

A Comparative Study of Serum Estrogen and Lipid Profile between Premenopausal and Postmenopausal Women

Dr. Jaimin Mahendrakumar Patel,

*Assistant Professor, Department of General Medicine, Dr. N. D. Desai Faculty of Medical Science & Research,
Dharmsinh Desai University, Nadiad, Gujarat, India,
Email id : dr_jmp30@yahoo.in*

Source of support : Nil

Conflict of Interest : None declared

KEYWORDS

Estrogen, Lipid profile,
Pre-menopause, Post-
menopause,
Cardiovascular disease

ABSTRACT

Background

Menopause is permanent cessation of menstruation. The effect of the hormonal changes associated with menopause on the serum lipid levels play important role in most cardiac related disorders associated with menopause.

Objectives

The present study was done to evaluate the serum level of lipid parameters in post and pre-menopausal women and to investigate the relationship of altered lipid levels to estrogen level in both groups.

Material and Methods

50 pre-menopausal and 50 post-menopausal women were selected for the study. Data was collected through clinical evaluation from questionnaires and laboratory investigations. Plasma estrogen and lipid profile determinations were done by using competitive binding immunoassay methods and enzymatic methods respectively. Student's unpaired T test and Pearson's test of correlation were used for the statistical analysis using Microsoft Excel. P-values of < 0.05 were considered to be statistically significant.

Results

The study showed that there was a statistically significant increase in serum Total Cholesterol (TC), Triglycerides (TG), LDL cholesterol, VLDL cholesterol in post-menopausal women and statistically significant decrease in HDL cholesterol level and serum estrogen level in post-menopausal women compared to pre-menopausal women. However, this altered lipid parameters did not correlate significantly with declined estrogen level in post-menopausal women.

Conclusion

Our study showed significant dyslipidemia in post-menopausal women; hence they are at increased risk of atherosclerotic cardiovascular diseases. However, further studies needed to establish the relation of dyslipidemia to serum estrogen level in post-menopausal women.

MANUSCRIPT

INTRODUCTION

Menopause means permanent cessation of menstruation at the end of reproductive life due to loss of ovarian follicular activity¹. The effect of the hormonal changes associated with menopause on the serum lipid levels play important role in most cardiac related disorders associated with menopause². Up to the age of 50 years, the prevalence of coronary artery disease (CAD) among women is lower than among men, but the incidence rises significantly after the menopause. The incidences of coronary heart disease have been observed to be increased in post-menopausal women until they become similar to the corresponding rates in men of similar age³. Multiple risk factors have been identified as contributory to the development of CAD. Hypercholesterolemia is a key factor in the pathophysiology of

atherosclerosis⁴. After menopause, there is loss of ovarian function. This results in adverse changes in glucose and insulin metabolism, body fat distribution, coagulation, fibrinolysis, vascular endothelial dysfunction and also derangement of lipoprotein profile. Lack of estrogen is an essential factor in this mechanism^{5,6}. Atherogenic alterations in lipid and lipoprotein profiles have been found in studies of surgically induced menopause and epidemiological studies comparing pre-menopausal women with post-menopausal women⁷. Whether dyslipidemia leads to significant increase in the development of coronary artery disease (CAD) is still controversial. The behaviour of lipoproteins during the menopausal transition and their relationship with the sex hormones and body fat distribution is still unclear³.

The present study is aimed at comparing the serum level of total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) between pre-menopausal and post-menopausal women and to study the relationship between the menopausal status and related hormonal variation of plasma lipid profile by serum estrogen level in both groups.

OBJECTIVES OF THE STUDY

- To study the difference in serum lipid profile in pre-menopausal and post-menopausal women.
- To investigate the relationship between the menopausal status and related hormonal variation of plasma lipid profile by serum estrogen level in pre- and post-menopausal women

MATERIALS AND METHODOLOGY

Study Design : Cross-sectional study

Study Population & Site : Pre- and Post-menopausal women attending the outpatient department of medicine, Dr. N. D. Desai Faculty of Medical Science and Research, Nadiad, Gujarat.

Sample size : 100 (50 pre-menopausal women and 50 post-menopausal women)

Collaboration Department : Department of Biochemistry, Dr. N. D. Desai Faculty of Medical Science and Research, Nadiad, Gujarat.

Inclusion Criteria for Pre-menopausal Women :

- Age > 35 years until she attains menopause

Inclusion Criteria for Post-menopausal Women :

- Attained natural menopause
- Not on Hormone Replacement Therapy
- Age up to 65 years

Exclusion Criteria:

- Known congenital and acquired heart diseases
- Systemic diseases - Hypertension, Diabetes mellitus, Hepatic and Metabolic diseases
- Chronic drug intake like Rifampicin, Phenytoin, Anticoagulants, Statins etc
- Thyroid dysfunction
- Smoking

After getting institutional ethics committee approval study commenced. After obtaining their informed consents, venous blood samples collected from subjects after an overnight fasting of 10-12 hours. For pre-menopausal women samples collected on 10th day of menstrual cycle in morning. After centrifugation, plasma separated and used for analysis.

The total cholesterol was calculated by enzymatic cholesterol oxidase and peroxidase method. Triglycerides was calculated by enzymatic GOD-POD (Glycerol Phosphate Oxidase and Peroxidase) method.

High Density Lipoprotein-HDL was calculated by Precipitation method.

Low Density Lipoprotein-LDL was calculated by Friedewald formula.

$$LDL = \text{total cholesterol} - (\text{high density lipoprotein} + \text{triglycerides}/5)$$

Very Low Density Lipoprotein-VLDL was calculated from level of triglycerides.

Very low density lipoprotein = triglycerides/5.

Quantitative determination of serum oestradiol is done by Chemiluminescence immunoassay method (CLIA).

BMI is calculated as follows: BMI = (weight in kg)/

(height in meters)² WHO Classification of Adult

Categories of BMI.^{8,9}

Data Analysis : All data obtained from the estimation was reported as the mean± standard deviation (SD) and student unpaired t-test was used for comparing mean± SD between the groups. Pearson’s correlation was applied to correlate between the parameters. The p value < 0.05 was considered as significant. All data was analysed using Microsoft Excel.

RESULTS

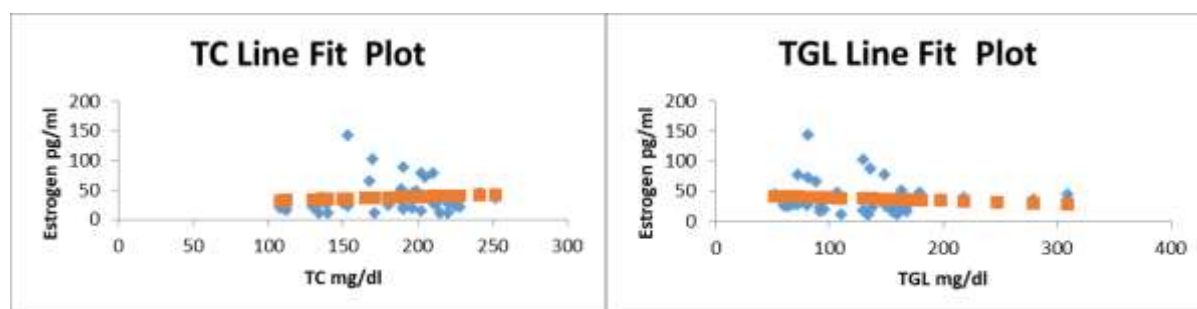
Table 1 : Comparison of parameters between pre and post – menopausal women

Serum biochemical parameters	Pre-menopausal Women n=50 (mean±SD)	Post-menopausal women n=50 (mean±SD)	P - Value
ESTROGEN (pg/ml)	156.59±62.91	37.35±25.41	<0.001
TC (mg/dl)	165.42±35.11	183.48±36.26	<0.05
TG (mg/dl)	101.56±47.50	134.82±54.30	<0.05
HDL (mg/dl)	49.30±10.46	39.28±11.38	<0.001
LDL (mg/dl)	99.08±26.80	120.70±28.76	<0.001
VLDL (mg/dl)	20.08±9.62	28.07±11.61	<0.001
BMI (kg/m ²)	25.24±4.41	26.29±5.17	>0.05

Table 1 shows a significant increase in serum Total Cholesterol (TC), Triglycerides (TG), LDL-cholesterol and VLDL cholesterol level in post-menopausal women as compared to those in pre-menopausal women (p<0.05 - significant or p<0.001 – highly significant). HDL cholesterol level and serum estrogen is significantly decreased in post-menopausal women compared to pre-menopausal women (p<0.001). According to above table there is no significant difference in BMI between pre and post-menopausal women (p>0.05).

Table 2 : Correlation between Serum estrogen and plasma lipid level of post-menopausal women

Estrogen	TC	TG	HDL	LDL	VLDL
Pearson’s correlation	0.10	-0.11	0.04	0.08	-0.22
P- value	0.48	0.45	0.80	0.55	0.12
Significance	NS	NS	NS	NS	NS



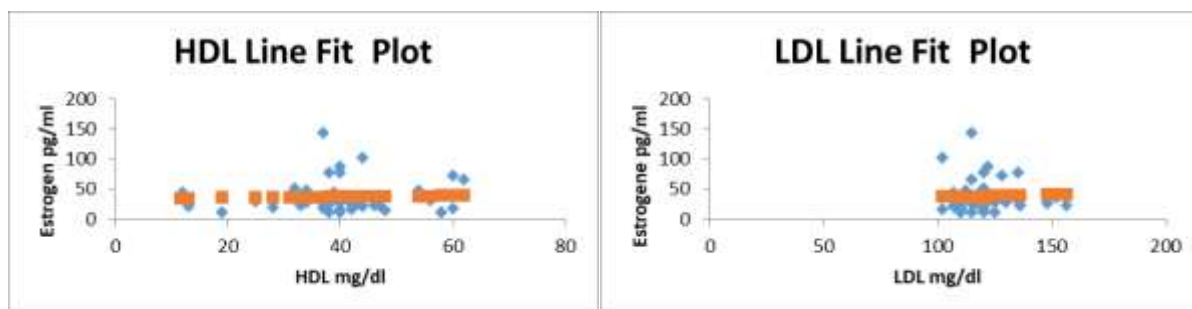


FIGURE 1 : Correlation between estrogen and total cholesterol (TC), triglycerides (TGL), LDL and HDL in post-menopausal women

Table 2 shows there is negative correlation between serum estrogen and triglycerides ($r = -0.11$), VLDL ($r = -0.22$) and positive correlation between estrogen and total cholesterol, LDL and HDL. However, there is no significance correlation between serum estrogen and all lipid parameters in post-menopausal women as suggested by p value > 0.05 in all parameters seen in table 2 and figure 1.

DISCUSSION

Cardiovascular diseases are multifactorial; dyslipidaemia is a major risk factor for atherosclerosis. Our study aimed to study the differences in lipid and hormonal status in post and pre-menopausal women and to investigate the relationship between the menopausal status and related hormonal variation with plasma lipid profile.

In Framingham cohort study, 2873 women were followed up for 24 years. Gordon T et al showed an increase in CVD incidence in postmenopausal women more than double compared to pre-menopausal women.⁹

Table 1 shows that postmenopausal women are having slightly higher BMI compared to premenopausal women, but p value is >0.05 and that is not significant. Study done by Srinivas Reddy Kilim et al¹⁰ also found increased BMI in post-menopausal women but not significantly ($p > 0.05$). However, Yasmeen Fatima et al¹¹ found significantly increased BMI in post-menopausal women in their study. Although women have 3 times higher risk of CVD if BMI is 29 or higher¹², our study did not show significantly higher BMI in post-menopausal women. Table 1 also shows Total Cholesterol, TG, LDL, VLDL values are increased among post-menopausal women compared to pre-menopausal women and difference is statistically significant ($p < 0.05$). And pre-menopausal women are having high HDL level than post-menopausal women and difference is statistically significant ($p < 0.05$). Our study showed significantly high level of serum estrogen in pre-menopausal women than post-menopausal women with p -value < 0.001 . This finding is in accordance with study done by Srinivas Reddy Kilim et al¹⁰ and Swarnalatha et al.¹³

The changes in the hormonal status after menopause such as low estrogen, increased luteinizing hormone and follicular stimulating hormone exert significant effect on plasma lipids and lipoproteins metabolism in post- menopausal women. Endogenous estrogen having a suppressive effect in lipase activity in the liver; low estrogen level before and after attaining menopause was correlated with high lipase activity in the liver^{14,15}. Subsequently, high lipase activity in the liver leads to a decrease in HDL2 cholesterol level and a small increase in solid LDL particle, which was correlated with increased atherosclerosis and CVD risk¹⁴. Moreover, estrogen also had an effect on regulation of lipoprotein lipase, and lipoprotein lipase is responsible for hydrolysing TG to chylomicrons and VLDL¹⁶; Therefore, decreased estrogen in menopause period could cause dysregulation of lipoprotein lipase and altered lipid parameters.

Study done by Yasmeen Fatima et al¹¹ showed positive significant ($p < 0.05$) correlation of estrogen with HDL and negative correlation with LDL, VLDL, TC, TG in post-menopausal women. Study done by Srinivas Reddy Kilim et al¹⁰ showed positive significant correlation between estrogen with HDL and negative correlation between estrogen with LDL in post-

menopausal women. Correlation of estrogen with lipid profile in study done by Swarnalatha et al¹³ showed significant positive correlation with HDL and negative correlation with LDL, VLDL, TC, TG after menopause. However, as shown in table 2 and figure 1, our study did not show significant correlation ($p>0.05$) between estrogen and altered lipid parameters in postmenopausal women. Similarly, study done by Ariadi et al¹⁷ did not show significant correlation between estrogen and total cholesterol, TG, LDL, and HDL. Since this study had a different result with several studies, therefore, the future study is needed about lipid profile in postmenopause and their correlation with estrogen level and another associated hormone such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

CONCLUSION

Menopause leads to altered lipid parameters by decreasing HDL level and increasing Total cholesterol (TC), Triglycerides (TG), LDL and VLDL cholesterol, which in turn increases the risk of cardiovascular diseases. As with other studies, our study also showed significantly altered lipid parameters in menopausal women. Therefore, regular screening of menopausal women for altered lipid profile is advisable to reduce the risk of cardiovascular diseases in older women and healthy lifestyle should be adopted to prevent future risk. However, in contrast to most studies, our study did not show significant correlation of decreased estrogen with altered lipid levels in menopausal women. Hence, further studies needed to establish the relation of estrogen along with other hormonal changes with dyslipidemia in menopausal women.

REFERENCES

1. D C Dutta: Textbook of gynaecology; 5th edition. 2008 : 55-61.
2. Do K A, A Green, J R Guthrie, E C Dudley, H G Burger, and L Dennerstein : Longitudinal study of risk factors for coronary heart disease across the menopausal Transition, American Journal of Epidemiology. 2000 ; 151 : 584-593.
3. Berg G, Mesch V, Boero L et al: Lipid and lipoprotein profile in menopausal transition. Effects of hormones, age, and fat distribution. Horm Metab Res. Apr. 2004 ; 36(4) : 215-220.
4. J C Igweh, I U Nwagha and J M Okaro: The effects of menopause on the serum lipid profile of normal females of south east Nigeria; Nigerian journal of physiological sciences. 2005; 520(1-2) : 48-53.
5. Bales A C: In search of lipid balance in older women; new studies raise questions about what works best. Postgrad. Med. 2000 ; 108 (7): 57-72.
6. S A Samaan and M H Crawford: Estrogen and cardiovascular function after menopause, Journal of the American College of Cardiology. 1995 ; 26 : 1403-1416.
7. Stampfer M J and W C Williet: A prospective study of postmenopausal estrogen and coronary heart disease, N.Engl.J.Med. 1999 ; 313 : 1044-1049.
8. K Park. Non Communicable Diseases and Conditions, Obesity. In: Park's Textbook of Preventive and Social Medicine. 21th ed. M/S Banarsidas Bhanot, 2011:369370.
9. Gordon T, Kannel WB, Huortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham study. Ann Intern Med 1978 Aug;89(2):157-61.
10. Srinivas reddy Kilim, Srinivasa rao Chandala : A comparative study of lipid profile and oestradiol in pre- and post-menopausal women. Journal of Clinical and Diagnostic Research. 2013 Aug, Vol-7(8): 1596-1598.
11. Yasmeen Fatima, Sreekantha, Ramesh : A comparative study of serum estrogen and lipid profile in pre-menopausal and post-menopausal women as atherosclerotic risk factors. International Journal of Clinical Biochemistry and Research, July-September 2017;4(3):237-241.
12. Shilpa S. Shende, M.V. Bimanpalli, I.C. Apte, Vishakha Vet al. Study of Lipid Profile and C Reactive Protein in Pre- and Post-menopausal Women. Journal of Clinical and Diagnostic Research. 2011 Dec;5(8):1544-1547.

13. Swarnalatha PK, Ebrahim NKC. A Correlative Study of Estrogen and Lipid Profile in Premenopausal and Postmenopausal Women. *International Journal of Biomedical and Advance Research (IJBAR)* 2012;03(11):818-821.
14. Randolph JF Jr, Zheng H, Sowers MR, et al. Change in follicle stimulating hormone and estradiol across the menopausal transition: effect of age at the final menstrual period. *J Clin Endocrinol Metab.* 2011; 96(3):746-754. <https://doi.org/10.1210/jc.2010-1746> PMID:21159842 PMCID:PMC3047231
15. Berg GA, Siseles N, Gonzalez AI, Ortiz OC, Tempone A, Wikinski RW. Higher values of hepatic lipase activity in postmenopause: relationship with atherogenic intermediate density and low density lipoproteins. *Menopause.* 2001; 8(1):51-7. <https://doi.org/10.1097/00042192-200101000-00009> PMID:11201516
16. Chatterjee C, Sparks DL. Hepatic lipase, high density lipoproteins, and hypertriglyceridemia. *Am J Pathol.* 2011; 178(4):1429-1433. <https://doi.org/10.1016/j.ajpath.2010.12.050> PMID:21406176 PMCID:PMC3078429
17. Ariadi A, Jamsari J, Yanwirasti Y, Siregar MFG, Yusrawati Y. Correlation between Estrogen Levels with Lipid Profile in Menopause Women in West Sumatera. *Open Access Maced J Med Sci.* 2019 Jul 15; 7(13):20842087. <https://doi.org/10.3889/oamjms.2019.627>