Original Article

Study of Lipid Profile and C Reactive Protein in Pre- and Post-menopausal Women

Biochemistry Section

SHILPA S. SHENDE, M.V. BIMANPALLI, I.C. APTE, VISHAKHA V. MAHAJAN, HARSHAL P. NARKHEDE

ABSTRACT

Background and Objectives: Menopause is the transition period in women's life when her normal ovarian function of ovulation ceases.There is less estrogen and progesterone secretion. Since cardiovascular disease (CVD) is the leading cause of death among post-menopausal women, the present study was undertaken to evaluate lipid profile status and C reactive protein (CRP) level in post-menopausal women and compare with pre-menopausal women.

Materials and Methods: 100 cases (post-menopausal women) were included in the study and 100 regularly menstruating women in the reproductive age group were taken as control. In both the study groups we have measured lipid profile which includes (Serum total cholesterol(TC), TG, HDL-C, LDL-C, VLDL-C), C-reactive protein(CRP) and Body mass index(BMI) as cardiovascular risk factors. Statistical analysis was done by students 't'-test.

Results: The results of this study shows significant increased level of serum total cholesterol, TG, LDL-C and VLDL-C in post-menopausal women compared to pre-menopausal women ($p<0.001$). While serum HDL-C level is significantly lower in cases compared to control($p<0.001$). Present study also show elevated mean LDL-C to HDL-C ratio (4.8 ± 0.73) in post-menopausal women compared to control($p<0.001$). There was also increased level of CRP and BMI in cases compared to control($p<0.001$).

Conclusion: The results of our study provide information that cardiovascular risk factors are elevated in post-menopausal women compared to pre-menopausal women so these women are at an increased risk of developing cardiovascular disease.

Key Words: Postmenopausal women, CRP, lipid profile, BMI, Cardiovascular disease (CVD)

INTRODUCTION

The incidence of cardiovascular disease is much lower in younger women than in men. This has led to popular misconception that cardiovascular disease is a disease of men and relatively rare in women. This however is not the case, with advancing age rate for women tend to approach those of men. One possible factor may be the different hormonal make up of the two sexes. Menopause is the end of menstruation and it is part of women's natural aging process. It is characterized by decrease level of estrogen and large number of hormonal changes [1].

It has been proposed that estrogen may be responsible for the protective effects seen amongst younger (pre-menopausal) women. Estrogen exerts cardioprotective action by maintaining high level of high density lipoprotein cholesterol(HDL-C) and lowering the low density lipoprotein cholesterol(LDL-C) and triglycerides(TG) [1, 2, 3, 4]. Loss of this protection after menopause may therefore be responsible for increased risk of developing cardiovascular disease in post-menopausal women [5, 6, 7, 8].

C-reactive protein an acute phase reactant synthesized in the liver is also a factor in the development of atherosclerotic plaque. Although CRP was initially believed to be only a marker of vascular inflammation, recent research indicates that it also plays an active role in atherogenesis [9]. Thus addition of CRP to traditional lipid screening improves the ability to predict cardiovascular risk.

In view of the above findings the aim of our study was to study the level of lipid profile, CRP and BMI in post-menopausal women and compare them with pre-menopausal women.

MATERIALS AND METHODS

Study population and Design

The present study was carried out in the Department of Biochemistry, Indira Gandhi Government Medical College and Hospital, Nagpur. The study protocol was approved by the institutional ethical committee. An informed written consent was obtained from all the study subjects who were enrolled in the study.

In order to estimate whether post-menopausal women have an increased risk of developing cardiovascular disease a total number of 100 cases (post-menopausal women) attending the Gynaecology out patient department(OPD) were included in the study. Also 100 regular menstruating women in the reproductive age group were included in the study as a control. Women with heart disease,diabetes melitus (DM), any neoplasia, arthritis or any other inflammatory disease and women taking hormonal replacement therapy were excluded from the study.

The majority of patients have similar diets and lifestyle with regard to their daily exercise. Body weight and height were recorded. The BMI was calculated as the weight (Kg) divided by height meter squared (m2).

Laboratory Assays

All blood samples were drawn in the morning after 12 – 14 hrs of fasting. Sample was allowed to clot for 30 minutes and then centrifuged. The separated serum was analysed for the following biochemical parameters.

- Serum total cholesterol by enzymatic method,Serum triglycerides (TG) by enzymatic method
- Serum HDL cholesterol by phosphotungstate precipitation followed by enzymatic method.
- Serum LDL Cholesterol and VLDL Cholesterol by Friedwald formula [10].
- Serum C- reactive protein by Turbilatex method.(Kit-MERCK laboratory). Principle: Latex particles coated with specific human anti-CRP are agglutinated when mixed with samples containing CRP. The agglutination causes an absorbance change dependent upon the CRP contents of the patient sample that can be quantified by comparison from a calibrator of known CRP concentration.

All the parameters were analyzed on semiautomatic analyzer (Transasia Erba Chem-5Plus)

STATISTICAL ANALYSIS

All statistical analyses were performed by using Graph Pad Prism Software. The data was expressed as Mean $\pm$ SD. Statistical analysis was carried by using students 't'-test and $P<0.05$ was considered as statistically significant. Pearsons correlation coefficient (r) was used to assess correlation between measured parameters.

RESULTS

We observed significant increase in serum total cholesterol(TC), triglycerides(TG), LDL-cholesterol and VLDL-cholesterol level in post-menopausal women compared to pre-menopausal women ($p<0.001$). HDL-cholesterol level was significantly decreased in post-menopausal women as compared to pre-menopausal women ($p<0.001$).Also in our study LDL-C to HDL-C ratio was significantly increased in cases compared to control ($p<0.001$). C reactive protein was significantly increased in post-menopausal women compared to pre-menopausal women ($p<0.001$).Body mass index (BMI) was also significantly increased in post-menopausal women compared to pre-menopausal women ($p<0.001$). We observed significant positive correlation between C reactive protein and BMI ($r=0.6$, $p<0.001$) in post-menopausal women. Significant positive correlation was also observed between triglycerides (TG) ($r=0.3$, $p<0.001$)and LDLcholesterol ($r=0.5$,$p<0.001$) with C reactive protein.

DISCUSSION

The major cause of death among post-menopausal women is cardiovascular disease which accounts for nearly 53% of all deaths in women over 50 years of age. When we consider the overall lipid profile as a marker for evaluation of cardiovascular risk, in the present study serum total cholesterol (TC), triglycerides (TG), LDL Cholesterol and VLDL Cholesterol level shows a significant rise ($P<0.001$) in post-menopausal women compared to pre-menopausal women while serum HDL Cholesterol level is significantly lower in post-menopausal women compared to control [Table/Fig-1], which is in accordance with previous studies by Maturana etal(2008) [11] and Alfonso Cano etal (2003) [12].

Increased serum triglyceride levels indicated in our results may be due to estrogen related decrease in activity of lipoprotein lipase (LPL) after the loss of ovarian function as stated by Stevenson et al (1993) [13] and Wild et al (1995) [4]

According to Arca et al (1994) [14] decrease in estrogen secretion with the cessation of ovarian function probably contribute to higher LDL Cholesterol level in post-menopausal women. Estrogen increases hepatic synthesis of LDL Cholesterol receptor for Apo-β 100 resulting in increase LDL Cholesterol uptake and therefore decreases circulating LDL levels. Thus its deficiency results in rise in LDL Cholesterol in post-menopausal women [4].

HDL Cholesterol is a standard risk profile for coronary heart disease (CHD). Estrogen increases HDL Cholesterol level by inhibiting hepatic lipase, the enzyme that destroys HDL Cholesterol. Present study also shows elevated mean LDL-C to HDL-C ratio in cases compared to control [Table/Fig-1] suggestive of increased cardiovascular risk in post-menopausal women. The Framingham study [15] reported that persons with LDL-C: HDL-C ratio greater than 5 are at high risk of developing CHD and person with LDL-C: HDL-C ratio between 2 and 5 are at intermediate risk of developing CHD. In comparison with Framingham study, our study shows LDL to HDL ratio 4.8+0.73 in post-menopausal women which suggest an intermediate risk of developing CHD in these women.

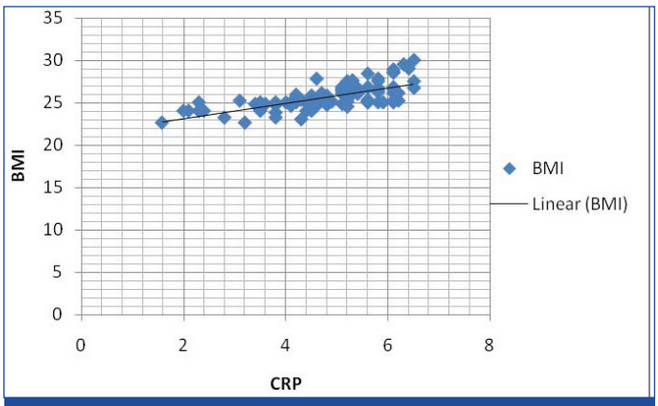
Body mass index was strongly associated with death due to CHD with the risk of CHD over 3 times higher among women with a body mass index of 29 or higher [16]. The finding of increased BMI in post-menopausal women was well supported by Wasir etal(2007)[6] and Tchernof etal (2002) [9].

From various studies it was found that C-reactive protein is a strong independent risk factor for cardiovascular disease among apparently healthy middle aged women [17-19]. Present study shows increased level of CRP in cases compared to control [Table/Fig-1] which point towards increased cardiovascular risk in post-menopausal women compared to control.

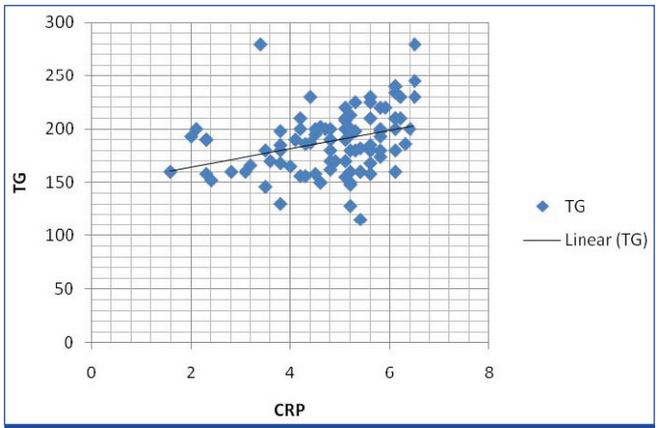
There was also positive coefficient of correlation between BMI and CRP levels [Table/Fig-2]. There are several mechanisms which may link adiposity with elevated CRP levels. It has been suggested that plasma CRP levels reflect the amount and activity of proinflammatory cytokines such as TNF- α, IL-1 and IL-6 which are implicated in the process of atherosclerotic plaque formation and acute coronary syndrome. In this regard, IL-6, which is

Biochemical parameters	Normal values	Premenopausal women (mean $\pm$ SD) n=100	Postmenopausal women (mean $\pm$ SD) n=100
Serum total cholesterol(mg/dl)	< 200	133.75$\pm$16.35	235.7$\pm$19.01*
Serum Triglycerides(mg/dl)	< 160	85.90$\pm$20.01	188.4$\pm$28.84*
Serum HDL cholesterol(mg/dl)	> 40	50.99$\pm$4.65	33.8$\pm$2.18#
Serum LDL cholesterol(mg/dl)	< 100	65.91$\pm$15.39	162.0$\pm$22.9*
Serum VLDL cholesterol(mg/dl)	< 32	17.2$\pm$4.04	37.4$\pm$6.56*
LDL-C/HDL-C	< 2	1.31$\pm$0.37	4.8$\pm$0.73*
CRP(mg/l)	< 1	1.08$\pm$0.86	4.8$\pm$1.11*
BMI (kg/m^2)	18.5-24.99	20.0$\pm$2.4	25.68$\pm$1.43*

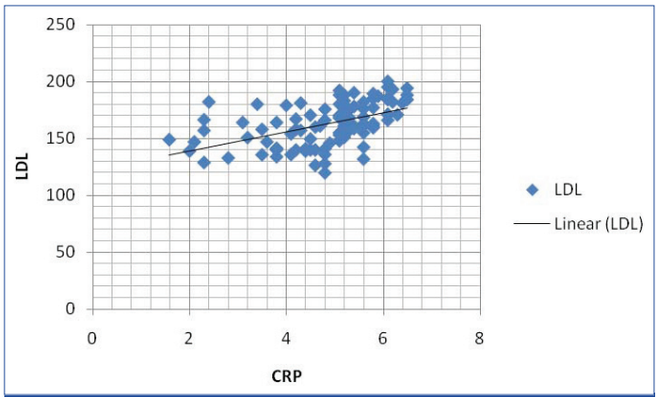
[Table/Fig 1]: Values of various parameters of lipid profile, CRP & BMI in study group
* Significantly higher ($p<0.001$) as compared to control
# Significantly lower ($p<0.001$) as compared to control



[Table/Fig-2]: Correlation of BMI with CRP



[Table/Fig-3]: Correlation of TG with CRP



[Table/Fig-4]: Correlation of LDL with CRP

induced by both TNF- α and IL-1,has been proposed to play a central role in the relationship between CRP and cardiovascular disease. The contribution of adipose tissue in IL-6 secretion has been proposed to be the link between plasma CRP and adiposity,as CRP synthesis in the liver is largely under the control of IL-6 [9, 20]. Thus adiposity is a significant predictor of plasma CRP in post-menopausal women.

We observed significant positive correlation between parameters of lipid profile such as TG, LDL with CRP level [Table/Fig-3 and 4]. This suggests that unfavourable lipid profile may facilitate the formation of foam cells in arterial wall increasing the inflammatory activity. Our results are in agreement with the findings of Tchernof etal (2002) [9].

In conclusion results of our study provide information that cardiovascular risk factors like lipids and lipoprotein conc, CRP and BMI are elevated in post-menopausal women compared to pre-menopausal women so these women are at an increased risk of developing cardiovascular disease. Considerable weightage should be given to prevent increase in the level of these parameters during midlife to reduce the later risk of developing coronary heart disease in these women.

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AUTHOR(S):

1. Dr. Shilpa Shende
2. Dr. M.V. Bimanpalli
3. Dr. I.C. Apte
4. Dr. Vishakha Mahajan
5. Dr. Harshal Narkhede

PARTICULARS OF CONTRIBUTORS:

1. Assistant professor, Department of Biochemistry, Indira Gandhi Government Medical College Nagpur, India.
2. Assosiate professor, Department of Biochemistry, Indira Gandhi Government Medical College Nagpur, India.
3. Professor and Head of Department, Department of Biochemistry,Indira Gandhi Government Medical College Nagpur, India.
4. Assistant professor, Department of Biochemistry Indira Gandhi Government Medical College Nagpur, India.
5. Assistant professor, Department of Biochemistry Indira Gandhi Government Medical College Nagpur, India.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Shilpa Shende
Assistant professor, Department of Biochemistry,
Indira Gandhi Government Medical College Nagpur, India
Phone: 9372128381
E-maildr.shilpashende@yahoo.com

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