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Association of C-reactive Protein With Atherogenic Index In Postmenopausal Women

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Abstract

Introduction: Dyslipidaemia, which has been more prevalent among postmenopausal women have made them more susceptible to cardiovascular risks and datas reporting association between C-reactive protein and dyslipidaemia is scarce.

Objective: To estimate and to find the association between serum C-reactive protein (CRP) and atherogenic index of plasma in postmenopausal women and determine the risk of cardiovascular disease with increasing years, compared with premenopausal women.

Methods: Height, Weight, BMI, Total cholesterol (TC), and their sub fractions: high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), and hs-CRP (high sensitive –CRP) were analyzed. Atherogenic index of plasma (AIP); log (TG/HDL –C) was calculated and compared between postmenopausal and premenopausal women. Spearman's (ρ) correlation was done to find the association between parameters. These parameters were also compared with 5 yrs post menopausal and 10 yrs postmenopausal women, to assess the cardiovascular risks with increasing years.

Results: There was statistically significant increase in hs-CRP, AIP and Triglycerides (P value: <0.05) and decrease in HDL-C (P value: 0.001) in postmenopausal women compared with premenopausal women. Significant positive correlation was found in hs-CRP with AIP, BMI, TG and negative correlation with HDL-C in postmenopausal women, (P value:<0.05).There was statistically significant derangement of lipid subfractions, increase in atherogenic index and hs-CRP (P value: <0.05) as the duration of menopause increased.

Conclusion: Elevated hs-CRP and its positive association with atherogenic index and BMI definitely adds significant value in assessing atherosclerosis and cardiovascular risks

Keywords: Post-menopausal women, Atherogenic index of plasma (AIP), hs-CRP, BMI

Introduction

Menopause, is a natural event in the reproductive cycle in all women characterized by cessation of menstrual cycles due to depletion of ovarian follicular reserve. The median age for the final menstrual period is about 51 years, when the oestrogen production is significantly reduced[1]. Decreased oestrogen during and after menopause have significant impact on physical, psychological and social wellbeing of the woman[2].The anti-atherogenic effect of oestrogens and the protection against cardiovascular diseases in women are well established[1].There are numerous evidences to indicate that menopause is associated with altered

lipid profile and central adiposity[3,4] that increases the risks of cardiovascular diseases. The adipose tissue behaves as an endocrine organ, secretes many adipocytokines which in turn is responsible for the hepatic synthesis of C-reactive protein[5]. As there are many evidences showing CRP as an independent predictor of cardiovascular risk, it prompted us to analyze and assess the association between C-reactive protein and obesity and the lipid profile in post menopause.

Materials and Methods:

Study design and participants: This case control study involved 50 premenopausal women (controls) aged between 30–40 years and 50 postmenopausal women (cases) aged between 50 – 70 years who attained natural menopause, which is defined as cessation of menstrual bleeding for more than one year. Inclusion criteria were women without diabetes mellitus, hypertension, cardiovascular diseases and those without any endocrine disorders and malignancy.

Women with signs of acute inflammation and women with history of menstrual disorders were excluded. Other exclusion criteria included pregnancy, renal diseases and those who had undergone surgical removal of ovaries and hormonal contraception. Informed written consent was obtained from the study group. Institutional ethical committee clearance was obtained. This study was conducted in compliance with the 1975 Helsinki declaration and its later amendments.

Data collection:

A detailed history was elicited for diabetes mellitus, hypertension, renal diseases, menstrual irregularities, surgical removal of ovaries, intake of contraceptive pills and pregnancy. Clinical examination which included weight, height, pulse, systolic and diastolic blood pressure were measured. Systemic examination was done to exclude hepatic and renal pathology.

Sample collection and biochemical measurements

Blood samples were collected after 12-h overnight fasting, and biochemical parameters such as fasting blood glucose (FBG), urea and Serum levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were measured spectrophotometrically using enzymatic procedures The atherogenic index of plasma (AIP) was calculated as the logarithmically transformed ratio of concentrations of TG to HDL-C by the formula log (TG/HDL –C)[12]. CRP levels were determined using a nephelometric assay (Nephelometer Analyzer, Siemens,Germany). The intra- and inter-assay coefficients of variation (CVs) for CRP and were 3.5% 6.0%, respectively.

Statistical analysis:

Analysis was done using SPSS VERSION 23. (IBM SPSS Inc.,Chicago,Illinois,USA). The Student t test was used for comparison of quantitative variables. Spearman's (ρ) correlation was done to find the association between parameters.These parameters were also compared with 5 yrs post menopausal and 10 yrs postmenopausal women, by ANOVA means test to assess the cardiovascular risks with increasing years. Linear regression analysis was done to find, which of the variable had significant association with CRP.

P values less than or equal to 0.05 were considered as significant.

Results:

The mean, standard deviation of clinical and biochemical parameters were depicted in Table 1 .The mean age, BP, fasting blood glucose, urea, creatinine was estimated to fulfill the exclusion criteria in the study population.There were statistically significant increase ($P<0.05$) in BMI,TC, TG, LDL-C and VLDL-C in the postmenopausal women compared to premenopausal women. There was decrease in HDL-C in the postmenopausal women when compared to the premenopausal women with p value being insignificant. The hs-CRP levels in post menopausal were significantly twice as higher as pre-menopausal women.

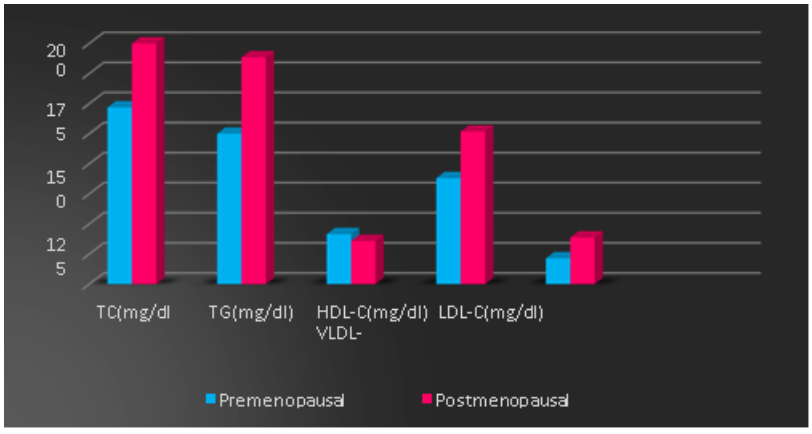
Table 1 Distribution of clinical and biochemical parameters

Volume 5, Issue 1; January-February 2022; Page No 1282-1287

Variables	Premenopausal (n=50)	Postmenopausal (n=50)	P value
Age	31±5	57±3	0.00*
BMI	24.2±2.1	28.4±2.4	0.03
Systolic BP(mmHg)	121±3	123±6	0.107
Diastolic BP(mmHg)	70±8	80±5	0.06
FBG(mg/dl)	79±9	88±7	0.89
Urea (mg/dl)	27±5	26±6	0.25
Creatinine (mg/dl)	0.6±0.3	0.7±0.3	0.814
TC(mg/dl)	146.81±24.58	202.70±20.08	0.000*
LDL-C(mg/dl)	88.08±19.59	126.75±25.92	0.001*
HDL-C(mg/dl)	41.52±10.52	35.85±10.14	0.061
TG(mg/dl)	125.00 ±50.35	188.50 ±87.63	0.008*
VLDL-C(mg/dl)	21.46±7.31	38.75±13.81	0.001*
AIP	0.47±0.25	0.67± 0.24	0.0091*
hs-CRP(mg/L)	0.99 ±2.81	2.32 ±1.48	0.001*

* p < 0.05 statistically significant

Fig 1 Bar chart showing distribution of lipid profile among the study group



This difference in lipid profile and AIP was more significant with 10 yrs post menopausal and 5 yrs postmenopausal women with more risks with increasing years.(Fig2)The AIP (log TG/HDL-C) was 0.67± 0.24 in post-menopausal women which was significantly higher , 0.47±0.25 than in pre menopausal women ($p<0.05$). (Fig3)

Volume 5, Issue 1; January-February 2022; Page No 1282-1287

Figure 2 Anova Means Test showing the difference with the duration of menopause

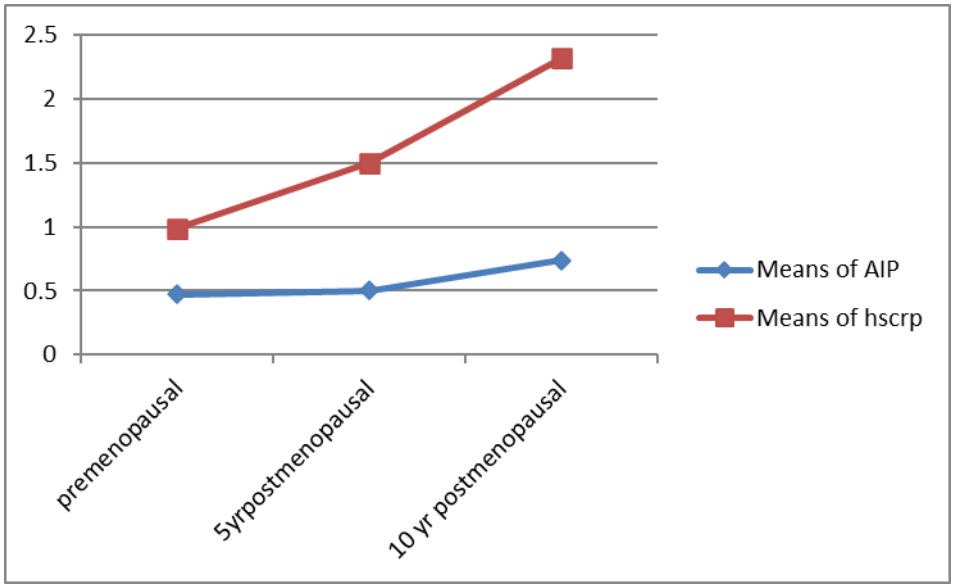
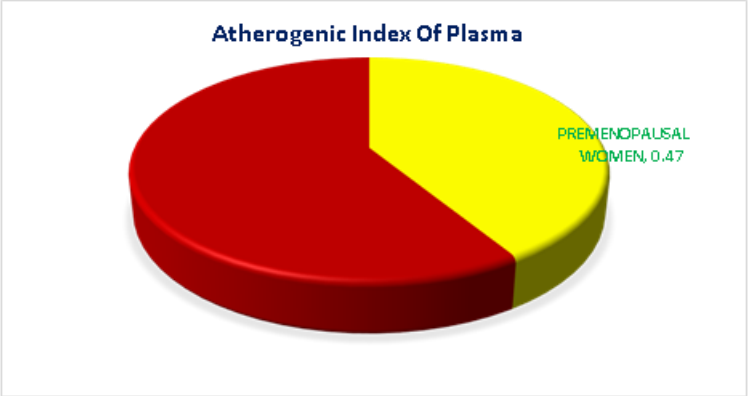


Fig 3 Pie Chart showing distribution of AIP among the study group



The association between hs-crp and other variables in pre-menopausal and postmenopausal women is presented in Table 2. In post-menopausal woman, the CRP was found to positively correlated with Triglycerides, BMI and atherogenic index of plasma and negatively correlated with HDL-C. In the control group, CRP had positive correlation with age and triglycerides.

Table 2 Spearmans correlation coefficient (ρ) between hsCRP and other parameters

Variable	cases		controls	
	ρ	P	ρ	P
Age	0.223	0.041	0.324	0.021
BMI	0.427	0.004	0.257	0.022
Triglycerides	0.280	0.001	0.191	0.011
TC	0.310	0.219	0.190	0.521
LDL-C	0.013	0.710	-0.182	0.684

Volume 5, Issue 1; January-February 2022; Page No 1282-1287

HDL-C	-0.413	0.01	-0.081	0.782
AIP	0.312	0.031	0.125	0.071

Linear regression analysis was done among post menopausal women, to find, which of the variable had significant association with CRP. As, shown in Table 3, in post menopausal women, BMI, Triglycerides, and AIP were significant predictors of CRP. And HDL-C is a negative predictor of CRP.

Table 3 Linear regression analysis with hs-crp as dependent variable

Independent variable	B	β	P
BMI	0.262	0.591	0.001
TC	-0.241	-0.149	0.381
Triglycerides	0.513	0.197	0.001
HDL-C	-1.710	-0.413	0.013
LDL-C	-0.091	-0.051	0.621
AIP	0.341	0.513	0.001

Discussion:

In this present investigation, there were statistically significant increase in hs-CRP and AIP (p:<0.05) in post-menopausal women, compared to their premenopausal counterparts. These results were consistent with the study conducted by Tchernof in 2002, in which Triglycerides and hsCRP were increased significantly in postmenopausal women[6].

The duration of menopause, in this study, also had impact on the lipid profile with statistically significant increase in the hs-CRP,TG, LDL-C and atherogenic index (p<0.05) and decrease in HDL-C. (p<0.05). Ting-Ting Wu et al have also reported similar results among postmenopausal women[7].These results confirm the dearrangements of lipid profile and rise in inflammatory markers in postmenopausal women[14,15].

Moreover, the significant association of hsCRP with BMI and atherogenic index in this present study, suggest that the adipose tissue being the main source of cytokines and interleukin 6, which is the major stimulant for the synthesis of hsCRP in liver[5]. These results reveals a significant mechanism in which adipose tissue increase the risk of CAD in postmenopausal women. Similar associations between CRP and BMI was reported in previous studies[6,8].

In a study by Lemieux et al[9], there was increased CRP levels among subjects with higher waist circumference (WC) i.e central obesity and Hak et al[10] reported in his study, a strong correlation of CRP with waist circumference (WC) after adjusting for BMI. Mendall et al[11] also reported a significant association of CRP levels with BMI among elderly men and women.

In our study after linear regression analysis, we found that CRP was predicted by BMI, Triglycerides and atherogenic index, which is similar to results of other studies.[11,12]

Among lipid parameters, there was negative correlation with CRP and HDL-C.This inverse association also reported by many studies supports the antiatherogenic and anti inflammatory properties of HDL-C[13].

In our study,there was no significant association of BMI and AIP in cases and the control group.

Conclusion:

To our knowledge, this is the first study to report the association between hs-CRP and atherogenic index of plasma in postmenopausal women. The Atherogenic Index of Plasma (AIP), which can be easily calculated from the standard lipid profile values, adjunct to raised hs-CRP values, significantly adds

Volume 5, Issue 1; January-February 2022; Page No 1282-1287

predictive value for the development of cardiovascular diseases than the individual lipid profile values. We have also found positive association of BMI and AIP with hsCRP in postmenopause. Therefore we suggest, AIP can be used for routine screening for CVD in women undergoing menopause along with dietary interventions and increased physical activity to curtail the development of central obesity.

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Volume 5, Issue 1; January-February 2022; Page No 1282-1287