Original Article

# Effect of menopause on lipid profile in relation to body mass index


## Abstract

**Background:** Menopause is a natural event in the ageing process and signifies the end of reproductive years with cessation of cyclic ovarian function as manifested by cyclic menstruation. Lipid profile is altered in menopause because of various reasons. **Objectives:** The study was aimed to compare the lipid profile in women with normal body mass index (BMI) = 18.9-24.9 and women with BMI = 25-29.9 in both pre- and post-menopausal group. **Materials and Methods:** Estimation of total cholesterol (TC) by CHOD-PAP Cholesterol Oxidase - Peroxidase + Aminophenazone + Phenol method, triglyceride (TG) by enzymatic calorimetric method, high density lipoprotein-cholesterol (HDL-C) phosphotungstic acid method, low density lipoprotein-cholesterol (LDL-C) by using Friedewald formula and very low density lipoprotein (VLDL) was done by using the formula -VLDL = TG/5 in 30 women selected in each group. **Results:** Our study revealed that serum levels of TC, TG and LDL-C were significantly higher in post-menopausal women in comparison to their pre-menopausal counterparts, irrespective of BMI ($P < 0.05$). Similarly, HDL-C levels were significantly lower in post-menopausal women as compared with pre-menopausal women of similar BMI ($P < 0.05$). **Conclusions:** We found that serum levels of TC, TG and LDL-C were significantly higher in post-menopausal women in comparison to their pre-menopausal counterparts, irrespective of BMI. Similarly, HDL-C levels were significantly lower in post-menopausal women as compared to pre-menopausal women of similar BMI. Since we found similar changes in women of different BMIs, the difference in hormonal status is the probable cause of altered lipid profile. Hence, all post-menopausal women irrespective of body weight and BMI should be strongly counseled to have proper physical exercise and dietary habits to avoid the possible cardiovascular complications.



**Key words:**
*Body mass index, lipid profile, menopause*


## Introduction

Sixty million women in India are above the age of 55 years. With women living longer than before, a majority would spend one third of their lives in post-menopausal stage. The health problems cropping up during this period are now obvious and better understood. It is therefore important to address all these menopause related diseases and apply prophylactic measures so that these women can lead an enjoyable and healthy life.

Menopause is a natural event in the ageing process and signifies the end of reproductive years with cessation of cyclic ovarian function as manifested by cyclic menstruation.[1] Menopause is an estrogen deficient state, but unlike other hormone deficient states, it is not a disease.[2]

The hormonal changes associated with menopause, e.g., low plasma levels of estrogen and marked increase in follicle stimulating hormone levels exert a significant effect on metabolism of plasma lipids and lipoproteins. Studies by Swapnali *et al*. and Kalavathi *et al*. have shown altered lipid profile in post-menopausal women.[3,4]

The risk of coronary artery disease (CAD) increases in women after menopause.[1,5] In addition, recent evidence


| Access this article online | |
|---|---|
| **Website:** www.cysonline.org | Quick Response Code |
| **DOI:** 10.4103/2229-5186.129331 | |



**Geetanjali Bade, Swati Shah[1], Pradeep Nahar[1], Savita Vaidya[1]**

*Departments of Physiology, All India Institute of Medical Sciences, New Delhi, [1]B.J. Medical College and Sassoon General Hospitals, Pune, Maharashtra, India*

**Address for correspondence:**
Dr. Swati Shah,
Department of Physiology, B.J. Medical College and Sassoon General Hospitals, Pune - 411 001, Maharashtra, India.
E-mail: sshah282@gmail.com

suggests that post-menopausal estrogen replacement therapy, which is commonly administered after bilateral oophorectomy is associated with a decreased risk of CAD.[6]

Increase in the incidence of cardiovascular disease is related to many risk factors such as increase in body weight, ageing process, dyslipidemia, physical inactivity, mental stress, smoking and alcohol intake.[5] As the incidence of CAD increases in women after menopause,[1] in the present study, we tried to correlate some of the risk factors associated with CAD to the hormonal changes taking place during menopause.

The objective of the present study was to compare lipid profile (a risk factor for CAD) between reproductive age group and post-menopausal group in women with normal weight and overweight women. Obesity, which can be measured commonly as body mass index (BMI) is a major factor affecting lipid profile. Hence, we hypothesized that the lipid profile will be altered in post-menopausal women irrespective of their BMI, compared with pre-menopausal women.

## Materials and Methods

The present study is of cross-sectional type. It was conducted from March 2008 to March 2009. The study protocol was approved by the ethical committee of the institute. All the subjects who participated in this study were interviewed in the ward. They were selected randomly by certain inclusion and exclusion criteria.

### Inclusion criteria

***Age groups***

1. About 60 women between 25 years and 35 years of age in reproductive age group, out of this 30 were of the normal weight (BMI: 18.9-24.9) and 30 were overweight (BMI: 25-29.9).
2. About 60 women between 45 years and 55 years of age in post-menopausal age group (whose menstruation had ceased 2 years back), out of this 30 were of the normal weight (BMI: 18.9-24.9) and 30 were overweight (BMI: 25,-29.9).[7]

All our subjects were having standard Indian diet and similar caloric intake. All the subjects were from similar socio-economic group.

### Exclusion criteria

The subjects with history of

1. Smoking, drinking alcohol, tobacco chewing.
2. Diabetes mellitus, hypertension (blood pressure >140/90 mm Hg) or family history suggestive of coronary heart disease (CHD).
3. Any major illness.
4. Taking drugs which are known to affect lipid metabolism, like statins were excluded from the study.

Before the actual study, written consent was taken from the selected subjects. Proper history of each subject was recorded. It included name, age, address, present medical illness, past history, family history, type of diet and menstrual history. Systemic examination of each subject was carried out.

***Estimation of serum levels of lipids***

Estimation of following parameters was done: Total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), very low density lipoprotein (VLDL).

***Collection of a blood sample***

From the women of reproductive age group, blood samples were collected during $6^{th}$-$10^{th}$ day of the menstrual cycle, as hormonal level varies with phases of the menstrual cycle. Serum lipid profile levels are more accurate when blood samples are collected 8-10 h after the last meal. Hence instructions were given to the subjects to take dinner at 9-10 p.m. and remain fasting overnight until blood samples were collected in the next day morning. Fasting blood samples were collected in the morning between 7 a.m. and 8 a.m. by venepuncture of antecubital vein, with all aseptic precautions. A test dose of 5 ml of blood was collected with disposable syringe in plain bulb. Clear, unhemolyzed serum was obtained by centrifuging blood at 3000 rpm for 15 min.

***Methods of estimation***

Estimation of TC was done by CHOD-PAP method. [Cholesterol + oxygen --(enzyme cholesterol oxidase)--> cholestenone + hydrogen peroxide. Hydrogen peroxide + 4-aminophenazone + phenol --(enzyme peroxidase)--> colored complex]

Estimation of HDL cholesterol was done by phosphotungstic acid method, of TGs by enzymatic calorimetric method, of LDL-cholesterol by using Friedewald formula[1,8] and of VLDL-cholesterol by using the formula:[7] VLDL = TG/5.

All the above mentioned investigations were done by a qualified biochemist who was blinded about the background and BMI of the patient, using the same kit. The assays were done on the day of collection of a blood sample.

BMI is also known as Quetelet's index.[9,10] It was calculated by following formula:

$$\text{BMI} = \frac{\text{Weight(kg)}}{[\text{Height(m)}]^2}$$

### Statistical analysis

All the values of the above parameters were arranged in a tabular form and analysis was done by SPSS software version 11( Chicago, USA ), by using Student's *t*-test and correlation. $P < 0.05$ was considered as statistically significant.

## Results

Table 1 describes the physical characteristics of premenopausal and postmenopausal group. There is statistically significant difference in weight and BMI of normal weight and overweight group (p<0.05). On comparison between women of reproductive age group and post-menopausal women with normal BMI, we found that, the levels of TC and TG were significantly higher in post-menopausal women than those of pre-menopausal women ($P < 0.05$). Although, HDL-C levels were significantly lower in post-menopausal women compared with pre-menopausal women ($P < 0.001$). LDL-C levels were also significantly higher in post-menopausal women compared to pre-menopausal women ($P < 0.001$). VLDL levels were slightly higher in post-menopausal compared to pre-menopausal women, but the difference between two mean values was not significant ($P > 0.05$) [Table 2 and Figure 1].

The comparison between overweight women from reproductive and post-menopausal age group revealed that TC, TG and LDL-C were significantly higher in post-menopausal women as compared to pre-menopausal women ($P < 0.001$). HDL-C levels were significantly lower in post-menopausal women than pre-menopausal women ($P < 0.05$) [Table 3 and Figure 2].

## Discussion

When compared to reproductive age group, in post-menopausal women there was an increase in TC, TGs, LDL-C and decrease in HDL-C level. These changes are independent of BMI [Table 2, 3 and Figures 1, 2]. Hence the changes in the lipid profile are most probably due to the difference in hormonal status of women. Several studies have shown similar results.[3,4]

A major effect of estrogen on lipid metabolism is up to the regulation of LDL receptors, resulting in increased clearance of LDL particles by hepatocytes and reduction in plasma LDL-C. The elimination of normal LDL-C is accelerated more than the clearance of small dense LDL particles. This results in the relative increase in small dense LDL particles. Subjects having a large amount of small dense LDL particles are characterized by increased plasma TG, reduced HDL cholesterol, higher fasting insulin levels and elevated visceral adipose tissue accumulation.[10] Thus estrogen improves the turnover of both normal and small dense LDL-C.

Remnants of TG-rich lipoproteins i.e., VLDL remnants and chylomicron remnants, are atherogenic particles that are being increasingly considered to be cardiovascular risk factors. Estrogen can reduce remnant concentrations by increased elimination through hepatic LDL receptors.

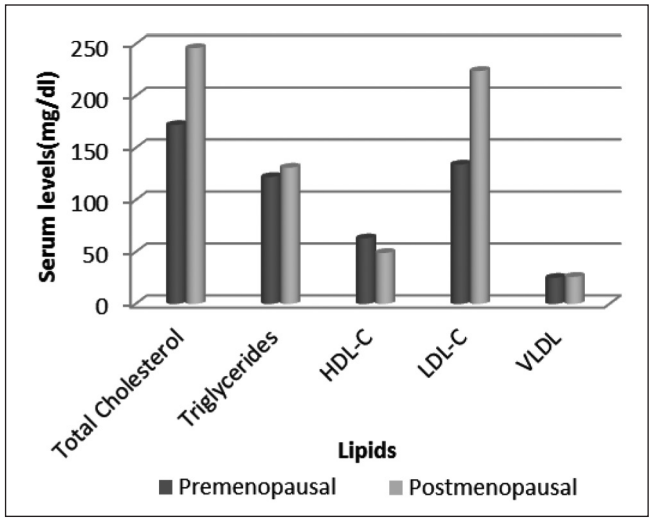


**Figure 1:** Comparison of lipid profile in pre- and post-menopausal women of normal weight

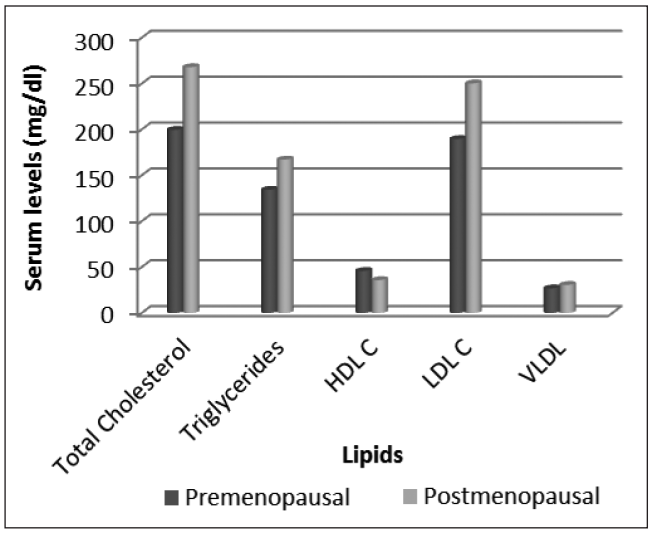


**Figure 2:** Comparison of lipid profile in pre- and post-menopausal overweight women

**Table 1: Physical characteristics of subjects**

| Parameters | Pre-menopausal women (mean ± SD) | | | Post-menopausal women (mean ± SD) | | |
|---|---|---|---|---|---|---|
| | Normal weight *n* = 30 (BMI 18.9-24.9) | Overweight *n* = 30 (BMI 25-29.9) | *P* value | Normal weight *n* = 30 (BMI 18.9-24.9) | Overweight *n* = 30 (BMI 25-29.9) | *P* value |
| Height (cm) | 152.76±8.08 | 155.43±7.09 | $P>0.05$ | 151.18±6.56 | 152.32±6.09 | $P>0.05$ |
| Weight (kg) | 52.49±8.31 | 65.15±5.32 | $P<0.05$* | 52.15±6.32 | 65.68±7.09 | $P<0.05$* |
| BMI (kg/m$^2$) | 22.40±2.36 | 27.12±7.67 | $P<0.05$* | 22.87±3.98 | 28.43±4.76 | $P<0.05$* |

*$P<0.05$ – Statistically significant; SD – Standard deviation

**Table 2: Comparison of lipid profile in pre-and post-menopausal women (BMI = normal)**

| Parameters | Pre-menopausal normal weight (BMI 18.9-24.9) | Post-menopausal normal weight (BMI 18.9-24.9) | *P* value |
|---|---|---|---|
| Total cholesterol | 172.06±27.41 | 246.62±29.19 | $P<0.05$* |
| Triglycerides | 122.76±21.73 | 131.22±18.99 | $P<0.05$* |
| HDL-C | 63±7.83 | 48.65±4.71 | $P<0.001$** |
| LDL-C | 133.62±28.9 | 224.21±30.98 | $P<0.001$** |
| VLDL | 24.55±4.34 | 26.24±3.80 | $P>0.05$ |

*$P<0.05$ – Statistically significant; **$P<0.001$ – Statistically highly significant; BMI – Body mass index; HDL-C – High density lipoprotein-cholesterol; LDL-C –Low density lipoprotein-cholesterol; VLDL – Very low density lipoprotein

**Table 3: Comparison of lipid profile in pre- and post-menopausal women (overweight)**

| Parameters | Pre-menopausal overweight (BMI 25-29.9) | Post-menopausal overweight (BMI 25-29.99) | *P* value |
|---|---|---|---|
| Total cholesterol | 199.67 25.78 | 268±23.19 | $P<0.001$** |
| Triglycerides | 134.32±21.89 | 167.23±19.90 | $P<0.001$** |
| HDL-C | 45.87±6.89 | 35.89±21.87 | $P<0.05$* |
| LDL-C | 189.67±23.45 | 250.32±28.67 | $P<0.001$** |
| VLDL | 26.89±2.76 | 30.67±4.56 | $P>0.05$* |

*$P<0.05$ – Statistically significant; **$P<0.001$ – Statistically highly significant; BMI – Body mass index; HDL-C – High density lipoprotein-cholesterol; LDL-C –Low density lipoprotein-cholesterol; VLDL – Very low density lipoprotein

Estrogen increases HDL cholesterol by several mechanisms, which mainly includes increased hepatic production of apolipoprotein A and decreased hepatic elimination of HDL2 cholesterol by reducing activity of hepatic lipase.[11,12]

Since during menopausal period estrogen level is low, all these actions are hampered resulting in increased TC and LDL-C level and decreased HDL-C level.

Decrease in the level of physical activity also plays a very important role in alteration of lipid profile during the post-menopausal period. Free fatty acids are the main source of energy during exercise. To mobilize the energy stored in adipose tissue for use during physical activity, stored TGs are hydrolyzed to form free fatty acids and glycerol. This conversion is catalyzed by an enzyme namely hormone sensitive TG lipase.[13] Exercise also increases activity of the enzyme lipoprotein lipase lining the capillary endothelium. Thus, exercise decreases serum levels of TC, TG and VLDL while reduced physical activity during the post-menopausal period elevates all these levels.[12] Moreover, Adrenal cortex and gonads are extremely active in LDL degradation.[13] As gonadal activity decreases during menopause, LDL level increases.

Thus depletion of estrogen, decreased physical activity and gonadal inactivity collectively alter lipid profile during the post-menopausal period resulting into increased incidence of CAD in post-menopausal women. BMI is an indicator of obesity which is an independent risk factor for CHD. Serum cholesterol level is also positively correlated with BMI. Starting at a BMI of ≈22 kg/m$^2$ an increase in weight equivalent to 1 BMI unit leads to a 4-5% increase in CAD mortality.[14,15] In our study,the comparison was done between pre-menopausal women with normal weight and post-menopausal women with normal weight. Similarly, we compared the same in overweight pre- and post-menopausal women. Hence the changes in lipid levels were not because of difference in BMI, but because of difference in hormonal status of women.

The biologic effects of estrogen replacement therapy are numerous, but the most likely mechanism to explain it's protective effect on cardiovascular disease is it's ability to alter lipid and lipoprotein levels. But along with these benefits there are certain risk factors of estogen replacement therapy. High doses of estrogen for moderately long periods increase the risk of endometrial carcinoma. However, addition of progesterone reduces this risk.[16-19]

Thus, the beneficial effects of hormone replacement therapy (HRT) are probably affected by various factors, including the age of onset of therapy, the presence of CAD, the type of estrogen and whether it is used in combination with progesterone, concurrent modification of other cardiac risk factors and duration of therapy. Until further prospective clinical trials are done, HRT should be considered in those women for whom the potential benefits exceed the potential risks, on the basis of an individualized patient evaluation.

Since the use of HRT and lipid lowering drugs is still controversial, it is important to counsel for proper diet and physical exercise. Exercise can help the post-menopausal women to increase HDL-C levels and reduce other lipid levels.[20] Low fat diet can help them to reduce their lipid levels. Some clinical trials have demonstrated a beneficial effect of dietary soy proteins on improving lipoprotein levels.[21]

### Limitation and scope

Smaller sample size is the limitation of our study. Along with standard lipid profile, estimation of Apolipoproteins could have given better idea about the effect of menopause. We have conducted the study in normal and overweight women. The study could have been extended in underweight women. This requires further research.

## Conclusion

As compared to reproductive age group, in post-menopausal women there is an increase in TC level, increase in TGs level, increase in LDL-C level and decrease in HDL-C level.

These changes are independent of BMI as the similar changes were found in women having normal weight as

well as overwight women in both pre- and post-menopausal women. These changes are favorable for development of atherosclerosis which is one of the important cause for CAD.

These changes are mainly due to the decreased level of estrogen in post-menopausal age which has got various effects on lipid metabolism. Since, HRT has its own limitations it can't be used as a routine treatment. It should be restricted to the particular group of patients. Majority of post-menopausal women should be guided to have proper physical exercise, dietary habits and if needed HRT and psychiatric help in order to have happy, healthy and enjoyable life after menopause.

## References


1. Usoro CA, Adikwuru CC, Usoro IN, Nsonwu AC. Lipid profile of postmenopausal women in Calabar, Nigeria. Pak J Nutr 2006;5:79-82.
2. Sultan N, Nawaz M, Sultan A, Fayaz M, Baseer A. Effect of menopause on serum HDL-cholesterol level. J Ayub Med Coll Abbottabad 2003;15:24-6.
3. Swapnali RK, Kisan R, Murthy DS. Effect of menopause on lipid profile and apolipoproteins. Al Ameen J Med Sci 2011;4:221-8.
4. Kalavathi L, Dhruvanarayan HR, Zachariah E. Plasma estradiol and lipid profile in perimenopausal women. Indian J Physiol Pharmacol 1991;35:260-2.
5. Gupta R, Rastogi P, Sarna M, Gupta VP, Sharma SK, Kothari K. Body-mass index, waist-size, waist-hip ratio and cardiovascular risk factors in Urban subejcts. J Assoc Physicians India 2007;55:621-7.
6. Crawford SL, Johannes CB. The epidemiology of cardiovascular disease in postmenopausal women. J Clin Endocrinol Metab 1999;84:1803-6.
7. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
8. Oliveira Ad, Mancini Filho J. Nutritional status and lipid profile of postmenopausal women with coronary heart disease. Arq Bras Cardiol 2005;84:325-9.
9. Park K. Park's Textbook of Preventive and Social Medicine. 20th ed. Jabalpur: M/S Banarsidas Bhanot; 2009. p. 345-9.
10. Tchernof A, Lamarche B, Prud'Homme D, Nadeau A, Moorjani S, Labrie F, *et al*. The dense LDL phenotype. Association with plasma lipoprotein levels, visceral obesity, and hyperinsulinemia in men. Diabetes Care 1996;19:629-37.
11. Medina RA, Aranda E, Verdugo C, Kato S, Owen GI. The action of ovarian hormones in cardiovascular disease. Biol Res 2003;36:325-41.
12. Satyanarayan U. Textbook of Biochemistry. 1st ed. Kolkata, India: Books and Allied Pvt. Ltd.; 1999. p. 293-339.
13. McArdle WD. Exercise Physiology, Energy, Nutrition and Human Performance. 3rd ed. Philadelphia, USA: Lea and Febiger; 1991. p. 398-623.
14. West JB. Best and Taylor's Physiological Basis of Medical Practice. 12th ed. Baltimore, USA: Williams & Wilkins; 1990. p. 741-53.
15. Walsh BA, Mullick AE, Banka CE, Rutledge JC. 17beta-estradiol acts separately on the LDL particle and artery wall to reduce LDL accumulation. J Lipid Res 2000;41:134-41.
16. Jousilahti P, Tuomilehto J, Vartiainen E, Pekkanen J, Puska P. Body weight, cardiovascular risk factors, and coronary mortality. 15-year follow-up of middle-aged men and women in Eastern Finland. Circulation 1996;93:1372-9.
17. Smith DC, Prentice R, Thompson DJ, Herrmann WL. Association of exogenous estrogen and endometrial carcinoma. N Engl J Med 1975;293:1164-7.
18. Antunes CM, Strolley PD, Rosenshein NB, Davies JL, Tonascia JA, Brown C, *et al*. Endometrial cancer and estrogen use. Report of a large case-control study. N Engl J Med 1979;300:9-13.
19. Gambrell RD Jr, Castaneda TA, Ricci CA. Management of postmenopausal bleeding to prevent endometrial cancer. Maturitas 1978;1:99-106.
20. Barclay L, Vega C. Physical activity improves lipid profile in postmenopausal women. Menopause 2007;14:115-22.
21. Barclay L, Lie D. Soy protein improves lipid profile in postmenopausal women. Menopause 2007;14:106-14.


**How to cite this article:** Bade G, Shah S, Nahar P, Vaidya S. Effect of menopause on lipid profile in relation to body mass index. Chron Young Sci 2014;5:20-4.

**Source of Support:** Nil. **Conflict of Interest:** None declared