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ORIGINAL ARTICLE

Novel Lipid Indices as a Better Marker of Cardiovascular Disease Risk in Postmenopausal Women

[1]Muruga Sirigere, [2]S Meera

ABSTRACT

Introduction: Cardiovascular disease (CVD) is the major leading cause of mortality in men and women around the globe. The incidence of CVD increases with age in both the sexes, whereas it has been noted that there is a marked increase in risk among women after menopause. The hormonal changes associated with the menopause like low level of plasma estrogen and marked increase in follicle stimulating hormone levels exert a significant effect on metabolism of plasma lipids and lipoproteins leading to atherosclerosis, thereby increasing the risk of CVD in postmenopausal women.

Objectives: To study the lipid profile parameters and to calculate and compare the lipid indices with lipid profile parameters in pre- and postmenopausal women.

Materials and methods: The study group included 90 women comprising 45 postmenopausal (cases) and 45 premenopausal (control) women. To estimate lipid profile, enzymatic method was used and for calculation of lipid indices appropriate formula was used.

Results: Altered lipid profile was observed in postmenopausal women, but it was not statistically significant. Atherogenic Index of Plasma, Castelli's risk index-I, atherogenic coefficient, and nonhigh-density lipoprotein cholesterol were significantly increased in postmenopausal women compared with premenopausal women, but there was no significant increase in Castelli's risk index-II.

Conclusion: Lipid indices may be considered as a better and cost-effective tool in assessing the risk of CVD in postmenopausal women.

Keywords: Cardiovascular disease, Lipid indices, Lipid profile, Postmenopause.

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[1]Postgraduate Student, [2]Professor and Head

[1,2]Department of Biochemistry, Mysore Medical College and Research Institute, Mysuru, Karnataka, India

Corresponding Author: Muruga Sirigere, Postgraduate Student, Department of Biochemistry, Mysore Medical College and Research Institute, Mysuru, Karnataka, India, Phone: +919620139932, e-mail: sirigeremax15@gmail.com

INTRODUCTION

The occurrence of atherosclerosis is less frequent in premenopausal women than in postmenopausal women. This is because of derangement of lipid profile which increases the risk of cardiovascular disease (CVD) in postmenopausal women.[1] Data from the Framingham study suggest that coronary artery disease (CAD) morbidity rate increases more rapidly in females than those of males after the age of 45 years.[2] A larger proportion of women (52%) than men (42%) with myocardial infarction die of sudden cardiac death before reaching the hospital.[3]

The World Health Organization defines menopause as "the permanent cessation of menstruation as a result of the loss of ovarian activity."[4] It is usually a natural transition which occurs in women in their late forties and early fifties, signaling the end of the fertile phase of women's life. In India, the median age of natural menopause is considerably earlier at 44 years.[5]

According to the various studies, women who underwent surgical menopause or had premature menopause showed increased prevalence of CAD and in whom plasma cholesterol levels and triglyceride (TG) levels are consistently increased after menopause.[6,7] A decrease in high-density lipoprotein (HDL) level and increase in low-density lipoprotein (LDL) level in postmenopausal women may be attributed to the cause of increased atherosclerotic heart disease.

Lipid profile estimation is considered as one of the standard tests to assess the risk of CVD. In the absence of abnormal lipid profile, the possibility of CVD cannot be ruled out. Various parameters of lipid indices have been studied to be sensitive risk markers of CVD and, moreover, lipid indices are calculated using formulas that can be used in all health sectors without the burden of cost-effectiveness. Hence, this study has been undertaken on the role of various lipid indices like Atherogenic Index of Plasma (AIP), Castelli Risk Index I and II (CRI-I and CRI-II), non-HDL cholesterol (NHDL-C), and atherogenic coefficient (AC) in assessing the risk of CVD in postmenopausal women with the following objectives.

OBJECTIVES

To study the lipid profile parameters, and to calculate and compare the lipid indices with lipid profile parameters in pre- and postmenopausal women.

MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry in association with the Obstetrics and Gynecology Department of our institution. Prior informed consent for collection of sample was taken from all the study subjects. Ethical clearance was obtained from the Institutional Ethical Committee. The total number of study subjects was 90. Based on the following inclusion and exclusion criteria, the cases and controls were considered for the study.

Inclusion Criteria

- Forty-five confirmed postmenopausal women attending the gynecology outpatient department were included in the study as cases.
- Forty-five regular menstruating premenopausal women were included in the study as controls.

Exclusion Criteria

- Known case of hypertension, obesity, diabetes mellitus, CVD, hepatic, metabolic and renal disease, any neoplasia, arthritis or any other inflammatory disease, and those who are on hormone replacement therapy or lipid-lowering drugs were excluded from the study.

Collection of Blood Samples

After getting informed consents from the subjects, 5 mL of blood was collected in a red plain vacutainer tube devoid of anticoagulant under aseptic condition from the subjects after overnight fasting of 12 to 14 hours. This, however, was done after the 7th day of the last menstrual period for premenopausal group.

Samples were centrifuged at 3,000 rpm to separate serum within 1 hour and the following lipid profile parameters were estimated:

- Serum total cholesterol (TC) by enzymatic Cholesterol oxidase- Phenol and 4 Aminoantipyrine method.
- Serum TG by enzymatic Glycerol phosphate oxidase- 4 chlorophenol and 4-Aminophenazone method.
- Serum HDL cholesterol by direct method.
- Serum LDL cholesterol by Friedwald's formula: [(TC HDL) TG/5].
- Very low density lipoprotein (VLDL) cholesterol by TG/5.

Lipid indices were calculated using the following formulas:

- AIP = log (TG/HDL)[8]
- CRI-I = TC/HDL[9-11]
- CRI-II = LDL/HDL[9-11]
- AC = (TC – HDL)/HDL[12]
- NHDL-C = TC – HDL[12]

Statistical Method

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ± standard deviation (SD) and results on categorical measurements are presented as number (%). Significance is assessed at 5% level of significance. Student's t-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between the two groups.

RESULTS

Table 1 depicts the lipid profile of pre- and postmenopausal women. The values of TC, LDL, VLDL, and TG were increased, and HDL values were decreased in postmenopausal women when compared with premenopausal women. However, these values are not statistically significant.

Table 2 represents the various lipid indices in pre- and postmenopausal women. The parameters AIP, CRI-I, AC, and NHDL-C show statistically significant results in postmenopausal when compared with premenopausal women, but CRI-II did not show statistically significant results.

DISCUSSION

In our study, there is an increase in the mean values of TC, TG, LDL and decrease in HDL levels in postmenopausal

Table 1: Lipid profile of pre- and postmenopausal women

	Premenopausal women (mean ± SD)	*Postmenopausal women (mean ± SD)*	*t-value*	*p-value*
TC	161.54 ± 32.72	178.81 ± 56.22	1.76	0.086
HDL	46.94 ± 14.61	43.13 ± 13.2	1.32	0.212
LDL	95.21 ± 30.71	105.91 ± 42.6	1.34	0.18
VLDL	21.84 ± 10.87	27.93 ± 17.44	1.80	0.08
TG	109.65 ± 54.08	139.65 ± 87.23	1.72	0.088

Values are measured in mg/dL

Table 2: Lipid indices in pre- and postmenopausal women

	Premenopausal women (mean ± SD)	*Postmenopausal women (mean ± SD)*	*t-value*	*p-value*
AIP	0.01 ± 0.29	0.12 ± 0.28	2.06	0.041
CRI-I	3.79 ± 1.44	4.47 ± 1.81	2.00	0.046
CRI-II	2.27 ± 1.14	2.73 ± 1.45	1.74	0.082
AC	2.79 ± 1.45	3.49 ± 1.83	2.07	0.048
NHDL-C	114.58 ± 32.89	135.68 ± 55.77	2.12	0.035

p-value < 0.05 suggests statistical significance

women when compared with premenopausal women. This altered lipid profile may be due to hormonal imbalance in postmenopausal women. However, these values were not statistically significant; this may be owing to reduced number of sample size. These findings of our study are in accordance with other studies done by Kalavathi et al[13] and Igweh et al.[14]

The study done by Varu et al[15] and Shinde et al[16] showed that mean levels of TC, TG, and LDL were significantly higher in postmenopausal women and these levels significantly increased with increase in duration of menopause. While the levels of HDL were significantly lower in postmenopausal women, these levels were significantly decreased with increase in duration of menopause.

In the absence of traditional risk factors like in the present study, with statistically insignificant TC, LDL, VLDL, and TG levels, chances of none identifying the risk of CAD will be more. In such scenario, there is need for some special tests that are required to be analyzed as risk factor of CVD. Such special tests are lipoprotein(a), plasma homocysteine, and small dense, undesirable type of LDL. These special tests may not be feasible in all health care centers as it is more cost-effective, lack of facilities, and insufficient resources. Hence, the calculated lipid indices play a significant role as risk factors for CVD in postmenopausal women.

In our study, we have observed that there is a statistically significant result obtained in AIP, CRI-I, AC, and NHDL-C among postmenopausal women when compared with premenopausal women. Studies done by Gaziano et al[17] and Dobiášová[18] showed that AIP is a strong predictor of myocardial infarction. In the present study, AIP is statistically significant in postmenopausal women, indicating a better marker. Studies by Nwagha et al[19] have shown that in situations where TG and HDL appear normal, AIP may be the diagnostic alternative and CRI-II was not statistically significant. The results of our study are in accordance with studies conducted by Siddiqui et al[20] and Mannangi et al.[21] In this study, though lipid profile values were increased in postmenopausal women, the values were not statistically significant, but lipid indices showed statistically significant results. This indicates that lipid indices may be used as a better marker to assess the risk of CVD.

CONCLUSION

From the current study, lipid indices seem to be the preferred parameter to assess the risk of CVD in postmenopausal women when compared with lipid profile. The lipid profile parameters can be used to derive these lipid indices in centers where there is limited availability of new and special markers and specialized equipments. Thus, the use of these lipid indices can be introduced as a routine parameter in complement with lipid profile in identifying high-risk individuals for CVD and drug management.

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