International Journal of Current Research and Review
DOI: http://dx.doi.org/10.31782/IJCRR.2020.12179

Scopus

Research Article

IJCRR
Section: Healthcare
Sci. Journal Impact Factor: 6.1 (2018)
ICV: 90.90 (2018)

Study of Lipid Profile, 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 cardioprotective mechanisms that are reduced with the beginning of menopause.

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

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

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.

Key Words: 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. Numerous hormonal changes 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 for 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 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 the 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

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ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)

Received: 20.06.2020 **Revised:** 18.07.2020 **Accepted:** 10.08.2020 **Published:** 08.09.2020

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 to an oestrogen deficiency are of growing in significance for women's health.[11]

Inadequacy of estrogen is a crucial factor that contributes to 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 the menopause period. Coronary artery disease (CAD) is 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 regularly menstruating females and investigating the relationship between menopause status and associated hormonal variability with plasma lipid concentrations.

MATERIAL AND METHODS

This cross-sectional study was carried out at Datta Meghe Medical College, Nagpur in collaboration with Jawaharlal Nehru Medical College Sawangi (Meghe) Wardha and 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 sportspeople

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 TC, TG 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 the Chemiluminescence Immunoassay kit, which is a two-step competitive binding immunoassay for the quantitative determination of 17-beta–estradiol.

STATISTICAL ANALYSIS

For quantitative data, calculated values were processed by using: arithmetic means, 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

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).

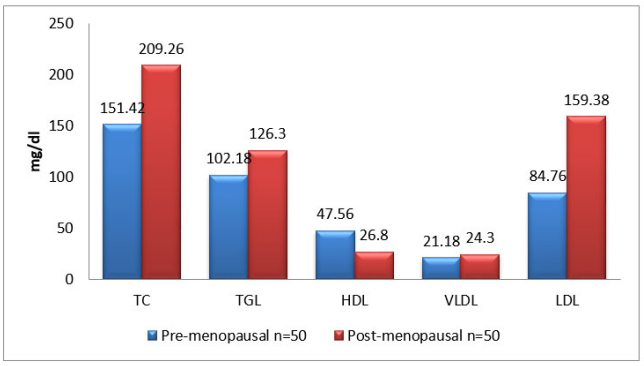

Figure 1: Comparison of lipid profile in pre and post-menopausal women

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/m²)	20.7 ± 4.3	23.9 ±4.12	>0.05

In our study, estradiol concentration in premenopausal women(168.48 ± 41.28) was observed to be significantly higher(p<0.001) than postmenopausal 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) (showed in table and graph no 1). 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) (showed in table no and graph no 2). [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 the increased fat accumulation and increased release of free fatty acids into circulation, and excessive free fatty acids provide a substrate for hepatic triglyceride 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 low-density lipoprotein (LDL) receptors in the Liver, is carried out by the effect of Estrogen on lipid metabolism. Estrogen works on the hepatocytes on these LDL receptors and contributes to the greater clearing of LDL-C particles.[25] By this process, the serum LDL-C levels are regulated. Lack of Estrogen following menopause increases hepatic 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 a 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 Very low-density lipoprotein (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 by modifying the relative risk factors during the menopause transition.

The High-density lipoprotein (HDL) was increased in pre-menopausal women relative to postmenopausal women in our study, and was statistically relevant ($P < 0.001$). These results correspond to studies performed by Shenoy and Vernekar (2015), [22] and Sapkota et al. in 2015.[23]

Estrogen raises HDL-C which is considered good cholesterol for CVS by the raised hepatic synthesis of Apolipoprotein -A and decreased hepatic removal of HDL2 cholesterol 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 post-menopausal women suggest that this group of people is at augmented risk of cardiovascular problems shortly. 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 cardio-protective impact.

The decreased cardiovascular protective HDL is an indicator that menopause is an independent risk factor for the development of the cardiovascular disease. Thus, it is necessary to encourage 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.

Acknowledgement: Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Conflict of interest: None

Source of funding: Nil

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