A Study of Lipid Profile and Estradiol for Evaluation of Cardiovascular Risk in Pre- and Post-Menopausal Women

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Abstract

Introduction: Following menopause, decreased oestrogen production from ovaries leads to lipoprotein profile derangement, drastic alterations in the metabolism of glucose and insulin, distribution of body fat, coagulation and fibrinolysis and vascular endothelium dysfunction. Oestrogens include many cardioprotective mechanisms that alter the vascular tone by enhancing the levels of nitrous oxide. Endothelial cells are stabilized by oestrogens, they augment antioxidant potential and alter fibrinolytic proteins. These are all cardio-protective mechanisms that are reduced with beginning of menopause.

Objectives: To evaluate the relation of oestradiol hormonal variation with plasma lipid concentrations in pre- and post- menopausal women.

Material and Method: 50 premenopausal women and 50 postmenopausal female were selected as subjects. Data were obtained via clinical assessment from laboratory investigations and questionnai.

Results: Serum levels of Total Cholesterol (TC), Triglycerides (TG), LDL-cholesterol, and VLDL-cholesterol in postmenopausal women were significantly elevated when matched with premenopausal women. For postmenopausal women, the level of HDL-cholesterol declined substantially. The concentration of estradiol in post-menopause women was significantly lower ($p<0.001$).

Conclusion: Menopause results in alterations in the lipid profile by reducing HDL and increasing total cholesterol (TC), triglycerides (TG), LDL-cholesterol and VLDL-cholesterol, thus raising the chances of cardiovascular disease. These shifts are due to decreased amounts of oestrogen that are observed in menopause.

Keywords: *Menopause, Oestrogen, Cardiovascular disease, Plasma lipids, Coronary heart disease.*

Introduction

Menopause refers to a state of complete menstruation cessation at the end of reproductive life because of loss of ovarian follicular function and menstrual cessation. There are numerous hormonal changes that occur after menopause in women and result in variations in lipid metabolism and increase the chances of coronary artery disease in women[1,2,3].

There are alterations in the metabolism of glucose and insulin, coagulation,distribution of body fat, fibrinolysis, and dysfunction of the vascular endothelium[3,4]. Coronary artery disease (CAD) is the major reason of death for women after the menopause. Post-menopausal women are 4 to 8 times more likely to die from CAD than from any other disease[5]. Framingham study results indicate

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that female CAD morbidity levels escalate faster than male morbidity rates after 45 years of age[6]. Numerous risk factors have been reported as responsible for CAD progression.

The incidence of CAD in women is lower up to the age of 50 years, but then the incidence in both men and women is similar[7]. As average lifespan in women is rising in terms of age and menopause remains relatively unchanged, so females are now spending more of their lives in post-menopause period. In India, 60 million women are over 55 years of age[8].

Oestrogen improves the permeability of the vessels by increasing production of nitrous oxide. Adequate Protein, Vitamins and Minerals intake is required for a healthy pregnancy[9]. It maintains a balanced profile of lipoprotein. It helps to maintain the endothelial cells, improves the antioxidant effect and changes the fibrinolysis protein. In menopause, all such cardioprotective functions are missing. Postmenopausal women face an elevated risk of developing cardiovascular disease and pre-eclampsia.[2,3,10]

A woman today, after the menopause, will live about a third of her life. After menopause the ovaries fail to produce significant quantities of oestrogen; thus, symptoms and diseases related with an oestrogen deficiency are of growing in significance for women's health[11].

Inadequacy of estrogen is a crucial factor that contributes in postmenopausal women's lipid metabolism derangement that is linked to increased cardiovascular risk[2,12]. Post-menopausal women currently account for over 30 per cent of India's female population at risk of CAD[13].

Low-density lipoprotein has been involved in coronary heart disease (CHD) progression. A predisposing factor for CHD is the accumulation of fatty plaques on the arterial walls (arteriosclerosis)[14].

Given comprehensive research on the effect of progestogens and oestrogens on lipoprotein and lipid metabolism[3,15,16]. It is not yet certain if changes in sex steroid levels are correlated with variations in lipid concentrations correlated with menopause period. Coronary artery disease (CAD) is evidently polyfactorial, and data of endogenous hormones could improve our assessment of CAD[17].

Our research aimed at finding variations in lipid status in menopause women and in regularly menstruating females and investigating the relationship between menopause status and associated hormonal variability with plasma lipid concentrations.

Material and Method

This cross-sectional study was carried out at Datta Meghe Medical College,Nagpur in collaboration with Jawaharlal Nehru Medical College Sawangi (Meghe) Wardha & Datta Meghe Institute of Medical Science (Deemed University) Maharashtra, India,between August 2019 to July 2020.

For this study, groups of 50 premenopausal women and 50 postmenopausal women were chosen randomly. The postmenopausal females who were studied were those with a history of natural menopause, who had menstrual cessation for at least one year. Those who had regular menstruation were premenopausal women who were studied.

Exclusion Criteria:

1. People with hypertension,
2. Cardiovascular disease,
3. Diabetes mellitus,
4. Hepatic,
5. Metabolic and renal disease
6. Those on exogenous hormones or hormone replacement therapy,
7. Lipid reduction medications.
8. Smokers,
9. Alcoholics,
10. Sedentary women
11. Skilled athletes or sports people

The research had been accepted by the Institutional ethical committee. Following a 12-14 hour overnight fasting, venous blood samples were obtained from subjects after obtaining their informed consents. But this was achieved for the premenopausal community on the 7th day of the last menstrual cycle. Samples were centrifuged, the plasma was separated, and analyzed.

The total cholesterol, triglyceride and HDL were estimated by an enzymatic method and serum LDL and

VLDL were calculated by using Friedewald's formula VLDL= TG/5.0 and LDL = TC - HDL - TG/5.0 (mg/dL)[18].

Oestradiol was estimated by using Chemiluminescence Immunoassay kit, which is a two step competitive binding immunoassay for the quantitative determination of 17-beta–oestradiol. Body Mass Index (BMI), as a measure of body fat was determined, based on height and weight of Pre-and Post-menopausal women It was calculated by following formula. Height was measured in Meter and weight was taken in Kgs.

Statistical Analysis: Data collected was entered into Microsoft Excel Worksheet and statistically analysed by using SPSS (Statistical Package for Social Sciences) version 23.0. For quantitative data, calculated values were processed by using: arithmetic mean, standard deviation and Student's 't' test. P value of< 0.05 was considered as statically significant.

Results

Table 1: Comparison of Plasma Lipids in Premenopausal and Postmenopausal Women

Plasma Lipids (mg/dl)	Pre-menopausal n=50	Post-menopausal n=50	P-Value
TC	151.42 ± 16.38	209.26 ± 27.48	< 0.001
TGL	126.3 ± 13.32	126.3 ± 13.32	< 0.001
HDL	47.56 ± 6.19	26.8 ± 5.4	< 0.001
VLDL	21.18 ±1.32	24.3 ± 2.40	< 0.001
LDL	84.76 ±20.32	159.38 ±29.42	< 0.001

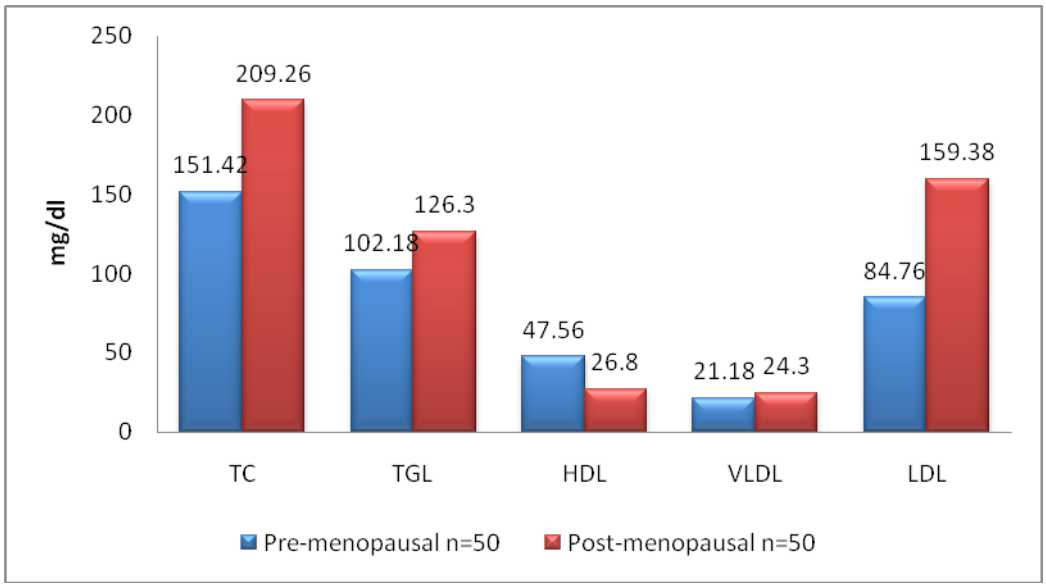

Fig-1: Comparison of lipid profile in pre and post menopausal women

In postmenopausal women, we found a significant rise in serum levels of Total Cholesterol (TC), Triglycerides (TG), LDL-cholesterol and VLDL-cholesterol compared with those in premenopausal women (p<0.001). The level of HDL-cholesterol in postmenopausal women was significantly reduced relative to that in premenopausal women (p<0.001) (Table 1 and fig 1).

[Table 2]: Comparison of Estradiol and BMI in Premenopausal and Postmenopausal Women

	Pre-menopausal n=50	Post-menopausal n=50	P-Value
Estradiol (Pg/ml)	168.48±41.28	42.32±11.20	< 0.001
BMI (kg/m^2)	20.7±4.3	23.9±4.12	>0.05

In our study, estradiol concentration in pre menopausal women (168.48 ± 41.28) was observed to be significantly higher (p<0.001) than post menopausal women (42.32 ±11.20) [Table-2].

According to the results of this study, there was no significant difference (p>0.05) in BMI between postmenopausal women (23.9±4.12) and pre-menopausal women (20.7±4.3) [Table 2].

Discussion

In postmenopausal women, we found a significant rise in serum levels of Total Cholesterol (TC), Triglycerides (TG), LDL-cholesterol and VLDL-cholesterol compared with those in premenopausal women (p<0.001). The amount of HDL-cholesterol in postmenopausal women was significantly lower than in premenopausal women (p<0.001).

Postmenopausal women in our cohort have demonstrated more significant dyslipidaemia than premenopausal women, in line with previous studies[19,20].

Our finding was comparable to the Ifueko (2013) analysis in which TC, TAG and LDL-C in postmenopausal women were significantly increased with "P" value < 0.001 than in premenopausal females[21]. Similarly, Shenoy and Vernekar (2015) observed a considerable increase in TC, TAG, and LDL-C but the HDL-C was not significantly increased in postmenopausal women compared to premenopausal females[22].

Our study results are consistent with other studies carried out by Kalavathi et al., where TC is shown to increase in postmenopausal females due to estrogen deficiency relative to premenopausal females and is statistically significant (P < 0.001) [12].

In our study, postmenopausal women had high TG and were statistically relevant (P < 0.001), relative to premenopausal women. Such results are consistent with other research carried out by Welty, Hallberg, and Svanborg[5,23]. For postmenopausal females, there is increased fat accumulation and increased release of free fatty acids into circulation, and excessive free fatty acids provide a substrate for hepatic TG synthesis[24].

In our study, in contrast with premenopausal women, postmenopausal women had elevated rates of LDL and were statistically important (P < 0.001). Those results are consistent with other studies[12]. Circulating estrogen regulates lipoprotein lipase (LPL). LPL catalyzes VLDL's hydrolysis to form intermediate-density lipoprotein and subsequently, LDL.

Regulation of various LDL receptors in Liver, is carried out by effect of Estrogen on lipid metabolism. Estrogen works on the hepatocytes on these LDL receptors and contributes to greater clearing of LDL-C particles[25]. By this process the serum LDL-C levels are regulated. Lack of Estrogen following menopause increaseshepatic TG and plasma LPL activity causing plasma LDL to concentrate and also contributes to LDL receptor down-regulation[26,27]. In our study, the VLDL was elevated and statistically significant (P < 0.001) in post-menopausal females relative to pre-menopausal females, and these results are consistent with studies by Welty [5].

Lack of Estrogen in postmenopausal women induces relative accumulation of small VLDL particles with cholesterol esters (CE) either due to elevated VLDL catabolism resulting in higher number of VLDL residual particles or increased cholesterol ester transfer protein activity[28]. The VLDL remnants are highly capable of interacting with smooth arterial muscle cells[29]. It is well known that VLDL alone constitutes a risk factor for cardiovascular diseases.

Anticipating the factors that impact the post-menopausal female's lipid profile will improve their cardiovascular risk profile by implementing strategies to control these mechanisms through modifying the relative risk factors during menopause transition.

The HDL was increased in premenopausal women relative to postmenopausal women in our study, and was statistically relevant (P < 0.001). These results

correspond to studies performed by Shenoyand Vernekar (2015)[22], and Sapkota et al. in 2015[23].

Estrogen raises HDL-C which is considered good cholesterol for CVS by raised hepatic synthesis of Apolipoprotein -A and decreased hepatic removal of HDL2 cholestrol by decreasing hepatic lipase enzyme activity. Because estrogen is reduced during menopause and this contributes to both of these functions being hampered[30].

The protective mechanism involving HDL could be due to its role in the transport of reverse cholesterol, resulting in the redistribution of cholesterol away from the artery wall and suppression of monocyte adhesion and antioxidant activity, which may avoid LDL oxidation[31]. In our analysis, we excluded the factors that could alter the lipid profile. BMI tests in pre- and postmenopausal women (P>0.05) do not indicate any important difference. So we concluded that those changes observed in these postmenopausal women's lipid profile are due to hormone estrogen deficiency and not linked to BMI. Similar findings have also been found in numerous other studies[12].

Conclusion

In the study,adverse changes in the lipid profile of postmenopausal women suggests that this group of people is at augmented risk of cardiovascular problems in the near future. Menopause contributes to increased lipid profile thus increasing the risk of cardiovascular disease. Postmenopausal females are at elevated risk of developing cardiovascular disease due to changes in lipid pattern and the loss of oestrogen's cardioprotective impact.

The decreased cardiovascular protective HDL is an indicator that menopause is an independent risk factor for the development of cardiovascular disease. Thus, it is necessary to encourage each and every postmenopausal woman to undergo screening for an abnormal lipid profile. Specific health education approaches are needed to prevent postmenopausal women from developing cardiovascular diseases.

In this high-risk population early and timely identification and primary prevention will reduce morbidity and mortality.

Ethical Clearance: Taken from institutional ethics committee.

Source of Funding: Self.

Conflict of Interest: Nil.

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