

THE RELATIONSHIP OF SERUM LIPID PROFILE AND SOME CARDIOVASCULAR RISK FACTORS IN APPARENTLY HEALTHY WOMEN IN TABRIZ, IRAN

Roghayeh Molani Gol¹, Maryam Rafraf², Mohammad Asghari Jafarabadi³

¹⁻³Faculty of Nutrition and Food Science, Tabriz University of Medical Sciences, Tabriz, Iran

Address for Correspondence:

Roghayeh Molani Gol

Faculty of Nutrition and Food Science, Tabriz University of Medical Sciences, Tabriz, Iran

Emails: rafrafm@tbzmed.ac.ir

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Contribution

MR designed the whole project as a supervisor. RMG contributed to data gathering and on-site study management. MAJ performed the statistical analysis. All authors contributed equally to the submitted manuscript.

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ABSTRACT

Objectives: To assess the relationship between serum lipid profile and some cardiovascular risk factors.

Methodology: This cross-sectional study consisted of pregnant and non-lactating women aged 30-55 years, selected by convenience sampling method from who referring health center in Tabriz, Iran from April to May 2017. Anthropometric measurements, blood pressure, fasting serum lipid profile, and dietary intakes of participants were evaluated data was analysis STATA of software. $P > 0.1$ was taken as significant.

Results: Total of 152 non pregnant women were included. Significant positive relationship were found between serum triglyceride (TG) and weight ($B = 2.23$ and $p = 0.032$), and between serum TG and total cholesterol (TC) with systolic blood pressure ($B = 1.58$ and 1.01 with $p = 0.059$ and 0.096 , respectively) and diastolic blood pressure ($B = 2.43$ and 1.56 with $p = 0.029$ and 0.027 , respectively) by multiple-adjusted quantile regression analyses. There were significant correlation between serum TC and daily zinc intake ($B = 7.93$ and $p = 0.003$) and between serum HDL-C with age ($B = -0.48$ and $p = 0.029$), waist circumference ($B = -0.86$ and $p = 0.025$), and waist-hip ratio ($B = -72.3$ and $p = 0.041$). No significant relationship were seen between serum lipids and other variables.

Conclusions: Serum TG and TC levels were associated with higher blood pressure and HDL-C levels increased with enhancing of central obesity. These findings emphasizes the role of lipid profile as cardiovascular risk factors in women. Effective strategies are necessary for improving dyslipidemia in women.

Key Words: Lipid profile, Cardiovascular risk factors, Blood pressure, Obesity, Women

INTRODUCTION

Dyslipidemia, as a metabolic abnormality, is an important public health problem and a common cause of morbidity all over the world.^{1,2} It is characterized by disorders in the levels of circulating lipids that related with many clinical indicators.³ The major risk factors for cardiovascular disease (CVD) include dyslipidemia, obesity, hypertension, diabetes mellitus, less physical activity, poor nutrition, low social economic status, smoking, age, inheritance, gender and ethnicity. Considerable evidence demonstrate that dyslipidemia, hypertension, obesity, and other cardiovascular risk factors are linked epidemiologically, clinically, and metabolically.⁴

Serum lipid profile has long been considered to be amongst the principal CVD risk factors in the general population.⁵ It is well known that high serum total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) are particularly important risk factors for coronary artery disease. Individuals with high blood cholesterol levels have a higher prevalence of hypertension and those with high blood pressure (BP) have a higher prevalence of hypercholesterolemia. Several studies have shown a positive association between serum triglyceride (TG) and coronary artery disease risk.⁴ Framingham Heart Study has concluded that a low high density lipoprotein cholesterol (HDL-C) level predicts the risk for coronary artery disease independently of other risk factors.⁶ The HDL-C is also a powerful antioxidant which inhibits LDL oxidation in the artery wall and prevents atherosclerosis.⁷ The typical dyslipidemia of obesity consists of increased TG and fatty free acid, decreased HDL-C with HDL dysfunction and normal or slightly increased LDL-C with increased small dense LDL.⁸

The pattern of lipid profile results is well established in the developed or advanced countries.⁹ Whereas, template of lipid abnormalities among Asians and their relative impact on cardiovascular risk have not been well characterized.¹⁰ On the other hand, dyslipidemia is highly prevalent among women.¹¹ While, in early clinical studies in dyslipidemia, women were not routinely included.¹² In Iran, the studies aiming at the analysis correlation of lipid profile and risk factors for CVD among the women are scarce. Therefore this study aimed at analyzing the relationship of lipid profile with some cardiovascular risk factors in apparently healthy women in Tabriz, Iran.

METHODOLOGY

This cross-sectional study was conducted on non-pregnant and non-lactating women aged 30-55 years, selected using convenience sampling method from who referred to health center in Tabriz during spring that is from April – May 2017. The study protocol was approved by the ethical committee of Tabriz University of Medical Sciences (Ethical code: IR.TBZMED.REC.1396.8). The sample size was calculated with regard to the prevalence of 39.8% pre-hypertension in Iran 13, and considering a 95% confidence level, a tolerable error of 20% and a power of 80% in two-tailed tests using G-Power 3.1.2 software. Exclusion criteria were: being pregnant or lactating, menopause, athlete, smoking and women having a history of the disease (such as heart disease, hypertension, diabetes, hepatic, kidney and nervous disease, cancer and etc.) or with use of medication (for example glucose, lipid and inflammatory lowering

drugs) or nutritional supplements (such as vitamin E, zinc and any antioxidants). All participants signed written informed consent and were informed of the study procedure.

Body weight was measured using a calibrated Seca scale and was approximately recorded to 0.5 kg. The participants were measured barefoot wearing light clothing. Height was measured using a mounted tape with the participants' arms hanging freely at their sides and was approximately recorded to 0.5 cm. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of height in meters. Waist circumference (WC) was measured at the midpoint between the lower costal margin and superior iliac crest after exhaling. Hip circumference was measured at the point where the buttocks extended the maximum. Measurements were taken with a tape measure in centimeters and rounded to 0.5 cm while the subject was standing. Waist-hip ratio (WHR) was obtained by dividing the size of the waist by the hip circumference.¹⁴

BP was measured on the right arm using a standard mercury sphygmomanometer together with an adult cuff after at least 5 min rest in a sitting position. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured as the first detectable sound and the disappearance of korotkoff sounds, respectively. The mean of the two readings was calculated for analysis.¹⁴

Venous blood samples (5 ml) were achieved from all participants next a 12 h overnight fast. Serum was separated using centrifugation and kept frozen at -70 °C until assay. Serum lipid profile measurements were done by using the commercial kits (ParsAzmoon kits, Tehran, Iran). TG, TC and HDL-C levels were obtained by enzymatic methods via the autoanalyzer (alcyon 300 automated biochemistry analyzer; Abbott laboratories, Abbott Park, IL, USA). When internal quality control met the suitable criteria, all samples were analyzed. Serum LDL-C was later calculated indirectly by the Friedewald formula: $LDL-C = TC - (HDL-C + TG/5)$.¹⁵ Information about the serum lipid profiles status of studied subjects has already been reported elsewhere.¹⁶

Data about daily dietary intakes was obtained by the 24-hour recall questionnaire for 3 d, with two weekdays and one weekend day, then analyzed by Nutritionist 4 software (First Data bank Inc., Hearst Corp., San Bruno, CA, USA).¹⁴

Statistical analysis were done by STATA software [ver.13] (Stata Corp, College Station, Texas 77845 USA). Normality of the numeric variables was checked by Kolmogorov-Smirnov test. To assess the relationship between serum lipid profile with studied variables, univariate and multivariate quantile regression modelling was used due to non-normal distribution of the dependent variables. In the multivariate model, the effect of confounders were adjusted and the simultaneous relationship of the predictors were assessed. In all analyses, P values less than 0.1 were considered as significant and 90% confidence intervals of the regression coefficients were presented.

RESULTS

In first, 160 participants recruited, which 8 participants excluded from the analyses due to either missing interview or anthropometric data. The final sample included 152 women. Table 1 shows the general and clinical characteristics of the study population. Mean age of women was 40.21 ± 5.85 years.

The correlation between serum TG concentrations and the other variables as shown in table 2. In the multiple-adjusted quantile regression analysis, serum TG was positively associated with weight ($p = 0.032$), SBP ($p = 0.059$), and DBP ($p = 0.029$). Serum TG was also inversely associated with daily dietary zinc

intake ($p = 0.003$) SerumTC correlation is shown in table 3. Serum TC correlation is shown in table 3.

Correlation of serum HDL-C levels with other variables as shown in table 4. In the multiple-adjusted quantile regression analysis, serum HDL-C was negatively associated with age ($p = 0.029$), WC ($P = 0.025$), and WHR ($p = 0.041$).

The correlation between serum LDL-C concentrations and the other variables as shown in table 5 No significant associations were found between LDL-C concentration and studied variables in the multiple-adjusted quantile regression analysis ($p > 0.1$).

Table 1: General, Clinical and Biochemical Characteristics and Dietary Intakes of Studied Women (n = 152)

Variables	Mean	SD	Frequency (n)	Percentage (%)
Age (years)	40.21	5.88		
Weight (kg)	76		13.59	
Height (cm)			158.05	5.78
BMI (kg/m ²)			30.48	5.05
WC (cm)			94.24	10.87
HC (cm)		111.32	9.96	
WHR			0.84	0.06
SBP (mmHg)			113.30	9.27
DBP (mmHg)		71.41		8.08
Serum TG (mg/dl)			124.55	69.47
Serum TC (mg/dl)	177.73		32.67	
Serum HDL - C (mg/dl)	50.52		14.54	
Serum LDL - C(mg/dl)	102.29		28.96	
Dietary intakes:				
Energy (Kcal/d)			1597.39	504.31
Carbohydrate (g/d)			246.38	82.64
Protein (g/d)			48.14	17.48
Fat (g/d)			49.67	18.18
Vitamin C (mg/d)	72.68		53.94	
Vitamin E (mg/d)	2.16	1.84		
Zin c (mg/d)			4.07	2.90

BMI, body mass index; WC, waist circumference; HC ,Hipcircumference; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

Table 2: Associations between Circulating TG Concentrations and other Variables in Women (n=152)

Variables	Unadjusted		Adjusted	
	B (90% CI) ‡	P-Value	B (90% CI)	P-Value
Age (years)	1.58 (-0.50 to 3.67)	0.212	1.04 (-0.69 to 2.77)	0.321
Weight (kg)	1.16 (0.40 to 1.91)	0.012	2.23 (0.52 to 3.93)	0.032*
BMI (kg/m ²)	2.50 (0.21 to 4.79)	0.072	-2.08 (-7.09 to 2.93)	0.493
WC (cm)	1.29 (0.24 to 2.35)	0.044	1.65 (-4.62 to 1.31)	0.357
WHR	276.69 (91.68 to 461.71)	0.014	212.5 (-62.1 to 487.3)	0.202
SBP (mmHg)	0.7 (-0.72 to 2.12)	0.418	1.58 (0.02 to 3.15)	0.059*
DBP (mmHg)	-0.86 (-2.41 to 0.68)	0.355	2.43 (4.25 to 0.60)	0.029*
Energy (Kcal/d)	-0.00 (-0.03 to 0.01)	0.684	-0.02 (-0.08 to 0.03)	0.555
Carbohydrate (g/d)	0.07 (-0.07 to 0.21)	0.421	0.25 (-0.01 to 0.53)	0.126
Protein (g/d)	0.15 (-0.56 to 0.87)	0.727	-0.98 (-2.06 to 0.10)	0.136
Fat (g/d)	0.55 (-1.23 to 0.12)	0.181	-0.43 (-1.28 to 0.40)	0.393
Vitamin C (mg/d) †	0.04 (-0.16 to 0.25)	0.703	0.08 (-0.10 to 0.27)	0.441
Vitamin E (mg/d) †	6.07 (0.09 to 12.06)	0.095	4.63 (-0.41 to 9.68)	0.131
Zinc (mg/d) †	2.71 (-1.00 to 6.43)	0.230	-7.93 (-3.55 to 12.31)	0.003*

TG, triglyceride; BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. P-value based on univariate and multivariate quantile regression.

* P<0.1 is significant.

‡ Confidence interval

† Daily intake

Table 3: Associations between Circulating TC Concentrations and other Variables in Women (n=152)

Variables	Unadjusted		Adjusted	
	B (90% CI) ‡	P - value	B (90% CI)	P-value
Age (years)	1(-0.12 to 2.12)	0.142	(-0.75 to 1.45)	0.602
Weight (kg)	0.15 (-0.33 to 0.63)	0.606	0.06 (-1.02 to 0.14)	0.923
BMI (kg/m ²)	0.63 (-0.74 to 2.00)	0.447	-1.37 (-4.57 to 1.81)	0.476
WC (cm)	0.52 (-0.07 to 1.13)	0.1521.00	(-0.88 to 2.90)	0.378
WHR	75.78 (-24.35 to 175.92)	0.212	-51.3 (-226.4 to 123.6)	0.628
SBP (mmHg)	0.24 (-0.42 to 0.90)	0.553	1.01 (0.01 to 2.01)	0.096 *
DBP (mmHg)	0.06 (-0.74 to 0.88)	0.8931.56	(2.72 to 4.02)	0.027
Energy (Kcal/d)	-0.00 (-0.01 to 0.01)	0.854	-0.01 (-0.05 to 0.02)	0.464
Carbohydrate (g/d)	1.11 (-0.07 to 0.07)	1.00	0.05 (-0.11 to 0.23)	0.583
Protein (g/d)	4.44 (-0.35 to 0.35)	1.00	-0.28 (-0.97 to 0.40)	0.492
Fat (g/d)	0.04 (-0.29 to 0.38)	0.839	0.43 (-0.10 to 0.97)	0.184
Vitamin C (mg/d) †	-0.02 (-0.13 to 0.09)	0.748	-0.08 (-0.20 to 0.03)	0.257
Vitamin E (mg/d) †	1.09 (-2.01 to 4.20)	0.561	0.63 (-2.58 to 3.84)	0.745
Zinc (mg/d) †	1.09 (-1.01 to 3.21)	0.392	2.17 (-0.61 to 4.96)	0.198

TC, total cholesterol; BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. P-value based on univariate and multivariate quantile regression.

* P<0.1 is significant.

‡ Confidence interval

† Daily intake

Table 4: Associations between Circulating HDL-Concentrations and other Variables in Women (n=152)

Variables	Unadjusted		Adjusted	
	B (90% CI) ‡	P-value	B (90% CI)	P-value
Age (years)	0.75 (0.45 to 1.04)	0.000	-0.48 (-0.12 to 0.85)	0.029*
Weight (kg)	-0.09 (-0.23 to 0.03)	0.237	-0.30 (-0.66 to 0.05)	0.164
BMI (kg/m ²)	-1.33 (-0.36 to 0.36)	1.00	-0.83(-1.89 to 0.23)	0.197
WC (cm)	0 (-0.13 to 0.13)	1.00-0.86	(-0.23 to 1.49)	0.025*
WHR	30.92 (7.28 to 54.55)	0.032	-72.3 (-130.5 to -14.1)	0.041*
SBP (mmHg)	1.11 (-0.16 to 0.16)	1.00	-0.11 (-0.44 to 0.22)	0.581
DBP (mmHg)	3.33 (-0.18 to 0.18)	1.000.14	(-0.24 to 0.53)	0.537
Energy (Kcal/d)	3.47 (-0.00 to 0.00)	1.00	0.00 (-0.00 to 0.01)	0.552
Carbohydrate (g/d)	1.39 (-0.02 to 0.02)	1.00	-0.03 (-0.09 to 0.02)	0.360
Protein (g/d)	-2.22 (-0.09 to 0.09)	1.00	0.01 (-0.21 to 0.24)	0.908
Fat (g/d)	1.11 (-0.08 to 0.08)	1.00	0.03 (-0.14 to 0.21)	0.726
Vitamin C (mg/d)†	0 (-0.03 to 0.03)	1.00	-0.00 (-0.04 to 0.03)	0.738
Vitamin E(mg/d)†	-0.42 (-1.17 to 0.31)	0.340	-0.41 (-1.48 to 0.65)	0.522
Zinc (mg/d)†	0.12 (-0.47 to 0.72)	0.731	0.321 (-0.70 to 1.14)	0.697

HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. P-value based on univariate and multivariate quantile regression.

* P<0.1 is significant.

‡ Confidence interval

† Daily intake

Table 5: Associations between Circulating LDL-Concentrations and other Variables Women (n=152)

Variables	Unadjusted		Adjusted	
	B (90% CI) ‡	P-value	B (90% CI)	P-value
Age (years)	0.47 (-0.37 to 1.31)	0.359	0.64 (-0.27 to 1.57)	0.249
Weight (kg)	0.18 (-0.17 to 0.53)	0.394	0.58 (-0.32 to 1.49)	0.291
BMI (kg/m ²)	0.52 (-0.37 to 1.43)	0.337	-1.92 (-4.61 to 0.75)	0.237
WC (cm)	0.25 (-0.20 to 0.72)	0.3580.64	(-0.95 to 2.23)	0.507
WHR	-25.96 (-101.02 to 49.10)	0.568	-65.9 (-213.25 to 81.28)	0.459
SBP (mmHg)	0.32 (-0.17 to 0.83)	0.281 0.43	(-0.40 to 1.27)	0.395
DBP (mmHg)	0.29 (-0.31 to 0.90)	0.421-0.87	(-1.85 to 0.09)	0.139
Energy (Kcal/d)	-0.00 (-0.01 to 0.00)	0.206	-0.02 (-0.05 to 0.01)	0.270
Carbohydrate (g/d)	-0.02 (-0.08 to 0.03)	0.424	0.06 (-0.08 to 0.20)	0.500
Protein (g/d)	-0.19 (-0.48 to 0.08)	0.246	0.01 (-0.56 to 0.59)	0.961
Fat (g/d)	-0.08 (-0.37 to 0.20)	0.639	0.37(-0.08 to 0.82)	0.176
Vitamin C (mg/d)†	-0.08 (-0.17 to 0.00)	0.117	-0.09 (-0.19 to 0.00)	0.124
Vitamin E(mg/d)†	0.82 (-1.82 to 3.47)	0.607	1.82 (-0.87 to 4.53)	0.265
Zinc (mg/d)†	-0.74 (-2.5 to 0.01)	0.483	0.04 (-2.30 to 2.39)	0.974

LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. P-value based on univariate and multivariate quantile regression.

* P<0.1 is significant.

‡ Confidence interval

† Daily intake

DISCUSSION

The association between dyslipidemia, obesity and hypertension is well established, and all have been found to be major risk factors for the development of CVD and cause of death.¹⁷ Our analysis provided a positive association between serum TG levels and weight. In the study conducted by Makhoul et al. on 330 men and women aged >18 years in Washington, which high TG concentration was positively associated with BMI.¹⁸ Collesse et al. also demonstrated that TG concentrations were significantly higher in obese subjects.¹⁹ In the study by Ugwuja et al. on 205 apparently healthy men and women aged 21-60 years in Nigeria, positive correlation was found between TG concentration and BMI, and obese subjects had significantly higher TG levels.¹⁷

In fact, dyslipidemia including high levels of TG is one of the characteristics of obesity. The hypertriglyceridemia with enhanced secretion of triglyceride-rich lipoproteins and impaired clearance of these lipoproteins is associated with abdominal obesity and increased levels of apolipoprotein C-III, a key regulator of TG metabolism. Besides, the hepatic over-secretion of large triglyceride-rich very low density lipoproteins (VLDLs) is linked to increased visceral adiposity.²⁰ Adipose tissue from different sites differs considerably in metabolism of TG and lead to hypertriglyceridemia.²¹ Therefore, weight loss significantly improves hypertriglyceridemia.²² It should be noted in present study the mean of BMI, WC and HC of all studied women were in obesity ranges. It is possible that the higher values of these obesity indexes contribute to mask any significant relationship between serum TG and BMI values in our sample.

Serum TG and TC levels in the current study were positively correlated with SBP and DBP. Similar results regarding TG levels and blood pressure, were obtained in the studies by Shimizu, and Pimenta et al.^{23,24} Some studies also have shown that in hypertensive patients compared to normotensives, BP had a significant correlation with high levels of serum TG and TC.¹⁰ Hypertension is recognized globally as a major risk factor for CVD, stroke, diabetes, and renal diseases. About 80% of hypertensive persons have comorbidities such as abnormalities in lipid metabolism, obesity and glucose intolerance.¹⁰ Hypertension and endothelial dysfunction have a bidirectional association. TG can become an independent risk factor for the early development of atherosclerosis and subsequently endothelial dysfunction. Therefore increased TG may promote high blood pressure.²³

In the present study, serum TG inversely associated with dietary zinc intake. A number of human studies have reported that zinc supplementation decreased serum TG levels.²⁵⁻²⁷ Several mechanisms are involved in this relationship. Zinc directly affects lipid metabolism, improve insulin secretion and sensitivity. Zinc deficiency with insulin resistance at the adipocytes results in increasing release of fatty acids into the circulation and their flux to the liver. Thus, zinc stimulates the assembly and secretion of VLDL and leading to hypertriglyceridemia.²⁸

According to the findings, serum HDL-C levels was negatively correlated with age. Some longitudinal studies frequently reported that HDL-C declined with aging.²⁹⁻³¹ Holzer et al. reported that aging is associated with altered composition of HDL-C.³² It was demonstrated that the age-related changes of liver sinusoidal

endothelium is one of the important reasons of dyslipidemia in aging. Age and gender are physiologic factors that have a strong influence on plasma lipid levels.³³ At older ages, HDL-C particles were less efficient at reverse cholesterol transport and were more susceptible to oxidative damage.^{34,35}

Obesity, especially central obesity, is probably the main cause of the metabolic syndrome, which includes all risk factors for CVD.⁸ In agreement to our study, Krause, and Rocha et al. reported that there was an inverse relationship between HDL-C concentration with WC and WHR.^{36,37} In the study by Bora et al. on 190 men and women with mean aged 45 years in India, decreased serum HDL-C strongly correlated with increased WC, and obesity was an important risk factor for reduction in serum HDL-C. Individuals with central obesity also had nearly 4 times greater odds for developing decreased HDL-C. A large proportion of the disease burden of low HDL-C dyslipidemia could be attributed to obesity. Moreover, Bora et al. found that 62.8% of decreased HDL-C among the centrally obese individuals was due to increased WC.³⁸

In general, the concentration of HDL-C is adversely altered in obesity, and HDL-C levels associated with both the degree and distribution of obesity. More specifically, intra-abdominal visceral fat deposition has an important negative correlation with HDL-C. Decreased HDL-C levels in obesity have been attributed to enhancement in the uptake of HDL-C by adipocytes and increased catabolism of apolipoprotein A-I on HDL particles.³⁸ HDL metabolism is also strongly affected by obesity because of the augmented number of remnants of chylomicrons and VLDL together with impaired lipolysis.⁹

LIMITATIONS

Some limitations of this study must be considered. Firstly, due to the cross-sectional nature of the study, data cannot be used to investigate the causal relationship between lipid profile and CVD risk factors. Furthermore, this study has a relatively small sample size and consists of a relatively homogeneous population of apparently healthy women, therefore it is not appropriate to generalize the findings to the general population. Thus, further studies are required in particular involving women of different age group and over the age of 50, in order to examine these associations and contribute to the early diagnosis of these risk factors for CVD.

CONCLUSION

This study showed that serum TG and TC were linked to hypertension and serum TG was also correlated with weight and dietary zinc intake. Decreased HDL-C levels could be largely attributed to aging and central obesity. These findings demonstrate the importance of establishing an early diagnosis, further prevention and control of the dyslipidemia, which may avert the CVD risk factors in females. Thus, public health efforts to challenge dyslipidemia, as a major strategy to reduce the burden of CVD and improve cardiovascular health status in our population are necessary.

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