VISCERAL ADIPOSITY INDEX AND ATHEROGENIC INDEX OF PLASMA: SURROGATE MARKERS OF CARDIOVASCULAR RISK IN POSTMENOPAUSAL WOMEN

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Abstract

Introduction: Cardiovascular disease has become a major cause of death especially in developing countries. This has raised serious concern especially on the health of postmenopausal women due to hormonal imbalance experienced at this transition. Early detection of cardiovascular disease is a key to its prevention. Therefore, this study aims to assess atherogenic index of plasma (AIP) and visceral adiposity index (VAI) as surrogate markers of cardiovascular risk in postmenopausal women.

Materials and Methods: This cross-sectional study recruited randomly a total of two hundred and seventy-six (276) participants which comprises of fifty four percent (54%) postmenopausal and forty six percent (46%) premenopausal subjects. Anthropometric variables such as blood pressure, body mass index, waist circumference, waist to hip ratio were measured while blood lipids and estradiol were estimated using standard methods. Visceral adiposity index, Atherogenic index of plasma, and other cardiovascular risk indices were calculated using standard formula.

Results: The result of the study revealed significantly higher ($p<0.05$) VAI, AIP, total cholesterol, triglycerides, very low-density lipoprotein, low density lipoprotein and other cardiovascular risk indices in postmenopausal women than premenopausal women. However, there was significantly lower estradiol in postmenopausal women when compared with premenopausal women but no significant difference observed in high density lipoprotein of postmenopausal and premenopausal women when compared.

Conclusion: It is therefore pertinent to note that postmenopausal women are at a greater risk for cardiovascular diseases and that VAI and AIP can be used as alternative screening tool for the evaluation of cardiovascular risk routinely.

Keywords: Postmenopausal women, Visceral Adiposity Index, Atherogenic Index of Plasma, Cardiovascular risk, Surrogate marker.

Introduction

Cardiovascular diseases (CVD) have become the major cause of death in Nigeria, with dyslipidemia, obesity and overweight being the major risk factors.[1] As the dynamics of life set in due to sedentary lifestyle, reduction in physical exercise, changes in diet, urbanization as well as aging takes the central stage, diabetes mellitus, hypertension and obesity begins to manifest as they are risk factors for cardiovascular diseases. World health organization in their 2021 report on cardiovascular diseases reported that over seventy – five percent of cardiovascular disease related death occurs in the low economies countries.[2] Postmenopausal health of women is fragile because, it comes with a lot of challenges due to the deficiency in the secretion of estrogen.[3] Shaw and colleagues[4] opined that, estrogen has a protective effect during the reproductive age on women hence they are late to the development of cardiovascular diseases like their male counterparts. There is increased visceral fat function in postmenopausal as part of endocrine system in secreting inflammatory markers that has a vital role in the occurrence of metabolic syndrome and cardiovascular diseases.[5] It is observed that the visceral fat takes part in the production of adipocytokines and participated in pro-inflammatory activities. Its dysfunction increased these secretion and activities that results in unfavourable lipid profile as well as decline in insulin sensitivity. Visceral adipose dysfunction is believed to be a predictor of cardio metabolic risk in individuals and this can be measured by visceral adiposity index (VAI). Monteleone and coworkers[6] reported that production of pro-inflammatory cytokines and adipokines in visceral tissues increase the propensity to atherosclerosis and cardiovascular diseases after menopause.

Visceral adiposity index is a mathematical equation that is gender specific which is observed to be a more potent predictor of visceral adipose dysfunction when compared to other traditional anthropometric variables such as body mass index, waist circumference and lipid profile.[7] Arderiu and colleagues[8] in their study observed that fat in the visceral and subcutaneous region play a vital role in the pathogenesis of cardiovascular diseases. The visceral adiposity index is reported to be an alternative means to measure visceral adipose tissue and can predict cardiovascular related disorders such as hypertension, diabetes mellitus, metabolic syndrome etc.[9] In an earlier study, Hosseinpanah et al,[10] identified VAI as an index of visceral fat function that correlate positively with cardiovascular events. Also, El Shikieri and coworkers[11] in their study suggested that VAI can be used as simple tool for checking adipose tissue dysfunction and cardiometabolic risk. Mohammadreza and colleagues[12] opined that VAI was a reliable indicator in identifying the risk of cardiovascular disease in females. In an earlier study by previous authors, [13] they observed that postmenopausal women have higher visceral adiposity index. On the other hand, atherogenic index of plasma (AIP) is logarithmic conversion of triglycerides and high-density lipoprotein cholesterol ratio and has been observed as a strong predictor of cardiovascular diseases in various populations. This is due to the fact that it is associated with particle size of all the lipoprotein cholesterol. Nwagha et al[14] in their study on postmenopausal women observed that AIP is positively associated with cardiovascular diseases.

The traditional anthropometric measurements such as body mass index, waist circumference, waist to hip ratio, waist to height ratio and the

lipid biomarkers have been used for the assessment of visceral adipose tissue.

Dysfunction and cardiovascular risk. However, these have been observed to be single parameters hence there is need to combine both the anthropometric variables as well as blood lipids parameters for the evaluation of cardiovascular risk. A search through the literature shows paucity of data on atherogenic index of plasma (AIP) and visceral adiposity index (VAI) among postmenopausal women in this locality. Hence the aim of this study is to evaluate atherogenic index of plasma and visceral adiposity index as surrogate markers of cardiovascular disease in postmenopausal women.

Materials and Methods

Study Area

This is a cross-sectional study conducted in Ekpan–Uvwie, a twin city to Warri, the commercial nerve centre of Delta State, Niger –Delta of Nigeria.

Study subjects

A total of two hundred and seventy-six (276) participants were recruited randomly for this study. This comprises of one hundred and twenty-six (126) premenopausal and one hundred and fifty (150) postmenopausal subjects. Participants consent was obtained verbally after explanation of the study protocol to them while ethical clearance was given with DT/MOH/EC/16/21. by the Ministry of Health Asaba.

Anthropometric measurements

Waist circumference was obtained using a flexible meter tape at the midpoint between the lower rib cage and the iliac crest. Participants were advised to wear light clothes without shoes and weight and height of the individual was obtained with a stadiometer while body mass index (BMI) was by multiplying body weight (kg) by square height (meters) (m^2). Blood pressure was measured with mercury in glass Accuson sphygmomanometer. The subjects were allowed to rest for some minutes while sitting comfortably. The suitable size cuff of was applied to the arm and inflated rapidly until when the reading was above the level where the pulse disappeared with about 30 mmHg and then deflated slowly. The Korotkoff sounds were observed at the brachial artery with stethoscope. The first Korotkoff phase I (first heart sound) is the systolic blood pressure while the Korotkoff phase v (at the point when the heart sound disappeared) is the diastolic blood pressure. This same procedure was performed for the other arm to rule out bias. The one with higher reading was recorded as the blood pressure.

Collection of blood Samples

After an overnight fast of about 6-8hours, about 6ml of fasting blood samples was obtained using aseptic precautions and dispensed in a plain container. This was allowed to clot and serum harvested after separation at 3000 revolution per minute in a centrifuge. The serum was kept frozen at -20^{o}C until ready for analysis.

Biochemical analysis

All biochemical analysts were analyzed by standard methods while ratios were calculated using standard formula. Total cholesterol estimated according to Richmond,[15] triglycerides was according to Trinder,[16] high density lipoprotein (HDL-C) was according to Burstein et al.[17] Very low-density lipoprotein and low-density lipoprotein was calculated using Friedewald equation by Friedewald et al.[18] Estradiol was estimated by enzyme immunoassay (ELIZA) method.

Calculation of Ratio

The various ratios were calculated with formula. Visceral adiposity index (VAI) was computed according to Amato et al, [19] Atherogenic Coefficient (AC) was by Ikewuchi and Ikewuchi,[20] Atherogenic Index of Plasma (AIP) by Dobiasova,[21] Cardiac Risk Ratio (CRR) and Non- High-density lipoprotein (NHDL) by Anie.[22]

Statistical analysis

Data were analyzed using statistical package for social sciences (SPSS) version 23. Differences in means were by student t- test at 95% confidence interval with p-value at < 0.05 while Pearson's correlation was used for association of variables.

Results

The result of the study as presented below shows postmenopausal subjects 150 (54%) while premenopausal subjects are 126 (46%) as shown in the Figure 1 below.

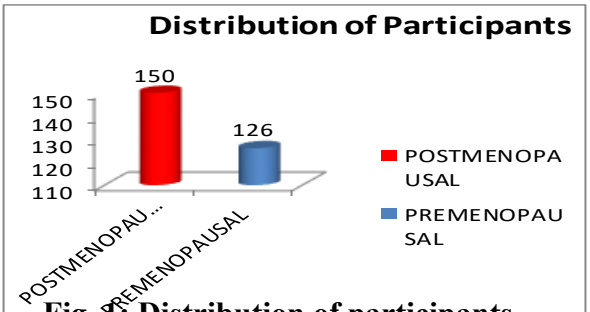

Fig. 1: Distribution of participants

Table 1 shows the anthropometric variables of premenopausal and postmenopausal subjects. Premenopausal subjects had significantly lower ($p<0.05$) blood pressure (mmHg) than postmenopausal subjects. The premenopausal subjects had significantly higher ($p<0.05$) body mass index (kg/m^2) than postmenopausal subjects when compared. There was a significantly higher ($p<0.05$) waist circumference in premenopausal subjects than postmenopausal subjects when compared. There was significantly higher ($p<0.05$) hip circumference (m) in premenopausal subjects than postmenopausal subjects. There was no significant difference ($p>0.05$) in waist to hip ratio between postmenopausal and premenopausal subjects when compared.

Table 2 shows lipid profile and cardiovascular risk indices of premenopausal and postmenopausal women. Premenopausal subjects had significantly lower ($p<0.05$) total cholesterol (mmol/l), triglycerides (mmol/l) than postmenopausal women when compared. There was no significant difference ($p>0.05$) in HDL (mmol/l) distribution between premenopausal and postmenopausal women when compared. Postmenopausal women had significantly higher ($p<0.05$) LDL (mmol/l) and VAI than premenopausal women when compared. Premenopausal women had significantly lower ($p<0.05$) AC, AIP, CRR and non-HDL (mmol/l) than postmenopausal women when compared. There was a significantly lower ($p<0.05$) estradiol in postmenopausal women than premenopausal women as shown in Figure 2. There was a negative association between the cardiovascular risk indices and estradiol as shown in table 4.

Table 1: Mean ± SD of anthropometric variables of premenopausal and postmenopausal female individuals.

Parameters	Premenopausal (n=126)	Postmenopausal (n=150)	t value	P value
SBP(mmHg)	124.28±19.13	136.56±30.65	-3.016	0.003*
DBP(mmHg)	77.82±12.21	80.06±15.85	-0.911	0.363†
Weight(kg)	90.73±17.52	78.16±17.80	3.797	0.000*
Height(m)	162.56±6.70	158.06±9.15	3.295	0.001*
BMI(kg/m^2)	34.31±6.47	30.94±6.23	2.734	0.007*
WC(m)	107.92±14.29	101.75±15.87	2.214	0.028*
HC(m)	117.68±13.52	110.81±11.72	2.697	0.008*
WHR	0.97±0.06	0.92±0.09	0.051	0.960†

***Not Significant** ****Significant**

Key:

SBP - Systolic blood pressure **WC -** Waist circumference
DBP - Diastolic blood pressure **BMI -** Body mass index
WHR - Waist to hip ratio **HC -** Hip circumference

Table 2: Mean ± SD of lipid profile and cardiovascular indices of premenopausal and postmenopausal female individuals

Parameters	Postmenopausal (n=150)	Premenopausal (n=126)	t value	P value
TC(mmol/l)	4.67±1.30	3.76±0.80	3.844	0.000*
TG(mmol/l)	1.68±0.53	1.35±0.43	3.276	0.001*
VLDL(mmol/l)	0.76±0.24	0.62±0.20	3.276	0.001*
HDL(mmol/l)	0.92±0.15	0.97±0.19	-1.559	0.121†
LDL(mmol/l)	2.99±1.31	2.18±0.81	3.410	0.001*
AC	4.30±1.78	3.11±1.39	3.582	0.000*
CRR	5.30±1.78	4.11±1.39	3.582	0.000*
NHDL(mmol/l)	3.75±1.39	2.79±0.93	3.760	0.000*
E_2(ng/ml)	21.93±17.69	53.13±32.69	5.090	0.000*

†Not Significant ***Significant**

TC - Total cholesterol **VLDL -** Very low-density lipoprotein
TG - Triglyceride **LDL -** Low density lipoprotein
CRR - Cardiac risk ratio **HDL -** High density lipoprotein
AC - Atherogenic coefficient **NHDL-** Non-high-density lipoprotein
E2 - Estradiol

Table 3: Mean ± SD of VAI and AIP of postmenopausal and premenopausal women

Parameters	Postmenopausal (n=150)	Premenopausal (n=126)	t value	P value
VAI	5.44±0.61	2.78±0.40	12.67	0.000*
AIP	0.23±0.16	0.13±0.16	3.479	0.001*

†Not Significant ***Significant**
AIP Atherogenic index of plasma
VAI Visceral Adiposity Index

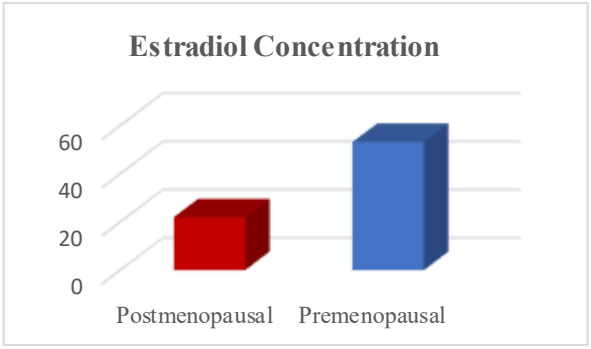

Fig. 2: Concentration of estradiol in postmenopausal and premenopausal women

Table 4: Correlations of cardiovascular risk indices with estradiol.

PARAMETER	Estradiol
AC	0.103**
AIP	0.059**
CRR	0.103**
NHDL	0.129**

**** Negative Correlation**

Discussion

Postmenopausal women health has become a thing of concern due to their propensity to non- communicable diseases. Our study examines visceral adiposity index (VAI) and atherogenic index of plasma (AIP) of postmenopausal women as markers of cardiovascular risk. There was a significantly higher ($p<0.05$) blood pressure among postmenopausal women than premenopausal women in this study, which is in tandem with earlier observation by Tyagi *et al.*[23] This higher blood pressure in postmenopausal women may be attributed to peripheral blood resistance which occurs in postmenopausal era as earlier observed by Ogwumike *et al.*[24] Also, the higher blood pressure may be due to loss of estradiol, as observed in this study, which is a potential vasodilator and antihypertensive, during child bearing years as earlier opined by Nie et al.[25] An earlier study by Thurston et al[26] observed that higher estrone level which is analog of estradiol enhance better endothelial function. Postmenopausal women had lower ($p<0.05$) BMI than premenopausal women but no significant difference ($p>0.05$) was observed in the WHR of postmenopausal and premenopausal women when compared. Postmenopausal women exhibited a higher ($p<0.05$) total cholesterol than premenopausal women.

This is in accordance with report of previous authors[27,28,29] which in their separate studies reported a higher total cholesterol in postmenopausal women when compared with premenopausal women but in contrast with other authors [30,31,32] which reported no significant difference between premenopausal and postmenopausal women. The increased total cholesterol may be attributed to the hypertrophy of the estrogen hormone in the postmenopausal women as seen in this study and earlier observed by Nie et al.[25] Postmenopausal women had significantly higher (P<0.05) triglyceride when compared with premenopausal women. This is in contrast to the work of Igweh and colleagues[31] that observed no significant differences in the triglycerides level of postmenopausal and premenopausal women. The increased triglycerides in this study may be attributed to the reduced level of estradiol present in postmenopausal women as seen in this study as a result of menopausal transition. No significant difference (p>0.05) between the HDL-C of postmenopausal and premenopausal women was observed. This is in accordance with earlier authors [28,29,32] observations that did similar work on premenopausal and postmenopausal women. Postmenopausal women had significantly higher (p<0.05) LDL when compared with premenopausal women. This is in tandem with earlier observation by Nie et al.[25] This implies that postmenopausal women have greater propensity in the development of cardiovascular diseases. Postmenopausal women had significantly higher (p<0.05) AC than premenopausal women. This implies that increase in age increases atherogenic coefficient which make such individuals more atherogenic. Comparing the AC value of 0.9 as earlier reported by previous authors[33] for non-diabetic non-obese subjects with 4.30±1.78 and 3.11±1.39 observed in this study for postmenopausal and premenopausal women respectively, it is therefore pertinent to state that premenopausal and postmenopausal women in this study have greater risk to cardiovascular disease. This study observed a significantly higher (p<0.05) cardiac risk ratio among postmenopausal women than premenopausal women. This is also same for the non - HDL when they were compared. The postmenopausal women had a non-HDL of 3.75±1.39 mmol/l while premenopausal is 2.79±0.93 mmol/l. When these values are compared with the cut-off values 3.3 mmol/l observed by Anie[22] and 1.2 ± 0.2 mmol/l observed by Adu et al[33] for non - diabetic subjects, it therefore implies that postmenopausal have a higher cardiovascular risk. The non-HDL-C is said to have a strong relationship with small dense LDL-C (sdLDL-C) levels[34] and its predictive importance for cardiovascular risk is better that low density lipoprotein.[35] The correlation between non-HDL and the small dense LDL gives an additional impetus for the use of non-HDL as a marker of cardiovascular diseases.[34]

Visceral adiposity index (VAI) of postmenopausal women was observed to be significantly higher (p<0.05) than VAI of premenopausal women. The VAI of postmenopausal was observed to be 5.44±0.61 and premenopausal 2.78±0.40. However, Amato et al[5] proposed the cut -off values for VAI as 1.92 for ages between 42 and 52 years, 1.93 for ages between 52 and 66 years and 2.00 for those ages over 66 years. Using this baseline as our reference, it therefore implies that there is visceral adipose tissue dysfunction in postmenopausal which enhance secretions of proinflammatory cytokines and adipokines and expose these subjects to cardiometabolic disorders as earlier observed by Monteleone et al[6].

Previous study by Hamzeh et al[36] reported an association between higher VAI and risk factors of cardiovascular diseases, which shows that the high VAI observed in this study is a pointer to higher risk of cardiovascular diseases in postmenopausal women. Postmenopausal women had significantly higher ($p<0.05$) AIP than premenopausal women. This is in accordance with report by previous authors[14,37] which reported similar results on women.

Also, there was a negative correlation between estradiol and cardiovascular risk indices of AC, CRR and AIP. This implies that estradiol and these cardiovascular risk indices are inversely proportional to each other; thereby lower estradiol is associated with higher risk to cardiovascular diseases. This study observed AIP value of 0.23±0.16 in postmenopausal women, and from the classification of cardiovascular risk by Dobiasova[21] that -0.3 to 0.1 as low risk, 0.1 to 0.24 as medium risk and >0.24 as high risk for cardiovascular diseases, postmenopausal women are exposed to medium risk of cardiovascular diseases. Our finding is in agreement with earlier report by El Shikieri[11] that observed postmenopausal women to exhibit medium (moderate) or high cardiovascular diseases based on AIP values. Menopause is therefore observed to be a risk factor in cardiovascular disease which was also opined earlier by Mohammadreza et al.[12] Atherogenic index of plasma (AIP) which is the logarithmic conversion of triglycerides and high density lipoprotein cholesterol ratio is observed to be strongly associated with atherosclerosis and cardiovascular diseases.[21] AIP is associated with the particle size of low-density lipoprotein, high density lipoprotein and very low-density lipoprotein, therefore acting as a very sensitive marker in cardiovascular diseases.[38] There is a positive correlation between AIP and cardiovascular diseases which is in tandem with earlier observation by Bo et al.[39]

Conclusively, this study revealed a high VAI and AIP including other indices of cardiovascular risk among postmenopausal women. This shows that these group of persons have greater propensity to cardiovascular diseases; therefore, VAI and AIP can be a suitable tool for the assessment or evaluation of CVDs in these subjects, reasons being that the methods is inexpensive, reliable and convenient in the early diagnosis of CVDs in populations.

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