group ($P < 0.001$). In the TPOAb⁺TgAb⁺ group, age, BMI, WC, SBP, FPG and TG were significantly lower than the control group, but the percentage of women, TSH, and HDL-C were observed to be significantly higher than the control group ($P < 0.05$).

Associations between increasing serum lipid levels and TgAb positivity

Table 2 presents the associations of serum lipid levels with TgAb positivity in the entire study population. After adjusting for age and gender in Model 1, the risk of TgAb positivity was positively associated with increasing levels of LDL-C. For every 1 mmol/L increase in LDL-C, the odds of having TgAb positivity increases by 8% (95%CI 1.00-1.16, $P = 0.044$). In contrast, there were no significant associations between increasing TG, TC, or HDL-C levels and TgAb positivity ($P = 0.413$, $P = 0.402$, $P = 0.125$, respectively). In Model 2, after further adjustment for BMI, WC, SBP and FPG, the positive association between LDL-C and TgAb positivity became more pronounced (OR 1.10, 95%CI 1.02-1.19, $P = 0.014$). Another finding includes that the risk of TgAb positivity was inversely associated with increasing levels of HDL-C (OR 0.80, 95%CI 0.67-0.96, $P = 0.014$). There was no significant association between increasing TG or TC levels and TgAb positivity ($P = 0.846$ and $P = 0.211$, respectively).

In the gender subgroup analyses, after full adjustment for age, BMI, WC, SBP and FPG, the relationships between increasing HDL-C (OR 0.74, 95%CI 0.60-0.91, $P = 0.005$) or LDL-C (OR 1.15, 95%CI 1.05-1.26, $P = 0.004$) levels and TgAb positivity were apparent only in female subjects (Table 2). There was no significant association between increasing lipid levels and TgAb positivity in male subjects (all $P > 0.05$) (Table 2).

Associations between increasing serum lipid levels and TPOAb positivity

Associations between increasing serum lipid levels and TPOAb positivity were investigated in the same manner and is presented in Table 3. In the entire study population, after adjustment for age and gender in Model 1, no significant association was found between any type of lipid parameter and TPOAb positivity

(all $P > 0.05$). Further adjustment for BMI, WC, SBP and FPG in Model 2, yielded similar results (all $P > 0.05$).

In the gender subgroup analysis for women in Model 1, the risk of TPOAb positivity was positively correlated with increasing levels of LDL-C (OR 1.11, 95%CI 1.01-1.24, $P = 0.041$). After full adjustment in Model 2, the trend became more significant between LDL-C levels and TPOAb positivity (OR 1.14, 95%CI 1.02-1.26, $P = 0.016$), no significant connection was observed between TG ($P = 0.377$), TC ($P = 0.153$) or HDL-C ($P = 0.064$) levels and TPOAb positivity (Table 3). For men, there was no significant relationship between any type of lipid parameter and TPOAb positivity (all $P > 0.05$) (Table 3).

Discussion

The present study focuses on the association between serum lipids and thyroid autoimmunity. We have shown the significant associations of increasing HDL-C and LDL-C levels with thyroid antibodies (TPOAb and TgAb) in the general population with normal TSH levels in a gender-dependent manner. Some literature has concentrated on the effects of thyroid autoantibodies on lipids [15]. However, few studies have explored the relationship between lipids and the positivity of thyroid autoantibodies. Especially, recent data have shown that serum lipids are novel risk factors for developing autoimmune diseases, such as systemic lupus erythematosus (SLE), celiac disease, idiopathic thrombocytopenic purpura (ITP) and Sjögren's disease [8,16]. Therefore, we aimed to evaluate whether similar associations can be observed in thyroid autoimmunity.

TSH is a pituitary gland hormone that plays a vital role in maintaining normal thyroid function. Abnormal levels of serum TSH can lead to dyslipidemia [17,18], and its association with serum lipid levels may be independent of thyroid hormone action [19]. Hence, our study was conducted in a normal TSH population. Interestingly, our findings suggested that TSH levels of the TgAb⁺ groups were higher than the negative control group even though TSH is within the reference range. Similar results have been reported in the previous studies [5,6,20] and may be explained by the fact that positivity for thyroid autoantibodies is associated with significantly higher risks of overt and subclinical hypothyroidism.

In the present study, we observed that lower concentrations of HDL-C were associated with a higher risk of TgAb positivity, which contrary to the result from an earlier study [15]. In this report, higher HDL-C levels were found in TPOAb⁻TgAb⁺ when compared with TPOAb⁻TgAb⁻. The likely explanation for this is that the statistical analysis methods used are different. Zhang et al. [15] analyzed the relationships between lipids and thyroid autoantibody by analysis of variance, which was statistically less robust than the binary logistic regression from our study. Furthermore, we found no association between HDL-C levels and TPOAb positivity. Several studies support our finding [6,7,21-24] but conflicting evidence have also been reported. For example, TPOAb was found negatively correlated with HDL-C levels in Iranian and Turkish studies by Tamer et al. and Mazaheri et al., respectively [3,4]. The reason for the discrepancy may be due to differences in the study design. These case-control studies had predominantly patients with HT who have higher titers of TPOAb and much higher risk of overt and subclinical hypothyroidism in comparison

to the general population. In contrast, a domestic study found that TPOAb was positively correlated to HDL-C levels [5], which is supported by the Copenhagen City Heart Study by Madsen et al. [8]. The Copenhagen Study reported U-shaped associations between HDL-C and autoimmune diseases, that is, high concentrations of HDL-C (> 77 mg/dL) is also associated with higher risk of autoimmune diseases. It seems to differ from the traditional perception of HDL-C as the “good cholesterol”. Possible explanations include: (i) the presence of residual confounding factors such as cancer, infection and other influence factors affected the results [25]; (ii) the presence of genetic variants [26] changed composition and function of HDL particles; and (iii) individuals who have high HDL-C (> 60 mg/dL) and very high HDL-C (> 100 mg/dL) concentrations are often grouped with participants with moderate concentrations. As a result of the above factors, researchers may not be able to observe this U-shaped relationship between HDL-C and autoimmune diseases [27,28].

Our data also suggested that increasing LDL-C levels were positively associated with TgAb and TPOAb positivity, which is supported by previous studies [5,7,24]. However, we did not find any association between TC levels and TgAb or TPOAb positivity, even though roughly seventy percent of serum TC is composed of LDL-C and the level of TC is usually parallel to that of LDL-C [5,29]. This lack of association observed in our study is inconsistent with previous reports. Kang et al. and Srivastava et al. reported that serum TC and LDL-C were positively correlated to TPOAb [5,7]. In another study, serum TC and LDL-C were found positively correlated to TgAb [24]. Since TC is the aggregate of cholesterol contained in various lipoproteins in the blood, including LDL-C, HDL-C, extremely low-density lipoprotein (VLDL), lipoprotein (a), and others, it is not ruled out that the association between TC and thyroid autoantibody may be affected by other cholesterol composition. Therefore, caution should be exercised when interpreting the results from the relationship of TC and LDL-C with the thyroid autoantibodies.

Moreover, we did not observe any association between TG and thyroid autoantibodies, which is consistent with several reports [4,6,21]. However, TG has also been observed to be positively correlated with TgAb and/or TPOAb in some studies [3,7,22]. These differences in findings could be due to geographical location, ethnicity, genetics, thyroid autoantibody cutoff values, sample size and statistical analyses methods.

Unexpectedly, we detected that the relationships between the serum lipids and thyroid autoantibody positivity were significant only in women. The disparate results from gender could be related to the immune system exhibiting sexual dimorphism in humans [30]. The unique effect of estrogen on the immune system may determine the susceptibility of women to autoimmune diseases and the greater immune response in women than in men [31].

Three main questions arise based on our study: First, what are the underlying mechanisms of the associations between serum lipids and thyroid autoantibodies? Evidence indicates that toll-like receptors (TLRs) play an essential role in the pathogenesis of AITD, HDL and LDL can inhibit and activate TLRs thus affect the progress of Graves' disease (GD) or HT, respectively [32-35]. In addition, reactive oxygen species (ROS) are necessary for thyroid hormone synthesis in physiological conditions, but excessive

ROS may result in thyrocytes apoptosis and necrosis. HDL and LDL are capable of modulating and stimulating oxidative stress further involvement in the development of AITD, respectively [36-38]. Further research is required in this field. Second, would management of blood lipids be beneficial to the patients at high risk of thyroid autoimmunity, given that lower serum HDL-C level or higher serum LDL-C level is associated with higher risk of this disease? Third, whether management of blood lipids could specifically prevent the onset of AITD in susceptible populations or decrease thyroid autoantibody titer? These questions of great clinical significance remain to be explored in the future.

To the best of our knowledge, this is the first report evaluating the issue of the association of serum lipids with thyroid autoantibody in the general population from a serum lipid perspective, and we unexpectedly identified that these relationships differed with gender. Moreover, in comparison to other reports, our study had a larger sample size and stronger statistical methods, which made the results more reliable. However, several limitations of this study should also be considered. First, due to the cross-sectional design of this study, the direction of any causal relationship could not be established. Second, this study was conducted in a single center, which suggests that the results may be inadequate to generalize to the broader population or even to different races. Finally, due to the lack of information on medication, smoking, alcohol consumption, and other concomitant autoimmune diseases, the results may also be affected by some unknown confounding factors.

In conclusion, we have shown the associations of increasing HDL-C and LDL-C levels with thyroid autoantibody positivity in the general population with normal TSH levels in a gender-dependent manner. This study highlights that lipid profiles may be new predictors of thyroid autoimmunity even when TSH is within the normal reference range. However, further validation is required in future prospective studies.

Declarations

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Conflicts of interest The authors declare that they have no conflict of interest.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Authors' contributions H.G. and W.W. contributed to the study conception and design. Material preparation and data collection and analysis were performed by J.L., Z.W., H.L. and J.F. and F.Q. The first draft of the manuscript was written by J.L. and Z.W. All authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval This retrospective study was approved by the Medical Ethics Committee of The First Hospital of China Medical University. Informed consent waiver was obtained to use deidentified data.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

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Tables

Table 1 Baseline characteristics of subjects according to thyroid antibody status

	TPOAb ⁺ TgAb ⁻	TPOAb ⁻ TgAb ⁺	TPOAb ⁺ TgAb ⁺	TPOAb ⁻ TgAb ⁻	<i>P</i> -value
Number (%)	184 (2.9)	800 (12.4)	937 (14.5)	4535 (70.2)	-
Men (%)	104 (56.5)	226 (28.2) ^b	191 (20.4) ^b	2637 (58.1)	<0.001
Age (year)	51.24 ± 10.69 ^b	47.18 ± 11.46	46.70 ± 10.90 ^a	47.77 ± 11.16	<0.001
BMI (Kg/m ²)	24.97 ± 3.26	24.39 ± 3.27 ^b	24.13 ± 3.39 ^b	25.23 ± 3.56	<0.001
WC (cm)	82.72 ± 10.38	80.04 ± 10.50 ^b	78.46 ± 9.92 ^b	83.96 ± 10.83	<0.001
SBP (mmHg)	130.08 ± 21.01	126.02 ± 19.79 ^b	124.18 ± 18.42 ^b	128.79 ± 19.05	<0.001
FPG (mmol/L)	5.23 (4.89-5.67)	5.08 (4.79-5.43) ^b	5.09 (4.84-5.42) ^b	5.16 (4.83-5.59)	<0.001
TSH (mIU/L)	1.66 (1.14-2.36)	1.68 (1.20-2.43) ^b	2.11 (1.43-3.12) ^b	1.55 (1.12-2.15)	<0.001
TPOAb (IU/ml)	17.41 (8.91-48.15) ^b	0.52 (0.24-1.16) ^b	158.26 (42.96-519.18) ^b	0.29 (0.12-0.58)	<0.001
TgAb (IU/ml)	2.21 (1.52-2.92) ^b	13.26 (6.05-51.11) ^b	45.23 (16.58-171.73) ^b	1.46 (1.04-2.03)	<0.001
TG (mmol/L)	1.23 (0.88-1.82)	1.18 (0.81-1.72) ^b	1.12 (0.80-1.70) ^b	1.34 (0.89-2.07)	<0.001
TC (mmol/L)	4.98 ± 0.90	4.98 ± 0.95	4.98 ± 0.89	4.94 ± 0.90	0.427
HDL-C (mmol/L)	1.35 ± 0.37	1.39 ± 0.37 ^b	1.43 ± 0.37 ^b	1.32 ± 0.37	<0.001
LDL-C (mmol/L)	3.16 ± 0.77	3.12 ± 0.82	3.11 ± 0.77	3.10 ± 0.80	0.646

BMI body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *FPG* fasting plasma glucose, *TSH* thyroid-stimulating hormone, *TPOAb* thyroid peroxidase antibody, *TgAb* thyroglobulin antibody, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

The data are presented as n (%), median (first quartile-third quartile) or mean ± SD

^a*P* < 0.05 compared to TPOAb⁻TgAb⁻ group

^b*P* < 0.01 compared to TPOAb⁻TgAb⁻ group

Table 2 Association of lipid levels with TgAb positivity

Each 1-mmol/L increase	Case/number (%)	Model 1	Model 2
Total			
TG	1739/6456 (26.9)	0.98 (0.93-1.03)	1.01 (0.95-1.06)
TC	1739/6456 (26.9)	1.03 (0.96-1.10)	1.04 (0.98-1.11)
HDL-C	1739/6456 (26.9)	0.88 (0.74-1.04)	0.80 (0.67-0.96) ^a
LDL-C	1739/6456 (26.9)	1.08 (1.00-1.16) ^a	1.10 (1.02-1.19) ^a
Women			
TG	1322/3298 (40.1)	1.01 (0.94-1.08)	1.04 (0.97-1.13)
TC	1322/3298 (40.1)	1.06 (0.98-1.15)	1.07 (0.99-1.16)
HDL-C	1322/3298 (40.1)	0.82 (0.67-1.00) ^a	0.74 (0.60-0.91) ^a
LDL-C	1322/3298 (40.1)	1.13 (1.03-1.24) ^a	1.15 (1.05-1.26) ^a
Men			
TG	417/3158 (13.2)	0.96 (0.89-1.03)	0.97 (0.90-1.05)
TC	417/3158 (13.2)	0.99 (0.88-1.11)	1.00 (0.89-1.12)
HDL-C	417/3158 (13.2)	1.03 (0.75-1.42)	0.96 (0.69-1.35)
LDL-C	417/3158 (13.2)	1.02 (0.89-1.16)	1.02 (0.90-1.17)

TG triglyceride, TC total cholesterol, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol

^a $P < 0.05$

Model 1: adjusted for age and/or gender

Model 2: further adjusted for BMI, WC, SBP and FPG

Table 3 Association of lipid levels with TPOAb positivity

Each 1-mmol/L increase	Case/number (%)	Model 1	Model 2
Total			
TG	1123/6456 (17.4)	0.95 (0.90-1.01)	0.98 (0.92-1.05)
TC	1123/6456 (17.4)	1.01 (0.94-1.09)	1.03 (0.96-1.11)
HDL-C	1123/6456 (17.4)	0.99 (0.82-1.20)	0.89 (0.73-1.09)
LDL-C	1123/6456 (17.4)	1.05 (0.96-1.14)	1.08 (0.99-1.17)
Women			
TG	828/3298 (25.1)	1.01 (0.93-1.09)	1.04 (0.96-1.13)
TC	828/3298 (25.1)	1.06 (0.97-1.16)	1.07 (0.98-1.17)
HDL-C	828/3298 (25.1)	0.89 (0.71-1.11)	0.80 (0.63-1.01)
LDL-C	828/3298 (25.1)	1.11 (1.01-1.24) ^a	1.14 (1.02-1.26) ^a
Men			
TG	295/3158 (9.3)	0.91 (0.82-1.00) ^a	0.93 (0.84-1.03)
TC	295/3158 (9.3)	0.97 (0.85-1.11)	0.98 (0.86-1.13)
HDL-C	295/3158 (9.3)	1.28 (0.90-1.80)	1.18 (0.82-1.71)
LDL-C	295/3158 (9.3)	0.98 (0.84-1.14)	0.99 (0.85-1.16)

TG triglyceride, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

^a $P < 0.05$

Model 1: adjusted for age and/or gender

Model 2: further adjusted for BMI, WC, SBP and FPG