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Evaluation of Risk Factors of Cardiovascular Disease on Hypertensive Post-Menopausal Women and Aged-matched Hypertensive Males

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ABSTRACT

***Background**: This study compared plasma lipids and glucose levels in hypertensive post-menopausal women with age-matched hypertensive men. **Methods**: This is a cross sectional study that involves 100 subjects attending out-patient department of Nnamdi Azikiwe University Teaching hospital hypertensive clinics and control subjects. 25 hypertensive post-menopausal women and 25 hypertensive male subjects both within the same age range of 50-60 years. Also 25 hypertensive pre-menopausal women and 25 non-hypertensive controls both within the age range of 30-40 years. The lipid profile parameters (Total Cholesterol (TC), Triglyceride (TG), Low density Lipoprotein (LDL-C), and High Density Lipoprotein (HDL-C)) and fasting plasma glucose were determined using standard methods. The study also assessed the anthropometric indices such as BMI, SBP and DBP in each group. **Results**: The mean levels of TC and TG were significantly lower in post-menopausal hypertensive females when compared with the hypertensive males ($p<0.05$). However, the mean plasma HDL-C and LDL-C did not show any significant difference between the two groups. The comparison of the mean levels of all the parameters in hypertensive males with the non-hypertensive controls showed a significant difference ($P < 0.05$). The mean levels of TC and LDL-C were significantly higher in hypertensive post-menopausal women when compared with hypertensive pre-menopausal females ($P<0.05$). **Conclusion**: This study showed that menopause had altered the plasma lipids of the hypertensive post-menopausal women, but not to the extent of putting them at the same atherosclerosis scale as their male counterpart.*

***Key words:** Hypertension, Menopause, Total cholesterol, Triglycerides.*

INTRODUCTION

The traditional risk factors for atherosclerotic disease include age, gender, hypertension, smoking, body mass index, diabetes and hypercholesterolemia.[1] The female gender is considered a protective factor in the development of atherosclerosis.[2] Studies have shown that premenopausal women have more protective effect on the development of Coronary Heart Disease (CHD) when compared with both men of a similar age and postmenopausal women.[3-5]

Estrogens affect the atherosclerotic process through a variety of mechanisms such as its lowering effect on total cholesterol and LDL-C,[6,7] Lipoprotein (a),[8] and its increasing effect on HDL-C.[9-11] Estrogen also has both acute vasodilatory effect on the vessel wall and an atheroprotective effect involving inhibition of smooth-muscle cell proliferation.[12]

The difference in cardiovascular risk between women and men at early ages disappears gradually after menopause and becomes equal for both sexes after ten years.[13-16] In this manner, cardiovascular diseases are considered to be the primary case of mortality in post-menopausal women.[17] Menopausal status is accompanied by unfavorable levels of cardiovascular risk factors, like changes in body fat, distribution from gynoid to android pattern, abnormal plasma lipids, increased sympathetic tone, endothelial dysfunction, vascular inflammation, and increased blood pressure.[18] Recently, postmenopausal women were reported to have the same prevalence of sub clinical carotids atherosclerosis as men matched with age and traditional risk factors.[19] Study also shows that oestrogen does not appear to provide a cardiovascular benefit in postmenopausal women with established coronary heart disease.[20] Moreover, it has been reported

that more post-menopausal female record an increased incidence of cardiovascular conditions.[17] The reason for this change in disease amongst women is not entirely clear, though however, it may be the observed association between atherosclerosis and hyperlipidemia.

Today, more African women live beyond 50 years, that is, post-menopause, a factor which should further heighten the risk of cardiovascular disease in them. As women age, their health is influenced by factors such as career, diet, physical activity level, the socioeconomic status and environment.[21] These changes, together with natural menopause, process of ageing, and hormonal changes in the reproductive system, affect the well-being of women.[22] The complex, interrelated nature of the process often makes it difficult to distinguish between the symptoms of ageing or those resulting from the loss of overian functions, and factors arising out of socioenvironmental conditions. Thus, we decided to compared men and women of the same age, traditional risk factors and socioeconomic and environmental status in other to ascertain their atherosclerosis status based on their lipid profile and glucose levels. It is hoped that the outcome of this study would improve our understanding of this growing subject and also help the management of menopause for which hormone replacement therapy is already being tried as a preventive measure against ischaemic heart disease arising from hyperlipidaemia.

METHODS

Study population and Design:

A total of 100 subjects, comprising 25 hypertensive post-menopausal women and 25 hypertensive men, both within the age bracket of 50-60yrs, and 25 hypertensive pre-menopausal women and 25 non hypertensive (men and women) both within the age bracket of 30-40yrs. They were all recruited after taking a thorough clinical history. Hypertensive women aged between 50 and 60 years, with absence of menstrual cycles for at least one year, were included. In all the groups, those that have any history of chronic illness, had undergone hysterectomy, and on hormone replacement therapy, were excluded from the study. The informed consent was obtained from all the participants, and the experimental protocol was approved by the Ethics committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi.

All the participants were instructed to refrain from food, alcohol and tobacco for 12 hours prior to recording and sample collection. They all underwent measurement of height, weight and basal blood pressure. Height was measured to the nearest 0.1 cm without footwear, using vertically movable scale. Weight was measured to the nearest 100 grams using a digital scale. A basal recording of blood pressure was done using Automatic Blood Pressure Monitor.

Sample Collection and Biochemical Analysis

5 mls of fasting venous blood samples were collected from all respondents for the analysis. A part was dispensed into fluoride oxalate bottles for glucose determination using standard enzymatic spectrophotometric method (Glucose Oxidase method). The remaining part was dispensed into a Na-EDTA bottle and the plasma separated and stored at -20ºC until analysis of Lipid profile.

The total cholesterol (TC) was estimated using enzymatic endpoint method. The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from hydrogen peroxide and 4 - aminoantipyrine in the presence of phenol and peroxidase.

High Density Lipoprotein (HDL) was estimated using enzymatic method. Low density lipoprotein (LDL and VLDL) and chylomicron fractions are precipitated quantitatively by the addition of phosphotungstic acid in the presence of magnesium ions. After centrifugation, the cholesterol concentration in the HDL fraction, which remains in the supernatant was determined.

Triglyceride (TG) was estimated using enzymatic method. The triglycerides are determined after enzymatic hydrolysis with lipases. The indicator is a quinoneimine formed from hydrogen-peroxide, 4-aminophenazone and 4-chlorophenol under the catalytic influence of peroxidase.

Glucose was estimated using glucose oxidase method. Glucose in plasma reacts with oxygen to give gluconic acid and hydrogen peroxide. This reaction is catalyzed by glucose oxidase enzyme. The hydrogen peroxide oxidizes the chromogen (4

- aminophenazone) in the presence of the enzyme peroxidase to give a colored compound that was measured spectrophotometrically.

The LDL-C was calculated by the previously established formula of friedwald. Body mass indix was calculated from measured height and weight. The TC : HDL ratio and averages (mean + SD) were determined.

Statistical Analysis

The version 20 of Statistical Package for Social Sciences (SPSS) was used in statistical analysis. All data were expressed as the mean ± standard deviations. The test of significant difference between two groups was done by the student T-test with $p<0.05$ being the cut-off point of significant.

RESULTS

The comparison of the mean levels of parameters between the hypertensive post-menopausal women and those of their male counterparts showed significant difference ($p<0.05$) in levels of triglycerides and total cholesterol. However, the results showed no statistical significant difference in the levels of age, BMI, HDL-C. LDL-C, TC: HDL, FBG, systolic BP, and diastolic BP in these two groups (Table 1).

Table 1. The mean levels of some parameters in the Hypertensive post-menopausal women and those of their male counterpart.

PARAMETERS	POST–MENO (25) mean ± SD	MALES (25) means ± SD	P =VALUES
AGE (yrs)	57.68 ± 2.45	57.80 ± 2.45	1.000
BMI (kgm^{-2})	28.51 ± 1.59	26.60 ± 1.80	0.080
TC (mmoL/L)	5.21 ± 0.81	5.92 ± 0.47	0.004
HDL-C (mmol/L)	1.15 ± 0.32	1.03 ± 0.28	0.722
LDL-C (mmol/L)	3.37 ± 0.44	4.06 ± 0.62	0.388
TG (mmol/L)	0.99 ± 0.04	1.64 ± 0.36	0.000
TC : HDL	4.78 ± 1.13	6.21 ± 1.90	0.104
FBG (mmol/L)	5.39 ± 1.78	5.8 ± 2.75	0.829
Systolic BP (mmHg)	174.80 ± 15.08	176.16 ± 20.82	0.987
Diastolic BP (mmHg)	107.80 ± 13.03	105.40 ± 15.06	0.862

The comparison of the mean levels of the parameters between the hypertensive post-menopausal women and those of hypertensive pre-menopausal women showed that there was statistical significant difference ($p<0.05$) between the mean levels of age, TC, LDL-C, FBG, systolic BP, and diastolic BP of the

hypertensive post-menopausal and that of hypertensive pre-menopausal women. The result also showed that there was no statistical significant different ($p>0.05$) between the mean levels of BMI, HDL-C, TC: HDL and FBG, of the hypertensive post-menopausal women and that of hypertensive pre-menopausal women (Table 2).

Table 2. The mean levels of the some parameters of the hypertensive post-menopausal women and those of the hypertensive pre-menopausal women.

PARAMETERS	POST-MENO (25) mean ± SD	PRE-MENO (25) mean ± SD	P-VALUES
AGE (yrs)	57.68 ± 2.75	38.68 ± 1.84	0.000
BMI (kgm^{-2})	28.51 ± 1.59	26.75 ± 1.83	0.123
TC (mmol/L)	5.21 ± 0.81	4.89 ± 0.65	0.000
HDL-C (mmol/L)	1.15 ± 0.32	1.25 ± 0.37	0.826
LDL-C (mmol/L)	3.75 ± 0.44	3.04 ± 0.06	0.03
TG (mmol/L)	0.99 ± 0.40	1.65 ± 0.62	0.000
TC : HDL	4.78 ± 1.13	4.21 ± 1.29	0.795
FBG (mmol/L)	5.39 ± 1.78	4.55 ± 1.09	0.336
Systolic BP (mmHg)	174.80 ± 15.08	150.52 ± 8.14	0.000
Diastolic BP (mmHg)	107.80 ± 3.09	93.64 ± 3.09	0.000

The comparison of the mean levels of the parameters between the hypertensive post-menopausal women and those of the non-hypertensive control individuals shows that there is statistical significance difference ($p<0.05$) between the mean levels of age, BMI, TC, HDL-C, LDL-C, systolic BP and diastolic BP of the hypertensive post-menopausal women and that of non-hypertensive control individuals. The result also shown that there were no statistical significant differences between the levels of TG, TC:HDL, and FBG of the hypertensive post-menopausal women and that of non-hypertensive control individuals (Table 3).

Table: 3. The mean levels of some parameters of the hypertensive post-menopausal women and those of non-hypertensive control individuals.

PARAMETERS	POST-MENO N = 25	CONTROL N = 25	P-VALUE
AGE (yrs)	57.68 ± 2.75	43.00 ± 8.94	0.000
BMI (kgm^{-2})	28.51 ± 1.59	23.92 ± 4.68	0.000

TC (mmol/L)	5.21 ± 0.81	4.50 ± 0.86	0.004
HDL-C (mmol/L)	1.15 ± 0.32	1.45 ± 0.60	0.018
LDL-C (mmol/L)	3.75 ± 0.44	2.25 ± 1.01	0.000
TG (mmol/L)	0.99 ± 0.04	1.22 ± 0.54	0.354
TC:HDL	4.78 ± 1.13	3.97 ± 3.58	0.569
FBG (mmol/L)	5.39 ± 1.78	4.19 ± 0.74	0.082
SBP (mmHg)	1.74.80± 15.08	115.36 ± 952	0.000
DBP (mmHg)	107.80 ± 13.03	70.88 ± 7.94	0.000

The comparison of the mean levels of the parameters between the hypertensive males and those of the non-hypertensive control individuals shows that there were statistical significant difference ($p<0.05$) between the mean levels of the all the parameters in hypertensive males and that of the non-hypertensive males control individuals (Table 4).

Table 4**.** The mean levels of some parameters of the hypertensive males and those of the non-hypertensive control individuals.

PARAMETERS	MALES N = 25	CONTROLS N = 25	P-VALUES
Age (yrs)	57.80 ± 2.45	43.00 ± 8.94	0.000
BMI (kgm^{-2})	26.60 ± 1.80	23.92 ± 4.68	0.005
TC (mmol/L)	5.92 ± 0.47	4.50 ± 0.86	0.000
HDL-C (mmol/L)	1.03 ± 0.28	1.45 ± 0.60	0.001
LDL-C (mmol/L)	4.06 ± 0.62	2.25 ± 1.01	0.000
TG (mmol/L)	1.64 ± 0.36	1.22 ± 0.54	0.015
TC:HDL	6.21 ± 1.90	3.94 ± 3.58	0.003
FBG (mmol/L)	5.82 ± 2.75	4.19 ± 0.74	0.008
Systolic BP (mmHg)	176.16 ± 20.82	115.36 ± 9.52	0.000
Diastolic BP (mmHg)	105.40 ± 7.94	70.88 ± 7.94	0.000

DISCUSSION

This study showed that the levels of TG and TC are significantly lower in hypertensive post-menopausal women than in their male counterpart. This shows that there is a lower tendency for hypertensive post-menopausal females to develop atheroma than males of their age. This outcome agrees with the situation reported in pre-menopausal hypertensive females, which showed that hypertensive child-bearing females stood less risk of atherosclerotic diseases, compared with men their age.[23] It also agrees with the findings in normal post-menopausal females, which reported that normal postmenopausal women, by plasma lipid analysis, stand less risk of atheroma-formation than their male counterparts.[24]

The female gender already largely shields these females from the risk of atheroma formation.[2] To further favour the females, oestrogen is known to have an inverse relationship with plasma lipid level.[25] Estrogens affect the atherosclerotic process through a variety of mechanisms such as its lowering effect on total cholesterol and LDL,[6,7] Lipoprotein (a),[8] and its increasing effect on HDL.[9,10] Estrogen also has both acute vasodilatory effect on the vessel wall and an atheroprotective effect involving inhibition of smooth-muscle cell proliferation.[12] Though menopause is associated with waning influence of oestrogen, aromatization in peripheral fatty tissues could partly sustain the oestrogen influence far into the postmenopausal period. This may be in operation in Nigeria females, with a BMI above pre-menopausal values.

Furthermore, the comparison between hypertensive post-menopausal women and non-hypertensive controls, and also between hypertensive men and non-hypertensive controls showed that both post-menopausal women and their male counterpart are at risk of developing CHD but tends to be more among hypertensive men. This is because all the parameters analyzed in this study were significantly higher in hypertensive men than in non-hypertensive controls, while there is no significant difference in the mean levels of triglyceride, TC:HDL, and fasting plasma glucose in hypertensive post-menopausal women and non-hypertensive controls. Thus, putting the hypertensive post-menopausal women less in the atherosclerosis scale than their male counterpart.

This study also showed that the level of LDL-C and cholesterol are significantly higher in hypertensive post-menopausal women than in hypertensive pre-menopausal women. This is in line with some studies that showed that pre-menopausal women have more protective effect on the development of CHD when compared with both men of a similar age and postmenopausal women.[3,5] Factors that may partly explain the positioning of the post-menopausal women on the atheroma scale than pre-menopausal women would include age,[1] higher BMI, diminishing oestrogen effect[23] and duration of the hypertension. These findings supported our present study as our results showed significantly higher levels of BMI, SBP, DBP, and age in post-menopausal women than in pre-menopausal women.

CONCLUSION

In conclusion, this study showed that menopause had altered the plasma lipids of the hypertensive females, but not to the extent of putting them at the same level of atherosclerosis risk scale as their male counterpart.

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