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Elevated Serum Visfatin, a Marker of Endothelial Dysfunction and Oxidative Stress in Obese Post Menopausal Women

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Abstract: *Cardiovascular disease is the leading cause of death in women and the* incidence increases *dramatically after menopause. The basic pathology of atherosclerosis is endothelial dysfunction (ED) which leads to pro-coagulant and pro-inflammatory state. Visfatin is an adipokine, preferentially expressed in visceral fat which activates pro-inflammatory cytokines in vascular smooth muscles and enhances oxidative stress, causing endothelial dysfunction. So, serum visfatin and oxidative stress status were analyzed in post-menopausal women. The study comprised of 55 post-menopausal women in the age group 45-55 years. They were divided into two groups based on body mass index (BMI) as obese (n=30) and non-obese (n=25). Serum visfatin was measured by ELISA method. Oxidative stress as (TBARS) and Total anti-oxidant status (FRAP) were measured using spectrophotometer. Serum Visfatin, a marker of endothelial dysfunction and TBARS, a measure of lipid peroxidation were found to be significantly elevated in obese women compared to non-obese women. Elevated serum visfatin levels and its positive correlation with BMI indicated that visfatin and concomitant enhanced oxidative stress in obese postmenopausal could increase the risk of CVD.*

Keywords: *CVD, endothelial dysfunction, oxidative stress, postmenopausal, Visfatin.*

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I. Introduction

Cardiovascular disease (CVD) is the leading cause of death in women in India [1,2]. Globally - deaths due to CVD accounts for 49% in female population [3]. The incidence increases dramatically after menopause, attributed to lack of estrogen and its cardio protective effects [4]. Estrogen has been shown to have cardio protective effects by increasing the production of apolipoprotein A1 and HDL-C [5]. Menopause is a risk factor for CVD as low estrogen has a detrimental effect on cardiovascular system [6]. But there are no consistent reports on cardio protective effect of estrogen. The basic pathology of atherosclerosis is endothelial dysfunction (ED) which is reduction in endothelial-dependent vasodilation (EDV), leading to pro-coagulant and pro-inflammatory state associated with diminished activity of nitric oxide [7]. Decreased production of NO, a potent vasodilator and reduced availability of other vasodilators (prostacyclin, endothelium derived relaxing factor- EDRF) and increased ROS and vasoconstrictors (Angiotensin-II, Endothelin-1) leads to endothelial dysfunction [8]. Hormonal changes such as low Estrogen and increased FSH and LH have significant effect on plasma lipid and lipoprotein metabolism [9]. Hence in post-menopausal women, there is alteration in body fat distribution and vascular remodelling which could increase CVD risk [10]. Adipose tissue secretes pro-inflammatory cytokines which act through transcription factors (Nuclear Factor-Kappa B) and NADPH oxidase and thereby induces oxidative stress [11]. Visfatin is an adipokine, preferentially expressed in visceral fat [12]. It directly activates pro-inflammatory cytokines in vascular smooth muscles and up regulates the level of inducible nitric oxide synthase (iNOS), forming peroxynitrite (ONOO• - a reactive nitrogen species) causing endothelial dysfunction [13]. Hence the present study was aimed to measure serum visfatin and oxidative stress status in obese and non obese post-menopausal women.

II. Materials And Methods

It was a cross-sectional study comprised of 55 post-menopausal women in the age group 45-55 years who attended Gynecology op department of Rajah Muthiah Medical College & Hospital. They were divided in to two groups as obese (n-30) and nonobese (n-25), based on Revised Guidelines issued by Prevention and Management of Obesity and Metabolic Syndrome Group [14]. Women with cardiac, renal, liver, thyroid diseases and cancer were excluded from the study. Ethical Clearance and informed written consent were

obtained. Anthropometric data and fasting blood samples (5 ml of venous blood) were collected for the study. Fasting plasma glucose, hemoglobin, lipid profile, alanine amino transferase, serum urea were estimated. Serum TBARS level and Total Antioxidant status (FRAP) were measured using spectrophotometer. Serum visfatin was assayed using ELISA method. Serum levels of FSH and LH were assayed using ELISA kits. Statistical analysis was done using SPSS 25.0 software. Unpaired't' test was done to determine the difference in biochemical parameters between two groups. Pearson correlation analysis was done to assess the relationship between BMI and serum visfatin, TBARS and FRAP. p value < 0.05 was considered significant.

Table- 1 Baseline Parameters in Post-Menopausal Women.

PARAMETER	GROUP I OBESE (n=30)	GROUP II NON-OBESE (n=25)	p value
AGE (years)	52.90 ± 4.83	50.12±5.75	NS
BMI	26.22 ± 0.45	20.75±3.16	<0.05
WHR	0.91±0.04	0.86±0.07	<0.05
SYSTOLE (mmHg)	114.67±8.19	115.76±12.33	NS
DIASTOLE (mmHg)	77.50±7.39	76.08±12.28	NS
Serum Urea (mg/dl)	27.50 ± 4.73	26.84 ± 3.02	NS
ALT (u/l)	28.17 ± 5.15	24.80 ± 7.78	NS

NS- not significant

Table- 2 Lipid Profile in Post-Menopausal Women.

PARAMETER	GROUP I OBESE (n=30)	GROUP II NON-OBESE (n=25)	p value
T. CHOLESTEROL (mg/dl)	211.90 ± 31.9	164.40 ± 2 6.62	<0.05*
HDL (mg/dl)	42.80 ± 2.05	42.76 ± 2.58	NS
LDL (mg/dl)	102.60 ± 35.64	99.64 ± 37.92	NS
VLDL (mg/dl)	32.94 ± 15.16	34.99 ± 18.79	NS

NS- not significant * shows p value <0.05, significant.** shows p value <0.01, significant

Table -3 Serum Visfatin, TBARS and Frap In Post-Menopausal Women

PARAMETER	GROUP I OBESE (n= 30)	GROUP II NON-OBESE (n= 25)	p value
TBARS (ng/l)	5.97 ± 1.00	4.48 ± 0.36	<0.05
FRAP(µmol/l)	209.27 ± 24.02	238.38 ± 38.61	<0.05
VISFATIN (nmol/mg)	19.58 ± 1.18	11.37 ± 5.12	<0.01**

Table 4 – Correlation Analysis of BMI with Parameters

PARAMETER	r value	p value	correlation
VISFATIN	0.951	0.001	Positive
TBARS	0.553	0.05	Positive
FRAP	-0.497	0.05	Negative

Fig.1 – VISFATIN AND TBARS - OBESE AND NON-OBESE

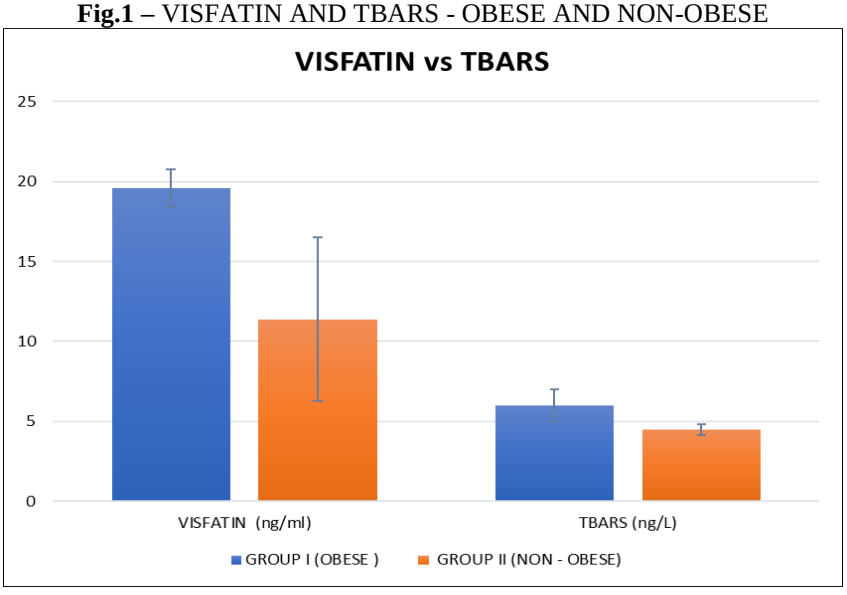


Fig.2 – FRAP - OBESE AND NON-OBESE

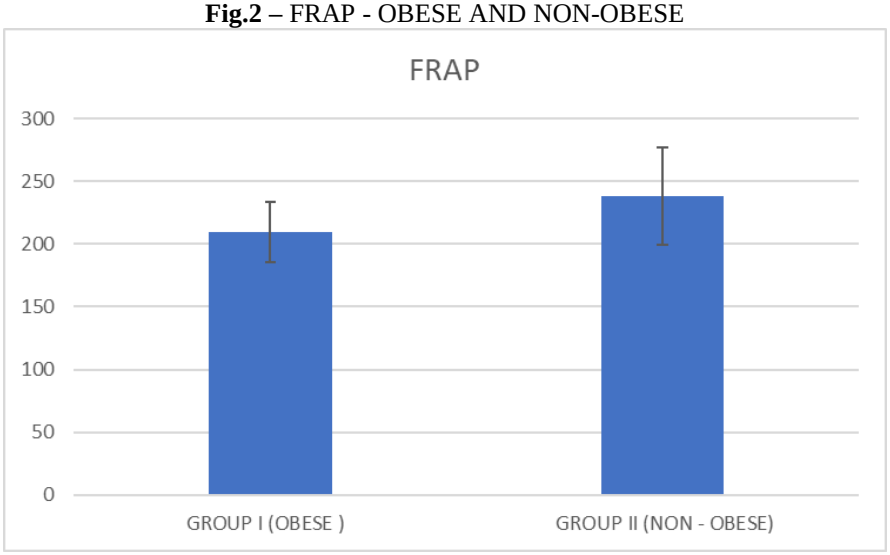
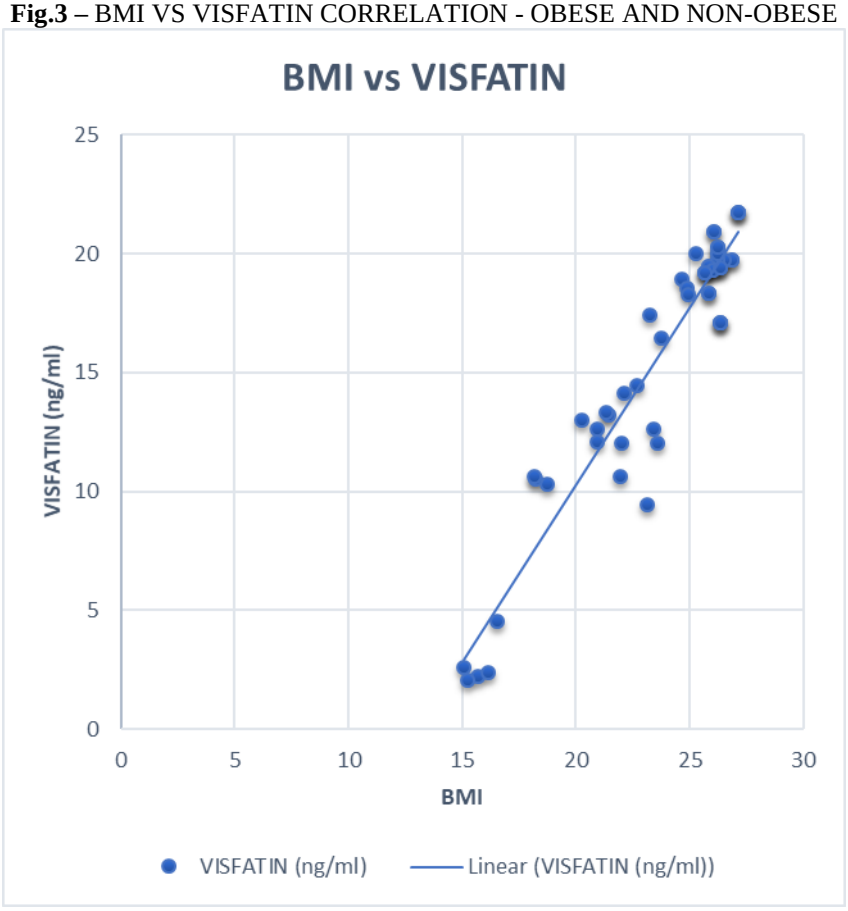


Fig.3 – BMI VS VISFATIN CORRELATION - OBESE AND NON-OBESE



III. Results

Table 1 shows baseline parameters in group I (obese) and group II (non-obese) post menopausal women. There was significant difference in WHR among the groups but no significant difference with respect to blood pressure, serum HDL-C, LDL-C, TGL , VLDL, AST and blood urea levels. Table 2 shows significant difference in total cholesterol in obese women. Table 3 shows serum visfatin and TBARS and FRAP in group I and group II post menopausal women. Serum visfatin and TBARS were significantly elevated in obese women and also there was a significant decrease in FRAP in obese. Table 4 shows Pearson correlation analysis between visfatin,TBARS and BMI. There was significant positive correlation between BMI and visfatin,TBARS in obese women and also there was significant negative correlation between visfatin and FRAP. In obese ,there was

about 1.5 fold increase in serum visfatin levels and TBARS was also significantly elevated in obese post menopausal women (fig.1) compared to non obese. There was significant decrease in FRAP in obese post menopausal women (fig.2). There is a strong positive correlation between BMI and visfatin (fig.3)

IV. Discussion

Menopause is a risk factor for CVD as low estrogen has detrimental effect on cardiovascular system [6]. But there are no consistent reports on cardio protective effect of estrogen. It was observed that there was a significant increase in serum total cholesterol level but no significant difference in case of LDL-C, HDL-C and TGL. It was observed that in obese postmenopausal women there was a significant increase of WHR. WHR and BMI were reported to have signifant association with CVD [15]. This could be due to fat redistribution and increased deposition in abdominal region.The incidence of cardiovascular disease among post menopausal women increases due to increased adiposity and vascular remodelling. There is increased central fat deposition in menopausal women and is considered as a risk factor for CVD. Visfatin plays a role in endothelial dysfunction. In the present study there was about 1.5 fold increase of serum visfatin levels in obese post menopausal women. Chang et al (2007) observed an increase in serum visfatin levels in diabetes mellitus, hypertension, and chronic kidney disease but they are ruled out in the present study. Haider et al observed that plasma visfatin concentration increased with abdominal obesity and type II DM and high concentration of plasma visfatin reduced after weight loss. Hence increase in visceral adipose tissue could be the factor for increase in serum visfatin levels[11], as supported by increased BMI and WHR. Endothelial Progenitor Cells (EPCs) in the circulation are regarded as an indicator of endothelial function and cardiovascular disease prognosis [16]. Shuchun Chen et al (2014) [17] has reported increased levels of serum visfatin, increased oxidative stress and decreased levels of antioxidants accompanied by decreased number of EPCs in obese population. In the present study, there was elevated visfatin, TBARS levels and decreased antioxidant status in obese postmenopausal women which could increase the CVD risk.

V. Conclusion

Increased serum visfatin level and oxidative stress observed in obese postmenopausal women could be due to visceral obesity as indicated by increase in BMI and WHR. Increase of serum Visfatin, a marker of endothelial dysfunction could enhance the CVD risk. Further studies are required to findout whether weight redution could decrease the CVD risk by reducing the serum levels of visfatin and oxidative stress in postmenopausal women.

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