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**Research Article**

# A comparative study of circulating plasma lipid components and superoxide dismutase activity in pre and postmenopausal women

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## ABSTRACT

**Background:** Menopause is associated with increased oxidative stress and decreased antioxidative activity in females which leads to increased risk of cardiovascular and many other diseases. The objective was to compare the lipid profiles and superoxide dismutase (SOD) activity of pre and postmenopausal women in an attempt to establish the fact that menopause is associated with increased oxidative stress.
**Methods:** A hospital based cross-sectional study was done at the department of obstetrics and gynaecology and biochemistry, Shri Mahant Indiresh Hospital, Dehradun, India. Out of total of 120 women, 60 women were in premenopausal group aged between 30-45 years and 60 women of 55-70 years of age group in post menopause status. Assessment of lipid profile was done by an automated chemistry analyzer (Vitors 5, I FS) and SOD activity was measured by colorimetric activity kit. Statistical analysis was done by Standard Microsoft Excel software.
**Results:** Mean serum SOD level in premenopausal women was 4.80±1.73 U/ml and in postmenopausal was 1.35±0.58 U/ml. This variation was found to be extremely significant ($p < 0.0001$). Changes in lipid components in pre and postmenopausal women showed that total cholesterol and triglycerides levels were higher in postmenopausal than premenopausal participants. These variations were also significant ($p = 0.0003$). Levels of HDL-C were lower in postmenopausal women than pre-menopausal group with a mean±SD of 51.5±12.20 mg/dl and 54.05±14.03mg/dl respectively.
**Conclusions:** Findings of this study corroborate the hypothesis that gradual loss of ovarian function is associated with a decrease in antioxidant status. Menopause also leads to changes in lipid components, which can predispose women to cardiovascular diseases.

**Keywords:** Antioxidants, Estrogen, Menopause, Oxidative stress, Superoxide dismutase, Total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, Triglycerides

## INTRODUCTION

Menopause a form of reproductive aging is defined as the permanent cessation of ovarian follicular activity and eventually, the menstrual cycle.[1,2] Menopause is associated with increase oxidative stress and decreased antioxidative activity in females, which leads to increased risk of cardiovascular disease and other major diseases. Accumulation of oxygen-derived free radicals (oxidative stress) is one of the established and thoroughly studied mechanisms of cell injury.

Free radicals are responsible for widespread and indiscriminate oxidation and peroxidation of lipids, denaturation of proteins, depolymerization of polysaccharides, breakage and modification of DNA or

any other cell structure, causing cell death or organ damage.[3] Antioxidants help to defend the body against free radical attack and human body has got well-developed endogenous antioxidant defence system like cellular enzymes and vitamins. Vitamin C forms the first line of antioxidant defence in human plasma exposed to a variety of oxidant insults.[4]

A group of antioxidants present in red blood cells (RBCs) that prevent lipid peroxidation consists superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase and reduced glutathione.[5]

Menopause is associated with decreased estrogen level in the body. Estrogens have free radical scavenging structures.[6] Estrogen exerts cardio protection action by maintaining high level of high density lipoprotein cholesterol (HDL-C) and lowering the low density lipoprotein cholesterol (LDL-C) and triglycerides (TG).

Loss of this protection after the menopause may therefore be responsible for increased risk of developing cardiovascular disease in postmenopausal women. Estrogen also plays a role in the increased production of neutrophil growth factors, which modulate neuronal growth survival and aging. In recent years, several studies have highlighted the alterations in antioxidant status in postmenopausal women.

Dyslipidemia is a major cause of cardiovascular diseases (CVD), which is the most common cause of male and female morbidity and mortality.[7] The incidence of CVD increases after menopause. This may be due to changes in the plasma lipid-lipoprotein levels that occur following menopausal transition. Elevated total cholesterol, LDL-C and triglycerides are more common in post than premenopausal women.[8-10]

Despite the extensive research on the effects of estrogen and progesterone on lipid and lipoprotein metabolism, it is not yet clear whether changes in sex steroid concentration associated with menopausal status are related to changes in lipid concentration.[11,12]

In view of this scientific background, present study was carried out to evaluate the changes in lipid profile and antioxidant status in both premenopausal and postmenopausal women.

## METHODS

The study was a cross-sectional study conducted over a period of 6 months (January 2015 to June 2015). A total of one hundred and twenty subjects visiting the Gynaecology out-patient department of Shri Mahant Indiresh Hospital, Patel Nagar, Dehradun, India participated in the study.

Out of these 60 subjects were pre-menopausal between 30-45 years of age while the remaining 60 were postmenopausal between 55-70 years of age. The subjects were of similar socioeconomic status (middle income group) and were residents of northern part of country around Dehradun, Garhwal, India.

### *Exclusion criteria*

Subject with diabetes mellitus, hypertension, endocrinal abnormalities, cardiovascular disease, receiving hormone replacement therapy or any other medication likely to adversely affect lipid profile and antioxidant status were excluded from the study.

The institutional ethics committee approved the study and informed consent was taken from all the subjects. Face to face interview was used to collect data from the participants.

All of the volunteers who agreed to participate in this study were asked to complete a pro forma about personal information like name, age, marital status and life style.

Under all aseptic conditions, 5 ml of blood samples were drawn from all the subjects. Blood samples were allowed to clot for 30 min and then were centrifuged at 3000 revolutions per minute (rpm) for 10 min. Serum separated from the clotted blood was refrigerated at -200C until analysis.

Serum total cholesterol, triglycerides and HDL-C were estimated by using VITROS 5600 automated dry chemistry analyzer. VLDL-C and LDL-C were calculated by using Friedewald's formula.[13] The SOD enzyme activity was measured by using commercial colorimetric activity kit from ARBOR.[14]

### *Statistical analysis*

Firstly data were coded in Microsoft excel software and then the various variables in the two groups were compared using Student's unpaired t-test. The p-value $\leq 0.05$ was considered to be significant.

## RESULTS

Results of the study are summarized in Table 1. Mean serum total cholesterol levels were found to be increased in postmenopausal women (197±33.74 mg/dl) as compared to the premenopausal women (171.95±40.33 mg/dl). This variation was statistically significant ($p < 0.05$).

Similarly mean serum triglyceride levels were significantly elevated in postmenopausal women. Mean serum SOD levels were significantly lower ($p < 0.0001$) in the postmenopausal group (1.35±0.58 U/ml) in comparison to premenopausal group (4.80±1.73 U/ml).

Our study also demonstrated decreased serum HDL-Cholesterol in postmenopausal women but statistically

this variation was not significant (p >0.05). Mean serum LDL-C and VLDL-C levels were found to be increased in postmenopausal women but these variations were also not significant (p >0.05).

**Table 1: Comparison of lipid profile and sod activity in premenopausal and postmenopausal groups.**

| Parameter | Mean±SD | | t-value | p-value | Significance |
|---|---|---|---|---|---|
| | Premenopausal group (n=60) | Postmenopausal group (n=60) | | | |
| Total Cholesterol (mg%) | 171.95±40.33 | 197±33.74 | 3.6901 | 0.0003 | HS |
| Triglycerides (mg%) | 120.90±36.26 | 157.65±66.53 | 3.757 | 0.0003 | HS |
| HDL-C (mg%) | 54.05±14.03 | 51.5±12.20 | 1.0624 | 0.2902 | NS |
| LDL-C (mg%) | 93.30±37.77 | 106.6±40.35 | 1.864 | 0.0648 | NS |
| VLDL-C (mg%) | 29.40±24.84 | 31.6±13.28 | 0.605 | 0.5463 | NS |
| SOD activity (U/ml) | 4.80±1.73 | 1.35±0.58 | 14.646 | <0.0001 | HS |

## DISCUSSION

Menopause is the permanent cessation of menstruation, which is retrospectively determined following twelve months of amenorrhoea.[15] The immediate symptoms of menopause are the effects of hormonal changes on various organ systems mainly on cardiovascular system. The average age of menopause is 50.5 years, but some women may enter menopause at earlier age. Cardiovascular disease is a leading cause of mortality in both men and women in industrialized world.

The various physiological risk factors for cardiovascular disease are complex and the incidence of cardiovascular diseases increases with age in both the sexes, but in women the risk increases markedly after menopause.[16] Estrogen increases HDL-C that is considered to be good cholesterol for cardiovascular system by increased hepatic productions of apolipoprotein-A and decreased hepatic elimination of $HDL_2$ cholesterol by decreasing the activity of hepatic lipase enzyme.

Since during menopause estrogen is low and which leads to hampering of all these functions.[17] Estrogen use is associated with elevation in HDL-C by up to 25% and HDL-C seems to be the best indicator of coronary heart disease risk in women.[18]

In the present study serum total cholesterol (TC) and triglycerides (TG) levels showed a significant rise (p <0.001) in postmenopausal women as compared to premenopausal women while serum HDL-Cholesterol levels were lower in postmenopausal women compared to premenopausal women (Table 1), which is in accordance with previous studies by Maturana et al and Alfonso et al.[19,20]

Increased serum triglycerides levels indicated in our study might be due to estrogen related decrease in activity of lipoprotein lipase (LPL) after the loss of ovarian function as stated by Stevenson et al.[9] The average HDL-Cholesterol in women is 55 to 60 mg/dl and a decrease in HDL-Cholesterol of 10mg/dl increases coronary heart disease risk by 40-50 percent.[21] We also observed increase in triglyceride, which could be due to hormonal effect on the lipid metabolism independent of age or can be attributed to age as given by few authors. Gandhi et al demonstrated triglycerides in plasma increased with age.[22]

Various studies conducted by different authors exhibit a fair measure of ambiguity with regard to the effect of menopause on SOD levels. Shrivastava et al reported that postmenopausal women had significantly lower concentrations of SOD in comparision to premenopausal women.[23] Krstevska et al observed that SOD levels were decreased in peri-menopausal and postmenopausal women as compared with normally menstruating women, however the variations were statistically non-significant.[24]

Bednarek T et al stated that SOD activity did not differ between pre and postmenopausal women.[25] However Gurdol et al found increased SOD activity in menopausal women, but only at an older age.[26] Present study showed a statistically significant (p <0.001) decreased SOD levels in postmenopausal women. Our study also demonstrated changes in lipid profile in pre and postmenopausal women which indicate that decreased estrogen levels are associated with increased oxidative stress and increased risk of cardiovascular disease due to significant alterations in serum lipid profile.

## CONCLUSION

It is concluded that oxidative stress in postmenopausal women causes potential oxidative injury in the cell, which causes pathology in this stage of life. Therefore antioxidants in the form of micronutrients and vitamins can be given as supplements in postmenopausal women along or as a substitute to hormone replacement therapy which itself is associated with serious side effects. Our

study also showed significant difference in cholesterol and triglycerides levels between pre and postmenopausal women.

Hence regular monitoring of women in menopausal transition with lipid profile would be helpful to prevent the age related risk of coronary heart disease. Limitation of the study was that the sample size was small, we had included only 120 subjects. Serum estrogen levels were also not estimated in our study.

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