Assessment of atherogenic indices and lipid ratios in the apparently healthy women aged 30–55 years

Roghayeh Molani Gol[1, 2], Maryam Rafraf[2], Mohammad Asghari Jafarabadi[3]

[1]*Student Research Committee, Tabriz University of Medical Sciences, Tabriz*
[2]*Nutrition Research Center, Department of Community Nutrition, Faculty of Nutrition and Food Science, Tabriz University of Medical Sciences, Tabriz, Iran*
[3]*Road Traffic Injury Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*

Abstract

Background: Cardiovascular disease (CVD) is the main cause of death worldwide and atherogenic dyslipidemia is an established risk factor for CVD. This cross-sectional study aimed to assess the atherogenic indices and lipid ratios, including atherogenic coefficient (AC), atherogenic index of plasma (AIP), cholindex (CI), Castelli risk index-1 (CRI-1), CRI-2, and non-HDL-C, in women living in the Tabriz, Iran during April–May 2017.

Material and methods: Anthropometric measurements, fasting serum lipids, and blood pressure of 150 women aged 30–55 years in Tabriz, Iran was evaluated. The atherogenic indices were calculated by the established formulas.

Results: The prevalence of high AIP, AC, CI, CRI-1, CRI-2 and non-HDL-C ratios were 64.5%, 36.2%, 20.4%, 77%, 7.2% and 44.7%, respectively. In the multiple-adjusted quantile regression analysis, significant relationships were found between CI ratio and diastolic blood pressure (DBP) (B = 3.76, p = 0.035) and between CRI-2 ratio and DBP (B = 0.005, p = 0.042) and age (B = 0.005, p = 0.031).

Conclusions: This study indicated that the majority of studied women had a high risk of CVD based on atherogenic indices. Further public health efforts are required to enhance awareness of women and healthcare providers about preventing and controlling CVD risk.

Key words: atherogenic indices; lipid ratios; dyslipidemia; cardiovascular risk factors; women

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Introduction

Cardiovascular disease (CVD) is the most important cause of death worldwide. The incidence of CVD is increasing all over the world, particularly in developing countries [1]. There are 17.5 million deaths annually due to CVD in the world. It has been estimated that 50% of all deaths per year are attributed to CVD in Iran [2], and these figures will increase because of growing CVD's risk factors [3]. In the past, the risk of heart disease in women has been underestimated due to the misperception that females are protected against CVD. In fact, CVD is the primary cause of mortality in women [4, 5].

Dyslipidemia is an established risk factor for CVD in the general population [6]. It was defined

Address for correspondence: Dr. Maryam Rafraf, Professor of Nutrition, Nutrition Research Center, Department of Community Nutrition, Faculty of Nutrition and Food Science, Tabriz University of Medical Sciences, Tabriz, Iran, Attarneishabori St., Daneshghah Avenue, Faculty of Nutrition and Food Science, Tabriz University of Medical Sciences, Tabriz, Iran, tel: +98 41 33357584, fax: +98 41 33340634; e-mail: rafrafm@tbzmed.ac.ir

as elevated triglycerides (TG), high low density lipoprotein cholesterol (LDL-C) and low high density lipoprotein cholesterol (HDL-C) levels [6]. Many clinical studies make effort to introduce better markers of atherogenic dyslipidemia that can predict the risk of CVD more precisely than classical biochemical indicators [7, 3]. These markers include new lipid ratios that are associated with an increased atherogenic potential [8].

Atherogenic index of plasma (AIP) [(logTG)/HDL-C] is a strong predictor of infarction, acute coronary events, atherosclerosis and CVD morbidity and its complications [9, 10]. In situations where all atherogenic parameters are normal, AIP may be the alternative screening tool [3]. Noumegni et al. reported that the 10-year risk of cardiovascular events among HIV-infected adults in Yaoundé, Cameroon, was significantly correlated with the AIP [8]. Results of a study by Ni et al. on patients undergoing coronary angiography, demonstrated that AIP was a significant independent predictor of all-cause mortality and cardiovascular events in women without prior myocardial infarction or coronary revascularization [11].

The atherogenic coefficient (AC), the ratio of non-HDL-C to HDL-C, is another ratio that relies on the significance of HDL-C in predicting the risk of CAD [12]. Cholindex (CI), the net effect of atherogenicity, is calculated by subtracting HDL-C from LDL-C. It is considered as the most independent predictor and relative risk value of coronary artery disease [13].

The Castelli risk indexes 1 (TC/HDL-C) and 2 (LDL-C/HDL-C) ratios are independent risk factors for CAD, which have a good predictive value for future cardiovascular events. Several studies reported that higher serum AC, CRI-1 and non-HDL-C were associated with increased risk of stroke independent of other potential confounding factors [14, 15].

In addition to dyslipidemia, other modifiable cardiovascular risk factors are hypertension, obesity, less physical activity, smoking, diabetes mellitus, low social economic status, and nutrition [16]. To our best knowledge, no published data are available about risk factors of CVD in women living in Tabriz, Iran. Hence, the present study aimed to evaluate atherogenic indices and lipid ratios and their association with other CVD risk factors in women living in Tabriz, Iran.

Material and methods

Study participants

The present cross-sectional study was carried out on 150 women aged 30–55 years who attended health centers in Tabriz and met the inclusion criteria of the study during April–May 2017. Our participants were selected by the convenience sampling method. 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 based on the correlation between AIP and waist circumference (WC) (r = 0.23) [3], and considering 95% confidence level and 80% power in two-tailed tests with STATA14 software to be 150 subjects. Of the 1182 target population, firstly160 women were selected and invited to study, then 10 subjects excluded due to uncompleted cooperation in the study. The final sample included 150 women. All participants signed written informed consent after being informed of the study procedure. Exclusion criteria were: athlete or having strenuous physical labor, being pregnant or lactating, smoking, and women with a history of the disease (such as kidney and nerve disease, heart disease, diabetes, hepatic, cancer and etc.) or with use of nutritional supplements or medication.

Anthropometric measurements

Body weight was measured using a calibrated beam scale while subjects wearing light clothing and barefoot and recorded to the nearest 0.5 kg. Height was measured using mounting tape with the participants' arms hanging freely at their sides and recorded to the nearest 0.5 cm. Body mass index (BMI) was obtained by dividing the weight in kilograms by the square of height in meters. Measurements of WC and hip circumference (HC) were taken with a tape measure in centimeters and rounded to 0.5 cm. WC was determined at the midpoint between the lowest rib and the iliac crest while the participant was standing and after expiration. Waist-hip ratio (WHR) was calculated by dividing the size of the waist by the HC [17, 18].

Blood pressure measurements

Blood pressure (BP) was measured twice in the morning by using a mercury sphygmomanometer together with an adult cuff, on the upper right arm, with the arm horizontally on a table, and subsequently 5 min rest in the 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 [17]. The mean of the two readings was calculated for analysis.

Biochemical assays

Venous blood samples (5 mL) were drawn from all participants after a 12 hours fasting. The serum

samples were separated from the whole blood by centrifugation and stored frozen immediately at –70°C until assay. Serum concentrations of TC, TG and HDL-C were evaluated by using the commercial kits (ParsAzmoon kits, Tehran, Iran) with using the autoanalyzer (Alcyon 300 Automated Biochemistry Analyzer; Abbott Laboratories, Abbott Park, IL, USA). When internal quality control reached the acceptable criteria all samples were analyzed. TC and TG were assayed with enzymatic methods using cholesterol esterase, cholesterol oxidase, and glycerol phosphate oxidase. HDL-C was measured after precipitation of the apolipoprotein B-containing lipoproteins [19]. LDL-C was calculated by the Friedewald formula: *LDL-C = TC – (HDL-C + TG/5)* [20].

The atherogenic indices were calculated using the following established formulas [15, 21, 22]:

$$AIP = log\ (TG/HDL\text{-}C)$$

$$AC = (TC–HDL\text{-}C)/HDL\text{-}C$$

$$CI = LDL\text{-}C – HDL\text{-}C\ (TG < 400\ mg/dL) =$$
$$= LDL\text{-}C – HDL\text{-}C + 1/5\ TG\ (TG > 400\ mg/dL)$$

The CI ratio in categorical form is as mmol/L.

$$CRI\text{-}1 = TC/HDL\text{-}C$$

$$CRI\text{-}2 = LDL\text{-}C/HDL\text{-}C$$

$$Non\text{-}HDL\text{-}C = TC – HDL\text{-}C$$

AIP values of < 0.11, 0.11 to 0.21, and > 0.21 are associated with low, medium, and high cardiovascular risk, respectively [3]. The following are the abnormal values for cardiovascular risk: AC > 3.0, CI > 2.07, CRI-1 >3.0, and CRI-2 > 3.3 [18]. Non-HDL-C < 130 mg/dL is considered as desirable [15].

Statistical analyses

Statistical analyses were performed by STATA software [ver.13] (Stata Corp, College Station, Texas 77845 USA). Normality of the numeric variables was checked by Kolmogorov-Smirnov test. Data were presented using mean (SD), and frequency (percent) for the normal and categorical variables, respectively. To assess the relationship between serum atherogenic indices with other 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 was adjusted and the simultaneous relationship of the predictors was assessed. The criterion to include the variables in the univariate analyses was using the significant variables. The R2 was used as a model fit measure. No interaction was examined. In all analyses, p values less than 0.05 were considered as significant and 95% confidence intervals of the regression coefficients were presented. Since this was a cross-sectional study, this choice preserves the power in the analyses, especially in the multivariate analysis.

Results

The mean age of women was 40.21 years. According to the AIP category, 70.4% of subjects were at high risk of CVD (Tab. 1). Abnormal AC, CI, CRI-1,

Table 1. Clinical and biochemical parameters of the studied women (n = 150)

Variables	Mean or n	SD or %
Age [years]	40.21	5.88
Blood pressure [mm Hg]		
SBP	113.30	9.27
DBP	71.41	8.08
Traditional lipid profiles [mg/dL]		
TG	124.55	69.47
TC	177.73	32.67
HDL-C	50.52	14.54
LDL-C	102.29	28.96
Nontraditional lipid profiles		
AIP (%)	0.35	0.26
< 0.11	23	15.1
0.11–0.21	22	14.5
> 0.21	107	70.4
AC (%)	2.72	1.03
≤ 0.3	95	63.8
> 0.3	55	36.2
CI (%)	51.77	3.42
≤ 2.07	119	79.6
> 2.07	31	20.4
CRI-1 (%)	3.72	1.03
≤ 3.0	33	23
> 3.0	117	77
CRI-2 (%)	2.17	0.82
≤ 3.3	139	92.8
> 3.3	11	7.2
Non-HDL-C [mg/dL] (%)	127.75	31.26
≤ 130	84	55.3
>130	66	44.7

AIP — atherogenic index of plasma; AC — atherogenic coefficient; CRI-1 — Castelli risk index-1; CRI-2 — Castelli risk index-2; CI — cholindex; DBP — diastolic blood pressure; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; Non-HDL-C — non- high-density lipoprotein cholesterol; SBP — systolic blood pressure; TG — triglyceride; TC — total cholesterol

CRI-2, and non-HDL-C ratios were identified in 36.2%, 20.4%, 77%, 7.2% and 44.7% of participants, respectively (Tab. 1).

In the multiple-adjusted quantile regression analysis that the simultaneous relationship of AIP, AC, CI, CRI-1, and CRI-2 indices with age, BMI, WHR, WC, SBP, and DBP were assessed, significant positive relationships were found between CI ratio and DBP and between CRI-2 ratio with age and DBP (Tab. 2).

Discussion

This research is the first study to examine the status of the atherogenic indices and lipid ratios in women living in Tabriz, Iran. The previous observations suggested that lipid ratios could be used for detecting subjects at higher risk of CVD and atherosclerosis when all values of lipoproteins seem normal and/or TG concentrations are elevated [12].

AIP ratio is shown to be associated with hypertension, diabetes, metabolic syndrome, insulin resistance, and the increased risk of cardiovascular events. Moreover, it may possess a better prognostic value than TC, LDL-C, and HDL-C concentrations. The background of this theory is that AIP is a surrogate for the concentration of atherogenic small dense LDL particles. Accordingly, such particles are more prone to the oxidation process and can subsequently induce the expressions of adhesion molecules on endothelial cells, which promote endothelial dysfunction [10]. In addition, AC ratio reflects the atherogenic potential of the entire spectrum of lipoprotein fractions [23]. CI ratio can also be used for the evaluation of all lipids risks for coronary artery disease in only one parameter [13].

In the present study, based on AIP category, 70.4% of subjects were indicated to be at a high risk of CVD. Based on our findings, high-risk AC and CI were also detected in 36.2% and 20.4% of the participants, respectively. Moreover, the prevalence rates of abnormal AC and CI ratios were higher in our subjects compared to the results of the study conducted by Olamoyegun et al. on semi-urban adults who were at least 18 years old [21].

According to the results, the most prevalent form of atherogenic indices was high CRI-1 (77%). It was shown that CRI-1 reflects coronary plaques formation as well as the thickness of intima-media in the carotid arteries of young adults [21]. Besides, an abnormal CRI-2 ratio was detected in 7.2% of the participants. CRI-2 ratio may provide a better risk assessment of coronary artery disease, since it con-

Table 2. Multiple-adjusted quantile regression analysis between some atherogenic indices and other risk factors in women

	AIP		AC		CI		CRI-1		CRI-2	
	B (95% CI)	p-value	B (95% CI)†	p-value*	B (95% CI)	p-value	B (95% CI)	p-value	B (95% CI)	p-value
Age	−0.000 (−0.00– 0.00)	0.588	−0.006 (−0.01–0.00)	0.122	1.10 (−2.26–4.47)	0.587	−0.006 (−0.01–0.00)	0.122	0.005 (−0.01– −0.00)	0.031*
BMI	0.000 (−0.00–0.00)	0.388	0.004 (−0.01–0.02)	0.715	4.74 (−4.3–1.3)	0.389	0.004 (−0.01–0.02)	0.715	0.006 (−0.00–0.02)	0.433
WHR	0.001 (−0.011–0.014)	0.833	0.278 (−0.76–1.3)	0.658	−7.73 (−5.8–4.2)	0.801	0.278 (−0.76–1.3)	0.658	0.301 (−0.50–1.1)	0.539
WC	−0.000 (−0.00–0.00)	0.410	−0.003 (−0.01–0.00)	0.643	−1.38 (−6.7–3.9)	0.670	−0.003 (−0.01–0.00)	0.643	−0.003 (−0.01–0.00)	0.446
SBP	0.000 (−0.00–0.00)	0.709	0.002 (−0.00–0.00)	0.543	−1.09 (−4.16–1.98)	0.557	0.002 (−0.00 –0.00)	0.543	0.001 (−0.00–0.00)	0.578
DBP	−0.000 (−0.00–0.00)	0.200	−0.007 (−0.01–0.00)	0.107	3.76 (2.87–7.24)	0.035*	−0.007 (−0.01–0.00)	0.107	0.005 (−0.01– −0.00)	0.042*

AIP — atherogenic index of plasma; AC — atherogenic coefficient; BMI — body mass index; CRI-1 — Castelli risk index-1; CRI-2 — Castelli risk index-2, CI — cholindex; DBP — diastolic blood pressure; SBP — systolic blood pressure; WC — waist circumference; WHR — waist-hip ratio; p-value based on univariate and multivariate quantile regression; *p < 0.05 is significant; †confidence interval

tains both atherogenic and protective lipid fractions [13]. In line with our results, in the study performed by Olamoyegun et al. on adults, abnormal CRI-1 and CRI-2 were identified in 55.2% and 16.8% of the population, respectively [21].

Non-HDL-C may be used to evaluate the atherogenic effects of LDL-C, TG, and VLDL-C in serum, which also reflects the contents of all atherogenic apolipoprotein-B-containing lipoproteins [13]. There is also a clear evidence that non-HDL-C is a strong predictor of cardiovascular risk and morbidity, and its predictive value even exceeds that of LDL [10]. Thus, it is recommended that non-HDL-C should be included in the routine lipid assessment of patients. According to the findings of this study, 44.7% of the included participants had high serum non-HDL-C. Similarly, Kumpatla et al. reported that 43% of type 2 diabetic patients had elevated non-HDL-C despite having an optimal LDL-C level. Thus, it was recommended that non-HDL-C should be included in the routine lipid assessment of patients [24].

Based on the results, the increased CI and CRI-2 ratios both were correlated with a higher DBP. In a study by Singh et al. on 50 women with pre-eclampsia, significant relationships were reported between some atherogenic indices and blood pressure [25]. Accordingly, it was suggested that lipids can cause hypertension through oxidative stress. It is noteworthy that oxidative stress promotes vascular smooth muscle cell proliferation, hypertrophy, and collagen deposition, which finally lead to the thickening of the vascular media and narrowing of the vascular lumen. Furthermore, lipid peroxides stimulate thromboxane synthesis and inhibit endothelial-derived relaxing factors resulting in vasoconstriction [25].

According to our results, the elevated CRI-2 ratio was associated with age. In this regard, the results of a study conducted by Kazemi et al. on 5207 individuals aged between 15 and 70 years old demonstrated that the atherogenic index increased with aging. It was also indicated that the catabolism of LDL-C decreases with increasing age [26]. Notably, a reduction in the activity of the LDL-C receptors in the liver is likely to be responsible for this age-related impairment of LDL-C catabolism and subsequently the increased LDL-C levels [4].

Based on our results, means of TG, TC, HDL-C, and LDL-C in the studied women were in the normal range partially. However, the obtained results on new generation lipid ratios indicated that, the studied women were at a high risk of CVD. These findings confirm that the lipoprotein-related indices are better tools in the assessment of cardiovascular risks compared to the conventional lipid profiles.

This study also had some limitations such as cross-sectional design and lack of a control group. Therefore, it is not possible to engage any cause-effective relationship between variables. Moreover, other risk factors of CVD such as individual's food habits and alcohol consumption were not examined in this study. The precise causes of the high prevalence of risk factors of CVD in our participants warrant longitudinal studies. The result of the current study may help policymakers in the implementation of a population-based strategy to screen, prevent, monitor, and control CVD in women.

Conclusions

This study indicated that the majority of studied participants had a high risk of CVD based on atherogenic indices, especially CRI-1 and AIP. Elevated DBP was associated with higher CI and CRI-2. Increased CRI-2 was also related to age. Further public health efforts are required to enhance awareness of women and healthcare providers about preventing and controlling CVD risk.

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Authorship

The whole project was designed and conducted by M.R., as a supervisor; and R.M.G. contributed to data gathering and on-site study management. Sampling methodology and statistical analysis were performed under the direction of M.A.J. All authors contributed to manuscript preparation and approved the final manuscript.

Conflict of interests

The authors declare no conflicts of interest, both financial and non-financial, for this study.

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