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ELEVATED SERUM HS-CRP AND LIPID PEROXIDATION LEVELS IN OBESE POST- MENOPAUSAL WOMEN

Biochemistry

Dr. M. Kotteswaran — Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Tamilnadu.

Dr. S. Sethupathy* — Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Tamilnadu. *Corresponding Author

Dr. K. Santha — Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Tamilnadu.

Dr. A. Mallika — Department of obstetrics and gynecology, Rajah Muthiah Medical College and Hospital, Annamalai University, Tamilnadu.

ABSTRACT

Postmenopausal women are more prone for cardiovascular disease due to decreased or complete absence of endogenous estrogen hormone. Cardiovascular disease (CVD) is the leading global cause of death, in that 49% of them are female population. The risk of CVD increases sharply after menopause and the exact underlying mechanism for association of post menopause with cardiovascular disease needs to be evaluated. So, we analyzed serum hsCRP, an inflammatory marker and lipid peroxidation levels in 55 Post-menopausal women in the age group of 45 to 55 years (obese: n=30 and non-obese: n=25) with no history of cardiac and other chronic disorders. Ethical clearance and written consent were obtained. hs-CRP was assayed by ELISA method and lipid peroxidation as thiobarbituric acid reactive substances (TBARS) was estimated using spectrophotometer. High sensitivity C - reactive protein (hs-CRP) and TBARS were found to be significantly elevated in obese post-menopausal women than in non- obese ($p<0.05$). There was significant positive correlation between hs-CRP and TBARS ($p<0.01$) in post-menopausal women. It is concluded that elevated oxidative stress and inflammation could increase the risk for CVD in obese postmenopausal women.

KEYWORDS

Post-menopausal women, hsCRP, Lipid peroxidation,CVD.

INTRODUCTION

Cardiovascular disease (CVD) is the leading global cause of death, in that 49% of them are female population(1). CVD risk increases sharply after menopause(2). Earlier study has stated that the menopause is a risk factor for CVD by decline in estrogen and progesterone production. Many studies have focused on the association between endogenous estradiol and subclinical CVD markers, with no consistent results. Ouyang et al,(3)did not find a significant correlation of estradiol levels with either Carotid Intima-media Thickness or coronary artery calcification in the study involving multi ethnic postmenopausal women aged 45–84 years. Some studies have shown a favorable effect of endogenous estradiol on the vasculature(4,5). Hence the exact underlying mechanism for association of post-menopause with cardiovascular disease needs to be evaluated(6). It has been reported that menopause is associated with changes in body composition and metabolic profile in overweight or obese women (2). Atherosclerosis is an inflammatory condition of large and middle-sized artery caused by oxidative stress (6). The pathogenesis of atherosclerosis was explained based on "Response to Injury Theory"(7). Oxidative stress is mainly due to reactive oxygen species (ROS). Imbalance of Nitric oxide (NO) and ROS is also involved in endothelial dysfunction. The defective NO production induces changes in the expression of vascular cell adhesion molecule-1, intercellular adhesion molecule-1 (ICAM-1), E-selectin and also affects the leucocyte cell ability to attach the endothelium. This results in increased infiltration of leucocyte cells locally in to the intima layer, which supports pro-inflammatory conditions and growth of atherosclerotic plaque(8,9). C-reactive protein (CRP) is produced by the liver on stimulation of several pro-inflammatory cytokines like IL-6 or TNF – α which are derived from monocytes/macrophages. It causes expression of ICAM-1 and VCAM-1 by endothelial cells and mediates Monocyte Chemoattractant Protein-1(MCP-1) induction ——(1012). CRP can also bind to and activate complement (13), as well as mediate LDL uptake by macrophages (14). However, when CRP remains chronically high in the absence of acute causes, there is an increased risk for CVD. Hence serum hsCRP and lipid peroxidation levels were analyzed in post-menopausal women to assess the CVD risk.

MATERIALS AND METHODS

Fifty Five post-menopausal women were selected for the Cross-Sectional Study from department of obstetrics and gynecology of Rajah Muthiah Medical College and Hospital, Annamalai University, Tamilnadu. Based on BMI as per revised consensus guidelines for Asian Indians and the World Health Organization (WHO) criteria(15). they are grouped into obese (n=30) and non-obese (n=25). The Post-menopausal women were in the age group of 45 to 55 years with no history of cardiac,thyroid diseases, liver diseases, renal diseases, cancer and no surgical history of hysterectomy. Institutional Human Ethics clearance and informed written consent were obtained.Venous blood was collected in the fasting state for plasma glucose, lipid profile, liver function tests and renal function tests.Serum hs-CRP was measured by ELISA plate reader and lipid peroxidation (TBARS) was measured using spectrophotometer.The Statistical analysis was done using SPSS -25 Software. Unpaired student t test for comparison and Pearson correlation analysis were applied. P value less than 0.05 was considered significant.

TABLE: 1. Baseline characteristics of OBESE and NON-OBESE Post-Menopausal Women.

PARAMETERS	GROUP I (OBESE) n=30	GROUP II (NON-OBESE) n=25	"P" Value
AGE (Years)	52.9 ± 4.83	50.12 ± 5.75	NS
BMI (Kg/m^2)	26.22 ± 0.54	22.46 ± 0.45	< 0.05*
WHR	0.91 ± 0.04	0.86 ± 0.07	<0.05*
BP (SYSTOLE) (mmHg)	114.67 ± 8.19	115.76 ± 12.33	NS
BP (DIASTOLE) (mmHg)	77.50 ± 7.39	76.08 ± 12.28	NS
Plasma Glucose (Fasting)(mg/dl)	80.00 ± 12.68	83.80 ± 15.16	NS
Plasma Glucose Post prandial) (mg/dl)	131.40 ± 13.51	120.56 ± 14.50	<0.05*
Total cholesterol (mg/dl)	211.90 ± 31.91	164.73 ± 26.62	<0.05*
Triglycerides (mg/dl)	164.73 ± 75.80	174.96 ± 93.97	NS
HDL-C (mg/dl)	42.80 ± 2.05	42.76 ± 2.58	NS
LDL-C (mg/dl)	102.60 ± 35.64	99.64 ± 37.92	NS
VLDL (mg/dl)	32.94 ± 15.16	34.99 ± 18.79	NS
ALT (u/l)	28.17 ± 5.15	24.80 ± 7.78	NS
Serum Urea (mg/dl)	27.50 ± 4.73	26.84 ± 3.02	NS

NS – Not significant

TABLE: 2. Serum Inflammmatory marker and lipid peroxidation levels in OBESE and NON-OBESE Post-Menopausal Women.

PARAMETERS	GROUP I (OBESE) n=30	GROUP II (NON-OBESE) n=25	"P" Value
hsCRP (mg/L)	4.75 ± 1.4	1.79 ± 0.89	<0.001*
TBARS (ng/ml)	5.97 ± 1.00	4.48 ± 0.36	<0.001*

Fig: 1. Serum Inflammmatory marker and lipid peroxidation levels in OBESE and NON-OBESE Post-Menopausal Women.

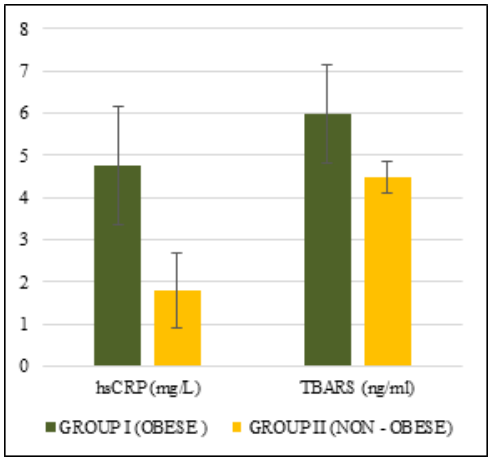

TABLE: 3. Pearson's correlation analysis of hsCRP with TBARS studied.

PARAMETERS	Pearson's correlation		correlation
	R value	P value	
TBARS	0.654	<0.001	Positive

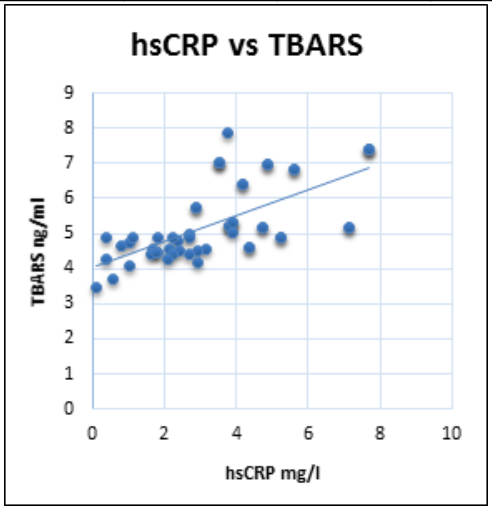

Fig: 2. Pearson's correlation analysis of hsCRP with TBARS studied.

RESULTS

T**able: 1.**There was no significant difference with respect to age, blood pressure, fasting plasma glucose, HDL-C, LDL-C, triglycerides, alanine amino transferase and blood urea levels. Waist hip ratio was significantly higher in obese.Even though there was significant difference in post prandial plasma glucose levels ($p < 0.05$), they were within normal range in both groups.Total cholesterol was found to be significantly increased in obese post-menopausal women.($p<0.05$)

T**able: 2.**High sensitivity C-Reactive Protein (hs-CRP) was elevated about two times in obese Post-menopausal women and TBARS was also significantly elevated in obese post-menopausal women than in non-obese. ($P< 0.05$)

T**able: 3.**Pearson correlation analysis was done between serum hsCRPwith TBARS. There was a significant positive correlation between them in post-menopausal women ($p<0.001$).

DISCUSSION

The risk of CVD increases sharply after menopause and the exact underlying mechanism for association of post menopause with cardiovascular disease needs to be evaluated. So, serum hsCRP and lipid peroxidation were analyzed in post-menopausal women and observed that hs-CRP level was elevated about two times in obese than in non-obese. CVD risk assessment based on hsCRP as per American Heart Association (AHA) guidelines, non-obese came under average risk (1.79 ± 0.89 mg/l) whereas obese came under high risk (4.75 ± 1.40 mg/l) (16). TBARS level was also significantly increased in obese post-menopausal women in comparison with non-obese. Even though serum total cholesterol was significantly increased in obese, there was no significant difference in LDL-C and HDL-C levels. Post prandial plasma glucose was significantly different among the groups but they were within normal range. It shows that obese are more prone for metabolic syndrome. Both groups were in similar age group and there was no significant difference. Since other disorders and inflammatory conditions were excluded, the significant elevation of hsCRP in obese could be due to chronic low-grade inflammation which is a risk factor for CVD. TBARS, a measure of lipid peroxidation was significantly elevated in obese indicating enhanced oxidative stress in obese. The significant positive correlation between hsCRP and TBARS indicates the close association of hsCRP with oxidative stress (TBARS) in post-menopausal women. Chronic low-grade inflammation and enhanced oxidative stress in obese post-menopausal women could increase the risk of Cardio vascular disease (CVD). Absence of estrogen alone in the pathogenesis of CVD in post- menopausal women could not be considered as recent study provided evidence that in the absence of estrogen there is a decline of negative feedback inhibition for FSH synthesis in pituitary gland which lead to increases in T:E ratio (Testosterone : estrogen ratio) and increases in FSH levels.FSH has an unfavorable effect on lipid profiles. FSH promotes lipogenesis and fat storage(17).So, the body composition and fat distribution changes occurduring the menopausal transition contributes risk factor in post-menopausal women through overexpression of pro-inflammatory cytokines(18,19).

CONCLUSIONS

It is concluded that obese post-menopausal women are more prone for oxidative stress induced chronic low grade inflammation and increased risk for CVD. Further studies are required to explore whether antioxidant supplementation would be helpful in reducing the CVD risk in postmenopausal women.

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