





## RESEARCH ARTICLE

# Assessment of cardiovascular risk in post-menopausal women in Ghana [version 1; peer review: 1 approved, 1 approved with reservations]

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## Abstract



**Background:** Cardiovascular diseases (CVD) continue to be a major cause of death among post-menopausal women. We sought to assess cardiovascular risk among pre- and post-menopausal women living within the Cape Coast Municipality by comparing the lipid profiles and other emerging biomarkers of CVD, i.e. the atherogenic index of plasma (AIP), visceral adiposity index (VAI), body adiposity index (BAI) and Castelli index I (CRI-I).

**Methods:** A comparative cross-section of 150 women (75 pre-menopausal women and 75 post-menopausal women) visiting the University of Cape Coast hospital for regular checkups were randomly recruited into the study. Socio-demographic and clinical characteristics of participants were obtained with the aid of a structured questionnaire. Blood pressure (BP) was measured and lipid profile was estimated using fasting blood samples. Other markers of cardiovascular risk such as BMI, AIP, VAI, BAI and CRI-I were estimated.

**Results:** We report elevated levels of total cholesterol (TC) ( $p < 0.0001$ ), low density lipoprotein (LDL) ( $p < 0.0001$ ), very low-density lipoprotein (VLDL) ( $p = 0.0021$ ), triglycerides (TG) ( $p < 0.0001$ ) and non-high-density lipoprotein (non-HDL-C) cholesterol ( $p < 0.0001$ ) in post-menopausal women compared with pre-menopausal women. High-density lipoprotein (HDL) ( $p < 0.0001$ ) was, however, decreased in post-menopausal women. Mean AIP ( $p < 0.0001$ ), VAI ( $p < 0.0001$ ), BAI ( $p < 0.0038$ ) and CRI-I ( $p < 0.0001$ ) were significantly increased in post-menopausal women compared to pre-menopausal women. We also

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report a positive correlation of TC, TG, VLDL and non-HDL with atherogenic markers AIP, VAI and CRI-I in post-menopausal women. A negative correlation of HDL with AIP, VAI, and CR in post-menopausal women was also observed.

**Conclusions:** Menopause could lead to changes in lipid profile to atherogenicity with associated increase in the risk of CVD. Atherogenic markers such as AIP, VAI, BAI, and CR can serve as potential biomarkers for predicting CVD.

### Keywords

Atherogenicity, menopause, Lipid profile, cardiovascular diseases

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## Introduction

Menopause is a permanent physiological state with cessation of menstruation attributable to the loss of ovarian function and reduction in the production of estrogen<sup>1</sup>. The average age of menopause is reported to be 51 years<sup>2</sup> but the age of natural menopause may vary from 40 to 58 years. This phase is characterized by variety of changes in socio-cultural, physiological and psychological states. These changes culminate into myriad of symptoms including insomnia, sweating, hot flashes, depressive mood, vaginal dryness and general discomfort<sup>3</sup>.

Cardiovascular diseases (CVD) are the major cause of death among post-menopausal women<sup>4</sup>. Studies have shown that premenopausal women have a low risk of CVD as compared to men but after menopause the level of risk increases<sup>5</sup>. Epidemiological data have revealed elevated risk of CVD in postmenopausal females compared to men of the same age<sup>6</sup>. Estrogen is the major female hormone that regulates many aspects of a female's development. Reduced circulating estrogen levels impeded ovulation as results of under stimulation of the hypothalamus to release follicle stimulating hormones<sup>7,8</sup>. Estrogen is known to possess both anti-atherogenic and cardioprotective effect by maintaining high levels of high-density lipoprotein (HDL-C) coupled with decreasing low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG)<sup>9</sup>. Several factors, including diabetes, hypertension, and atherosclerosis among others can lead to CVD in women. The World Health Organization (WHO) has ranked CVDs as the number one cause of death, with global estimation of about 17.7 million deaths in 2015<sup>10</sup>.

Current data have shown that Castelli risk index I and II which are estimated as TC/HDL-C and LDL/HDL-C ratios respectively predict cardiovascular risk accurately than conventional lipid profile indices such as serum TC and serum triglycerides<sup>11,12</sup>. Similarly, comparison of individual lipid ratios in subjects of the Framingham Heart Study unarguably indicates that lipid ratios are significantly more useful predictors of CVD than the individual levels of LDL or HDL<sup>12</sup>. Many clinical studies have also made efforts to introduce better markers of atherogenic dyslipidemia that can predict the risk of CVD to be useful for evaluating response to treatment instead of the classical ratios<sup>13</sup>. Notable among these markers is the atherogenic index of plasma, which has proven to be a strong marker for the prediction of atherosclerosis and coronary heart disease risk<sup>14</sup>.

Menopausal health has received little attention due to high illiteracy rate, poverty and a possible lack of understanding of the clinical dynamics associated with it, irrespective of the fact that menopause is a key risk factors for dyslipidemia which affects cardiovascular health of women. Compared with men, the diagnosis of CVD in women is difficult due to hormone-related changes and difference in sex in the clinical manifestation of CVD. Such limitations and challenges present the need for an increased consciousness of the significance of CVD as a major public health issue for older women. This study therefore sought to assess the cardiovascular risk between pre and post-menopausal woman in the Cape Coast municipality by comparing the lipid profiles and other emerging biomarkers of CVD such as

atherogenic index of plasma visceral adiposity index and basal adiposity index.

## Methods

### Study area and population

We conducted this comparative cross-sectional study among a convenience sample of 150 women between June 2017 and August 2018 at Cape Coast, the capital of the Central Region of Ghana. No attempts were made to control for bias in recruitment. This Region covers an area of approximately 9826 square kilometres or 4.1% of Ghana's land area. The study participants were apparently healthy pre- and post-menopausal women.

### Inclusion criteria

The inclusion criterion used for the study was healthy postmenopausal women aged 40–55 years serving as cases while premenopausal women within the age of 30–40 years were used as comparative controls.

### Exclusion criteria

Those with known cardiovascular and metabolic diseases such as hypertension, diabetes, renal or hepatic disorders, menstrual disorders and those on hormonal replacement therapies were excluded from the study. Also, pregnant and lactating women, women with known thyroid diseases, heavy smokers and alcoholics were not included in the research.

### Ethical approval and consent to participate

Ethical approval for the research was sought from the Institutional Review Board of University of Cape Coast (UCCIRB/CHAS/2017/83). All information regarding the study including the purpose, risks, procedures, and benefits were made known to the participants before seeking for written informed consent.

### Blood sample collection, lipid profile and fasting blood glucose measurement

From each participant, 4 mL of venous blood samples were collected from each participant with a sterilized syringe and needle after an overnight fast (12–14 hours) and dispensed into a gel separator tube. Blood samples were analyzed using a fully automated chemistry analyzer (Mindray BS240. Mindray Bio-Medical Electronics Co., Ltd) to estimate the total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), VLDL, TG and non-HDL. Fasting blood glucose was measured with the URIT glucometer (URIT G26<sup>®</sup>, URIT Medical Electronic, UK).

### Anthropometric measurements

For body mass index (BMI) estimation, height was measured to the nearest centimetre without shoes with a stadiometer (Seca 217, 40 Barn Street B5 5QB Birmingham, United Kingdom) and weight was measured to the nearest 0.1 kg, with a bathroom scale (Zhongshan Camry Electronic Co. Ltd, Guangdong, China). BMI was calculated as a ratio of weight (kg) to height squared (m<sup>2</sup>). This was used to categorize participants as underweight (<18 kg/m<sup>2</sup>), normal (18–24 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>) and obese (>30 kg/m<sup>2</sup>) according to WHO criteria<sup>15</sup>.

### Measurement of blood pressure

Blood pressure measurements were performed according to the American Heart Association recommendations<sup>16</sup>. Measurements of blood pressure were performed using an automatic validated device (Omron HEM711DLX, UK) on the superior left limb. The subjects were made to sit with the legs uncrossed and arm supported at the height of the heart with cuff adapted to the size of the arm. Blood pressure was measured as the mean values of duplicate measurements. Grading of hypertension recorded as follows; “normal” when the systolic blood pressure (SBP) was < 120 mmHg and diastolic blood pressure (DBP) was <80 mmHg “pre-hypertension” when SBP = 120–139 or DBP = 80–89 and “hypertension” when SBP = 140–159 or DBP = 90–99<sup>17</sup>.

### Atherogenic indices

Atherogenic indices estimated included AIP (log (TG/HDL)), visceral adiposity index (VAI) ( $VAI = \left( \frac{WC}{36.5 + (1.89 \times BMI)} \right) \times \left( \frac{TG}{0.81} \right) \times \left( \frac{1.52}{HDL} \right)$ ), body adiposity index (BAI) ( $BAI = \frac{100 \times \text{hip circumference in m}}{\text{height in m} \times \sqrt{\text{height}}} - 18$ ), non-HDL(TC – HDL) and CRI-I(TC/HDL)<sup>18</sup>.

### Data analysis

Data for the study were analyzed using GraphPad prism (6.01) and R statistical software package version 3.0.1. Exploratory analysis was done for descriptive statistical indices such as frequencies, percentages and mean  $\pm$  standard deviations. Tables were obtained from exploratory analysis. Student's t-test was performed to compare pre and post-menopausal groups for

anthropometrics, lipid profiles and atherogenic indices. Fisher's exact test or Chi-square test were employed where deemed fit to assess the association between proportions of variables in pre and post-menopausal groups. Crude and adjusted odds ratios (aOR) at 95% confidence interval (CI) were evaluated for Fisher's exact test outcome. Correlation analysis was done using Spearman's rho moment correlation analysis for lipid profile and atherogenic indices among the study participants. Significance level was determined at  $P < 0.05$ .

## Results

### Participant background

A total of 150 pre and post-menopausal women were enrolled into the study with a significantly older post-menopausal group (59.63 $\pm$ 7.419,  $P < 0.0001$ ) compared to the pre-menopausal group (32.28 $\pm$ 8.820). Also, the post-menopausal group had an elevated SBP ( $P = 0.0003$ ), DBP ( $P = 0.0822$ ), FBS ( $P = 0.0004$ ) as well as a higher BMI compared to the pre-menopausal women (Table 1). Complete demographic information, alongside all other variables measured, are available as *Underlying data*<sup>19</sup>.

### Cardiovascular and atherogenic markers

Serum TC, TG and NON-HDL-C were significantly increased in post-menopausal women compared to pre-menopausal women ( $p < 0.0001$ ). In addition, there was an observed significant increase in LDL-C ( $p < 0.0001$ ) and VLDL ( $p = 0.0021$ ) levels in the post-menopausal women. In comparison with pre-menopausal women, atherogenic markers (AIP, VAI, BAI and CRI-I) were significantly elevated in post-menopausal women ( $p < 0.0001$ ) (Table 2).

**Table 1. Comparison of anthropometric, blood pressure and fasting blood sugar measurements among pre and post-menopausal women.** Data presented as mean  $\pm$  SD.

Variable	Pre- menopausal	Post-menopausal	p-value
Age (years)	32.28 $\pm$ 8.820	59.63 $\pm$ 7.419	< 0.0001
Weight (kg)	61.16 $\pm$ 10.08	6.21 $\pm$ 8.82	0.4969
Height(m)	1.59 $\pm$ 0.06	1.56 $\pm$ 0.062	0.0001
WC (cm)	75.36 $\pm$ 9.67	82.53 $\pm$ 8.68	<0.0001
HC(m)	0.93 $\pm$ 0.13	0.87 $\pm$ 0.08	0.2513
WC/HC	0.87 $\pm$ 0.61	0.95 $\pm$ 0.09	0.9733
BMI (kg/m <sup>2</sup> )	24 $\pm$ 3.644	25.57 $\pm$ 2.883	0.0039
Under weight	5(6.7)	1(1.3)	0.0804
Normal	40(53.3)	33(44.0)	
Overweight	30(40.0)	41(54.7)	
SBP (mmHg)	112.3 $\pm$ 7.591	116.7 $\pm$ 6.960	0.0003
DBP (mmHg)	75.33 $\pm$ 5.285	76.8 $\pm$ 4.976	0.0822
FBS (mmol/L)	5.515 $\pm$ 0.6247	5.865 $\pm$ 0.5547	0.0004
Low	3(4.0)	0(0)	0.1037
Normal	31(41.3)	25(33.3)	
Pre-diabetes	41(54.7)	50(66.7)	

WC, waist circumference; HC, hip circumference; WC/HC, waist to hip ratio; FBS, fasting blood sugar; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

**Table 2. Comparison of Lipid profile and other atherogenic biomarkers among pre and post-menopausal women.**

Variable	Pre-Menopause	Post-Menopause	P-value
TC (mmol/L)	4.130±0.4758	5.889±0.6545	< 0.0001
HDL-C (mmol/L)	1.941±0.5831	1.111±0.2106	< 0.0001
LDL-C (mmol/L)	3.036±0.6797	4.449±0.7094	< 0.0001
VLDL (mmol/L)	0.3381±0.4217	0.5043±0.1803	0.0021
TG (mmol/L)	0.576±0.2869	1.087±0.3612	< 0.0001
NON-HDL (mmol/L)	2.189±0.8091	4.778±0.7299	< 0.0001
AIP	-0.5333±0.2251	-0.02147±0.1839	< 0.0001
VAI	0.6431±0.9652	1.907±1.907	< 0.0001
BAI	28.31±6.576	31.08±4.847	0.0038
CRI-I	2.366±1.009	5.523±1.318	< 0.0001

TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; VLDL, very low-density lipoprotein; TG, triglycerides; AIP, atherogenic index of plasma; BAI, body adiposity index; CRI-I, Castelli index I.

Higher levels of TC, LDL-C, AIP, BAI and CRI-I, as well as low levels of HDL-C, were all crudely associated with post-menopausal women ( $p < 0.0001$ ). However when the data was adjusted for age and BMI, only elevated levels of TC [aOR=76.58 (95%CI=5.880-2439.396),  $P=0.0032$ ], LDL-C [aOR=11.76 (95%CI=1.934-90.816),  $P=0.011$ ], BAI [aOR=41.19 (95%CI=6.7511-321.0692),  $P=0.0001$ ], CRI-I [aOR=818.824 (95%CI=51.900-29515.961),  $P=0.0001$ ] as well as low levels of HDL-C [aOR=11.76 (95%CI=1.934-90.816),  $P=0.011$ ] were significantly associated with post-menopausal women (Table 3).

In post-menopausal women, we report a positive correlation of TC with all the cardiovascular and atherogenic markers except HDL-C whilst HDL-C on the other hand showed a significant negative correlation with all the atherogenic and cardiovascular markers with the exception of BAI, which wasn't significant (Figure 1).

## Discussion

Although CVD is the major cause of death and disability in women, it usually starts about 10 years late in men of the same age. It is also true that CVD are the major cause of mortality in post-menopausal women<sup>4</sup>. The patterns of dyslipidemia that leads to CVD and its associated complications have been linked with hormonal changes associated with menopause. Estrogen is known to possess both anti-atherogenic and cardioprotective effect by maintaining an acceptable balance between pro/anti-atherogenic and cardiovascular risk markers<sup>9</sup>. We therefore sought to assess cardiovascular and atherogenic risk among pre and post-menopausal women in the Cape-Coast municipality.

In comparison to pre-menopausal women, we report elevated levels of TC ( $p < 0.0001$ ), VLDL, TG ( $p < 0.0001$ ), LDL-C ( $p < 0.0001$ ) and NON-HDL cholesterol ( $p < 0.0001$ ) in post-menopausal women. This is in line with earlier findings by Pardhe *et al.*, who

also reported significantly increased levels of TG, TC, LDL-C and reduced levels of HDL-C among Nepalese women<sup>4</sup>. Adverse changes in lipids and lipoprotein independent of age has been linked to menopause<sup>20</sup>. Among all the risk factors for CVD, the major indication suggests an association of estrogen with the observed discrepancies in lipids and lipoproteins<sup>12</sup>. Earlier studies have reported an increase in the release of free fatty acids into circulation due to high-fat accumulation leading to elevated hepatic triglycerides synthesis<sup>21</sup>. In addition, a reduction in estrogen after menopause increases plasma lipoprotein lipase (LPL) and hepatic TG lipase activity thereby causing accumulation of plasma LDL-C<sup>22</sup>. However, HDL-C was significantly decreased in post-menopausal women which is in tandem with the findings of previous studies<sup>23,24</sup>. Available evidence shows that as HDL-C increases by 0.026 mmol/ml, there is a reduction in risk of cardiovascular diseases, with a 4.7% decrease in mortality rate of CVD<sup>25</sup>. Changes in plasma lipid is known to partly increase the incidence of cardiovascular disease following menopausal transition<sup>20,24</sup>.

Newly emerging atherogenic markers such as AIP, VAI, BAI and CRI-I have been used to assess cardiovascular risk and atherogenicity among various disease states including hypertension<sup>26</sup>, diabetics<sup>27</sup> and among HIV patients<sup>11</sup>. Our results revealed that, markers of atherogenicity including AIP ( $p < 0.0001$ ), VAI ( $p < 0.0001$ ), BAI ( $p < 0.0038$ ) and CRI-I ( $p < 0.0001$ ) were significantly increased in post-menopausal women. This is in line with a study by Nwagha *et al.*, which reported a significantly reduced AIP levels among pre-menopausal women confirming the alteration of lipid profile in menopause<sup>26</sup>. The use of lipid ratios as prognosticators of cardiovascular risk cannot be overemphasized. In fact, variations in lipid ratios such as CRI-I and CRI-II have been reported to be better predictors of risk reduction in coronary heart disease compared to the absolute lipoproteins or lipids<sup>28</sup>.

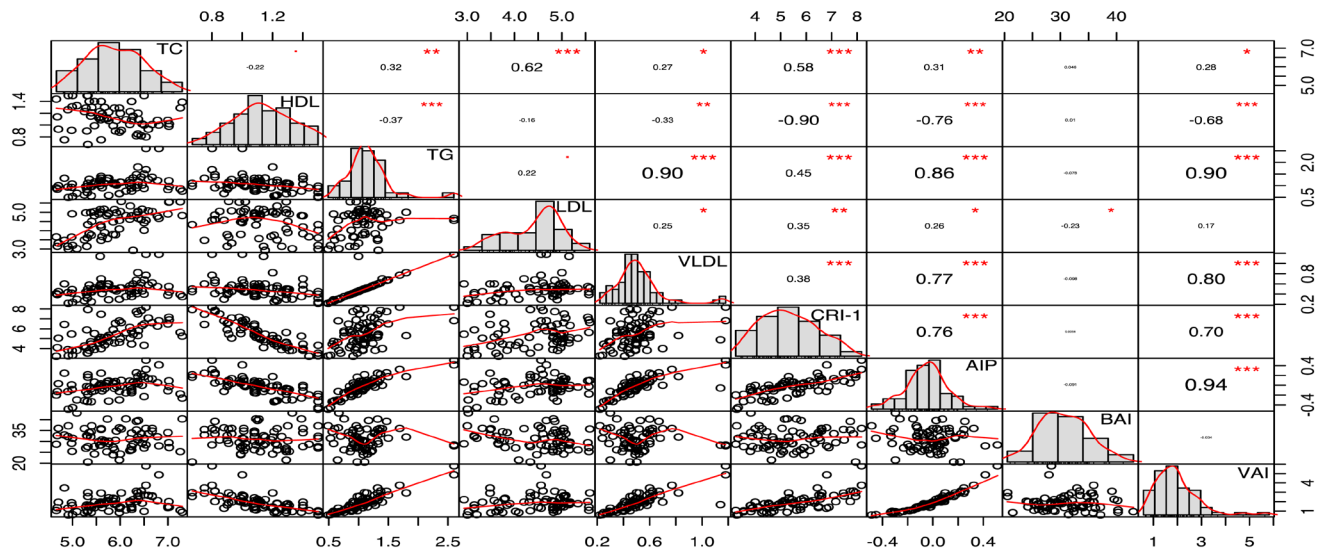
**Table 3. Crude and adjusted odds ratios of lipid variable and markers of atherogenicity associated with menopausal status of study participants.**

Variable	Crude OR (95%CI)		aOR (95%CI)	P-value
<b>TC</b>				
LOW	0.4286(0.01635 to 11.23)	0.7115	NA	
Normal	*reference			
High	474.5(59.09 to 3810)	<0.0001	76.58(5.880-2439.396)	0.0032
<b>HDL-C</b>				
Low	24.65(7.277 to 78.69)	<0.0001	11.76(1.934-90.816)	0.011
Normal	*reference			
<b>LDL-C</b>				
LOW	6.83(0.3596 to 129.7)	0.0855	1.164×10 <sup>-5</sup> (0.162- 2.022×10 <sup>4</sup> )	0.996
Normal	*reference			
High	29.06(3.793 to 222.6)	<0.0001	16.86(1.641-433.443)	0.0343
<b>VLDL</b>				
Normal	*reference			
High	0.7396(0.1597 to 3.425)	0.6987	4.32×10 <sup>7</sup> (1.992×10 <sup>-60</sup> -1.789×10 <sup>40</sup> )	0.993
<b>TG</b>				
Low	9.65×10 <sup>-9</sup> (NA to 2.67×10 <sup>71</sup> )	0.933	4.73×10 <sup>-8</sup> (2.5×10 <sup>-9</sup> , 1.379×10 <sup>71</sup> )	0.993
Normal	*reference			
High	1.808(0.1601 to 20.42)	0.6272	15.77(0.122-15974.386)	0.336
<b>AIP</b>				
low	0.005(0.001 to 0.02)	0.0001	0.262(0.020-3.046)	0.2885
normal	*reference			
high	4.103(1.372 to 11.76)	0.0218	2.61(0.363-18.652)	0.334
<b>BAI</b>				
low	0.4(0.07202 to 2.246)	0.2949	0.16(0.0045-39194)	0.27
normal	*reference			
high	54.17(19.46 to 133)	<0.0001	41.19(6.7511-321.0692)	0.0001
<b>CRI-I</b>				
low	0.5039(0.02176 to 11.67)	0.6654	7.02×10 <sup>-6</sup> (NA-8.35×10 <sup>112</sup> )	0.9965
normal	*reference			
high	467.2(87.58 to 2492)	<0.0001	818.824(51.900-29515.961)	<0.0001

NA, odds ratio value not given by R statistical package; aOR, age- and BMI-adjusted odds ratio; CI, confidence interval; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; VLDL, very low-density lipoprotein; TG, triglycerides; AIP, atherogenic index of plasma; BAI, body adiposity index; CRI-I, Castelli index I.

Higher levels of TC, LDL-C, AIP, BAI and CRI-I as well as low levels of HDL-C were all crudely associated with post-menopausal women; however, after correction for age and BMI, AIP was not significantly associated to postmenopausal status with a marked reduction in the significance levels of the other parameters (Table 3). This confirms the significant intersection between cardiovascular risk and aging<sup>29</sup>. We also report a positive correlation of TC, TG, and VLDL with atherogenic

markers AIP, VAI and CRI-I in post-menopausal women. Upsurge in the levels of TG in isolation has been shown to increase AIP in women than in men but its influence can be neutralized by the levels of HDL<sup>30</sup>. Others have reported an association of CVD progression with the size of LDL-C and HDL-C, with the lesser size showing great atherogenic potential<sup>31</sup>. There is indeed a strong relationship between cholesterol etherification rate in HDL plasma (FERHDL) and



**Figure 1.** Scatter plot and correlation matrix between lipid profile and atherogenic markers among Post-menopausal women.

lipoprotein particle sizes, which is considered as a risk marker of coronary artery diseases. Lately, VAI has demonstrated to be a potent marker of adipose distribution and function indirectly conveying cardiometabolic risk<sup>32</sup>. Among post-menopausal women, VAI was shown to predict cardiometabolic risk in association with visceral fat<sup>33</sup> while positively correlating with peripheral glucose usage during euglycemic hyperinsulinemic clamp<sup>32</sup>. Among our study population, post-menopausal women showed increased body adiposity with a high percentage of body fat than pre-menopausal counterparts. An easy but effective determination of adiposity is needed to assess the magnitude of cardiovascular disease for the development of suitable management and preventive strategies. Confirmatory studies in different ethnicities have consistently revealed the overestimation and underestimation of adiposity at low and higher body fat percentages, respectively, by BAI<sup>34</sup>. Therefore, it is important to carefully interpret BAI values along with other anthropometric and cardiovascular markers.

Our results also indicated there was a significant increase in BMI, blood pressure and fasting blood sugar in post-menopausal women in contrast with pre-menopausal women. The increase may be attributed to the reduction in the production of estrogen, which may be associated with amplified cardiovascular risk in post-menopausal women. Surgical or naturally induced menopause increases the risk of CVD<sup>35</sup> and the changeover may be associated with changes in body composition, with a considerable increase in the waist-to-hip ratio during menopause coupled to a possible increase in BMI<sup>36</sup>. Research has demonstrated the upsurge in the release of nitric oxide and the production of prostacyclin within the arterial endothelial cells by estrogen, culminating into the induction of a vasodilatory effect leading to a drop in BP<sup>37</sup>. Furthermore, estrogen

again reduces the synthesis of thromboxane A<sub>2</sub> by platelets with vasoconstriction properties<sup>38</sup>. Hence the absence or a reduction in the estrogen levels during menopause may increase blood pressure due to an increase in peripheral resistance. Also, when estrogen production is low, there is reduced stimulation of the liver to synthesize renin. This is a rate-limiting step in the renin-angiotensin-aldosterone system leading to vasoconstriction with subsequent increase in blood pressure<sup>39</sup>. On the other hand, urbanization, affluence, changing dietary habits and sedentary lifestyles can also be implicated for the above findings<sup>40</sup>. Even though a significant association of increased cardiovascular risk with post-menopausal status was found in this study, our findings may be limited by the smaller sample size used and hence a larger sample size would have provided more stability to our conclusions.

## Conclusion

Menopause could lead to changes in lipid profile in the direction of atherogenicity and increase the risk of CVDs. Atherogenic markers such as AIP, VAI, BAI, and CR can serve as potential biomarkers for predicting CVD and can be used together with other markers.

## Data availability

### Underlying data

Zenodo: Assessment of cardiovascular risk in post-menopausal women in Ghana. <http://doi.org/10.5281/zenodo.3228917>.

## Grant information

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**Christian Obirikorang** 

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## Overview and General Recommendations:

Thank you for the opportunity to review this manuscript which highlights the need for CVD risk assessment among postmenopausal women. Fat mass accumulation is one of the significant changes that occur with advancing age and its peaks around the menopausal, and it is associated with metabolic and haemodynamic derangement. The research interests of the paper is that it adds to already existing knowledge on menopause and CVD risk. Despite the fact that menopausal transition is associated with physiological changes which affects the health status of women, little data exist in Ghana. Thus highlighting the relevance of the paper in context.

I found the paper to be overall well written and much of it to be well described. I felt confident that the authors executed careful and thorough processing of methods to generate the data. The design of the study combined with data processing strategy makes the data set seem quite useful for the purpose. However, there are few concerns which a minor revision is warranted.

First, the authors placed too much emphasis on lipids and anthropometry given little attention to the constellation of metabolic abnormalities (also called metabolic syndrome) and hypertension which are potent indicators of CVD. Lipids abnormalities or atherogenic indices alone does not explain 100% of CVD risk prevalence among postmenopausal women. Dyslipidaemia increases the risk of coronary artery disease among and lipid peroxidation promote atherosclerosis. Thus making the single emphasis on dyslipidemia relevant. However, for general CDD risk, I strongly recommend that the authors should include MetS and hypertension, which will give the relevance of the study in context.

## Minor Revisions:

At the abstract section, the authors should correct "comparative cross-section" and change it to

“comparative cross-sectional study”.

At the results section, the mean blood pressure were within the recommended range for both groups. Thus, the first sentence should be revise: Also postmenopausal group had elevated BP should be change to “a higher BP levels were observed among postmenopausal women..... or something similar.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Chemical Pathology

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 24 June 2019

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**Bashu Dev Pardhe** 

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The fact relies on that cardiovascular diseases (CVDs) are more prevalent in women after menopause; the researchers compare the lipid profile and atherogenic index in pre- and post-

menopausal women.

They included a total of 150 women and estimated BP, FBG and lipid profile and finally, they determined the atherogenic markers like BMI, AIP, VAI, BAI, and CRI-I for the interpretation. They found a significant rise in lipid profiles except for HDL-C in post-menopausal women compared with pre-menopausal women. Mean AIP, VAI, BAI, and CRI-I ( $p < 0.0001$ ) were significantly increased in post-menopausal women compared to pre-menopausal women. Higher levels of BAI and CRI-I were significantly associated with post-menopausal women after even adjusted for age and BMI factors.

At the same time, they reported a positive correlation of TC, TG, VLDL-C and non-HDL-C with atherogenic markers AIP, VAI and CRI-I in post-menopausal women. With these findings, they conclude that postmenopausal women have an adverse change in lipid parameters with an increased atherogenic index and they are more prone to have cardiovascular diseases.

### Comments:

1. I found the manuscript interesting from an epidemiological point of view, which has the value to describe the lipid profile and atherogenicity in a group of pre and postmenopausal women from Ghana.
2. The age range for postmenopausal women was 40-55 years and for pre-menopausal was 30-40 years in the method section. In the result section (table 1), the mean age of post-menopausal women was reported to be  $59.63 \pm 7.42$ . How is this possible?
3. Socio-demographic factors like lifestyle interventions, education levels, social status, ethnicity, etc. may also influence the findings of this study. It will be useful (and interesting) to have a table with a more complete description of the women included in the study.
4. The author mentioned, "We, therefore, sought to assess cardiovascular and atherogenic risk among pre and post-menopausal women in the Cape-Coast municipality." The selection criteria and sample size do not reflect this statement.
5. The selection of the study population is not clearly defined. They approach for the convenient sampling, it is better to define inclusion and exclusion criteria for both pre and post-menopausal women separately. They recruit healthy women attending the hospital. The question remains why healthy women do attend the hospital. Were they completely healthy or apparently healthy?
6. Wide range of age of study population required larger sample size. Even author mention that the sample size limit this cross-sectional study, this relative smaller sample size may sometimes miss-lead the conclusion.
7. I recommend including significance of atherogenic index (AIP, VAI, and BAI) in introduction section because this study focused on the investigation of these parameters.
8. Table 1:
  1. The average weight of post-menopausal women ( $6.21 \pm 8.82$  kg)?
  2. I recommend using the same SI unit (cm or m) for height, WC and HC.
  3. I recommend using the maximum 3 digits after decimal and uniform for all variables

(all tables and figure).

4. Mention the criteria to define pre-diabetes in study population at least in the method section.
9. It is better to include the abbreviation section in the manuscript. Please use cardiovascular diseases (CVDs), very low-density lipoprotein cholesterol (VLDL-C).
10. Title of the tables should not be end with a full stop.
11. Even though the findings are more interesting, interpretation and discussion part is poor. The author reported the association of the atherogenic index with menopausal status with respect to adjusted for age and BMI. The discussion part is poor to justify this analysis.
12. There are some typo errors especially in abbreviations (mainly on abstract) and grammatical errors in the manuscript.

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**

Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Metabolic diseases, Enzymology (Cytochrome P450)

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

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