

# Fasting Lipid Profile in Pre- and Post-Menopausal Women: A Prospective Study

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## Abstract

**Introduction and Aim:** Menopause is a phase of woman's natural aging process and is marked by the cessation of ovarian function. The increased incidence of cardiovascular risk in the post-menopausal women may partly be due to hormonal changes leading to derangement of lipid metabolism. The present study is aimed at determining the degree of dyslipidemia in pre- and post-menopausal women.

**Materials and Methods:** This prospective study comprised 124 women, 47 pre-menopausal aged between 25 and 45 years and 77 post-menopausal aged between 55 and 70 years. Serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) direct, low-density lipoprotein cholesterol (LDL-C), and very LDL-C (VLDL-C) were evaluated in both the groups and data were statistically analyzed using SPSS software version 16.

**Results:** In our study, we found significantly high levels of serum TC, serum TGs, serum LDL, and serum VLDL ( $234.77 \pm 58.13$  mg/dl,  $156.86 \pm 70.56$  mg/dl,  $146.49 \pm 52.70$  mg/dl, and  $31.92 \pm 13.76$  mg/dl) in post-menopausal subjects when compared with pre-menopausal subjects ( $201.60 \pm 48.50$  mg/dl,  $125.81 \pm 69.96$  mg/dl,  $124.09 \pm 42.71$  mg/dl, and  $25.28 \pm 13.98$  mg/dl). However, there was no statistically significant difference in the HDL-C fraction levels between the two groups.

**Conclusion:** Post-menopausal women are at increased risk of developing cardiovascular disease due to change in the lipid pattern and loss of cardioprotective effect of estrogen. Predicting the factors affecting the lipid profile in post-menopausal women, adopting strategies to control these mechanisms by modifying the relative risk factors during menopausal transition may improve the cardiovascular risk profile in these women.

**Key words:** Cholesterol, Lipid profile, Menopause

## INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death among the post-menopausal women. Post-menopausal women are 4-8 times more likely to die of CAD than of any other disease.<sup>1</sup> Data from the Framingham study suggest that female CAD morbidity rates accelerate more quickly than do those of males after the age of 45 years.<sup>2</sup> Multiple risk factors have been identified as contributory to the development of CAD.

Menopause is the permanent amenorrhea, which lasts at least for a period of 1-year due to the cessation of ovarian function.<sup>3</sup> This results in changes in metabolism of glucose and insulin, body fat distribution, coagulation, fibrinolysis, and vascular endothelial dysfunction.<sup>4</sup> It has been proposed that estrogen exerts cardioprotective action among pre-menopausal women by maintaining high level of high-density lipoprotein cholesterol (HDL-C) and lowering the low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG).<sup>5-8</sup> Lack of estrogen is an essential contributory factor in the derangement of lipid metabolism in post-menopausal women which is associated with increased cardiovascular risk.<sup>9</sup> Currently, post-menopausal women account for more than 30% of the female population at risk for CAD in India.<sup>10</sup>

The present study is aimed at determining the degree of dyslipidemia in pre- and post-menopausal women.

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Modification of specific factors that increase the risk of the disease appears to be the most effective means to decrease the impact of CAD on women's health.<sup>11</sup>

## MATERIALS AND METHODS

This is a prospective study conducted on a group of 124 women, 47 pre-menopausal women aged between 25 and 45 years and 77 post-menopausal women aged between 55 and 70 years at a tertiary referral hospital. Subjects with cardiovascular disease, diabetes mellitus, hypertension, obesity, pregnancy, familial hypertriglyceridemia, history of hysterectomy, oophorectomy, those on exogenous hormone or hormone replacement therapy, heavy exercise, intake of lipid-lowering drugs, or any surgery were excluded from the study. After an overnight fasting of 12-14 h, about 5 ml of venous blood was drawn under aseptic precaution in a sterile plain vacutainer from selected subjects. Serum was allowed to clot, and then separated by centrifugation and used for biochemical analysis.

Total cholesterol (TC) was measured using established enzymatic methods of Allain *et al.*<sup>12</sup> TG was isolated enzymatically by glycerol-3-phosphate oxidase - phenol + aminophenazone method as described by Schettler *et al.*<sup>13</sup> HDL-C direct was isolated by enzyme selective protection method of Williams *et al.*<sup>14</sup> LDL was calculated using the Friedewald formula:

$$\text{LDL-C} = \text{TC} - (\text{HDL-C} + \text{TG}/5)$$

Very LDL-C (VLDL) was calculated using the formula:

$$\text{VLDL-C} = \text{TG}/5^{15}$$

All the analytes were measured using Agappe Diagnostics kit on Biolis 24i autoanalyzer. The quality check was done by running two levels of quality control material.

### Ethics

Study subjects were randomly selected after an informed consent and ethical clearance from the ethical committee were obtained and were in accordance with the Helsinki Declaration of 1975 that were revised in 2000.

### Statistics

The results obtained were statistically analyzed and compared between different groups of the study. Baseline characteristics of the study participants are expressed in mean  $\pm$  standard deviation. Comparison of mean was done by independent samples *t*-test. The statistical analysis was performed using SPSS 16.0 version computer software for windows. Statistical significance was considered at  $P < 0.05$  and highly significance at  $P < 0.001$ .

## RESULTS

The mean age for pre-menopausal women was 34.9  $\pm$  6.71 years and that for post-menopausal women was 59.2  $\pm$  10.2 years.

Serum TC, TGs, LDL-C, and VLDL-C fractions were compared between the two study groups. Serum TC levels were found to be increased in post-menopausal subjects when compared with pre-menopausal subjects which was statistically significant. TG levels were found to be increased in post-menopausal subjects when compared with pre-menopausal subjects which was statistically significant. LDL-C levels were found to be increased in post-menopausal subjects when compared with pre-menopausal subjects which was statistically significant. VLDL-C levels were found to be increased in post-menopausal subjects when compared with pre-menopausal subjects which was statistically significant. However, we observed that there was no statistically significant difference in the HDL-C fraction levels between the two groups (Table 1).

Table 2 shows the HDL/LDL ratio between the two groups. HDL/LDL ratio was seen to be higher in post-menopausal women when compared to pre-menopausal women.

## DISCUSSION

The present study was undertaken to evaluate the levels of serum cholesterol and its subfractions in pre- and post-menopausal women.

The incidence of cardiovascular disease after menopause may be partly caused by changes in the plasma lipid levels that

**Table 1: Comparison of serum cholesterol and its subfractions between the study groups**

Biochemical parameters	Premenopausal women (n=47)	Postmenopausal women (n=77)	P values	Significance
TC	201.60 $\pm$ 48.50	234.77 $\pm$ 58.13	0.001	$P < 0.05^*$
TG	125.81 $\pm$ 69.96	156.86 $\pm$ 70.56	0.019	$P < 0.05^*$
HDL-C	52.15 $\pm$ 14.98	55.84 $\pm$ 22.11	0.314	$P > 0.05$
LDL-C	124.09 $\pm$ 42.71	146.49 $\pm$ 52.70	0.015	$P < 0.05^*$
VLDL-C	25.28 $\pm$ 13.98	31.92 $\pm$ 13.76	0.011	$P < 0.05^*$

\*Significant  $P < 0.05$ , non significant  $P > 0.05$ , TG: Triglycerides, TC: Total cholesterol, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol

**Table 2: HDL/LDL ratio in pre- and post-menopausal women**

Study subjects	HDL	LDL	HDL/LDL
Premenopausal women	52.15	124.09	1:2
Postmenopausal women	55.84	146.49	1:3

HDL: High-density lipoprotein, LDL: Low-density lipoprotein

occur following the menopausal transition.<sup>16-18</sup> Deposition of fatty plaques on arterial walls (arteriosclerosis) is a predisposing factor for coronary heart disease.<sup>19</sup> The increased risk of CAD following menopause is mainly related to the endocrine influences on lipid profile especially when other risk factors such as blood pressure, blood sugar, and body weight are normal. Estrogens have a major beneficial effect on cholesterol metabolism and appear substantially to reduce the risk of atherosclerosis and cardiovascular disease in post-menopausal women.<sup>20</sup>

The mean age in the post-menopausal women is  $59.2 \pm 10.2$  years and in the pre-menopausal women is  $34.9 \pm 6.71$  years. The mean age in post-menopausal women is greater than that of pre-menopausal women. There is difference in age between both groups of women because it is difficult to design studies that can separate the effects of the normal aging process from natural menopause which occurs between 45 and 50 years.<sup>9</sup>

The findings in our study are in accordance with other studies done by Kalavathi *et al.*, Muzzio *et al.*, and Matthews *et al.*, where the TC is seen to increase in post-menopausal women due to estrogen deficiency when compared to pre-menopausal women and is statistically significant ( $P < 0.05$ ).<sup>9,16,21</sup>

In our study, when compared to pre-menopausal women, post-menopausal women were having high TG and were statistically significant ( $P < 0.05$ ). These findings are in accordance with other studies done by Welty and Hallberg and Svanborg.<sup>1,22</sup> In the post-menopausal women, there is increased fat accumulation and increased release of free fatty acids into the circulation, and excessive free fatty acids provide substrate for hepatic TG synthesis.<sup>23</sup>

It was observed in our study that the menopausal status is unlikely to alter HDL-C level since no significant differences were found regarding its levels between the pre- and post-menopausal women. This finding was in accordance with certain previous studies done.<sup>24-27</sup>

In our study, post-menopausal women had high levels of LDL when compared to pre-menopausal women and was statistically significant ( $P < 0.05$ ). These findings are in accordance with other studies.<sup>9,28,29</sup> Lipoprotein lipase (LPL) is regulated by circulating estrogen. LPL catalyzes

the hydrolysis of VLDL to form intermediate-density lipoprotein and later LDL. Estrogen deficiency after menopause increases the plasma LPL and hepatic TG lipase activity causing plasma LDL to accumulate and also leads to down-regulation of LDL receptors.<sup>21,28,30</sup>

In our study, the VLDL was increased in post-menopausal women when compared to pre-menopausal women and was statistically significant ( $P < 0.05$ ), and these findings are in accordance with studies done by Swapnali *et al.*,<sup>28</sup> Welty<sup>1</sup> and Matthews *et al.*<sup>16</sup> Estrogen deficiency in post-menopausal women causes relative enrichment of small VLDL particles with cholesteryl esters (CE) either due to the increased catabolism of VLDL with resulting increased number of VLDL remnant particles or increased activity of cholesterol ester transfer protein or both.<sup>11</sup> These small VLDL particles are highly atherogenic as they contain more CE molecules per particle.<sup>31</sup> The VLDL remnants have a high capacity for interacting with arterial smooth muscle cells.<sup>32</sup>

In our study, the HDL/LDL ratio was increased in the post-menopausal group, and it has been shown that HDL/LDL ratio is a significant predictor for development of atherosclerosis.<sup>33</sup>

## CONCLUSION

Menopause leads to changes in lipid profile by elevating TC, TGs, LDL-C, and VLDL-C, thus increasing the risk for cardiovascular disease. Due to the change in the lipid pattern and loss of cardioprotective effect of estrogen, post-menopausal women are at increased risk of developing cardiovascular disease. There are many studies showing the beneficial effects of hormone replacement therapy on the lipid profile in post-menopausal women.<sup>34,35</sup> Furthermore, there are several studies which disagree on the beneficial effects of hormone replacement therapy in patients with cardiovascular disease.<sup>36</sup> Predicting the factors affecting the lipid profile in post-menopausal women, adopting strategies to control these mechanisms by modifying the relative risk factors during menopausal transition may improve the cardiovascular risk profile in these women.

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