

Research Article

Metabolomic Alterations in Postmenopausal Women: Experience in a Metropolitan City of South-Eastern Nigeria

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Abstract

Background: The decline in levels of some hormones during menopause has been associated with metabolic syndromes, particularly cardiovascular diseases, and cardiovascular diseases have been ascribed to hyperlipidemia, insulin resistance and lifestyle changes. **Aim:** This study investigated changes in lipid profiles, insulin levels, and body weight in post-menopausal women in Enugu metropolis, an urban town in South-eastern Nigeria. **Method:** This was a cross-sectional study and involved 150 post-menopausal women aged 55 to 70 years. One hundred and five (105) pre-menopausal women aged 25 to 40 years were used as controls. Lipid parameters (total cholesterol – TC, high-density lipoprotein – HDL, low-density lipoprotein – LDL, very low-density lipoprotein – VLDL, and triglycerides – TG) and insulin levels were determined spectrophotometrically, while body weights were determined using a digital Weighing Balance. **Results:** The results of the study showed that TC, LDL, VLDL and TG were significantly higher in post-menopausal women than in pre-menopausal women ($p \leq 0.001$). These parameters also showed positive correlations with the age of the post-menopausal women. Conversely, HDL was significantly lower in post-menopausal women than in pre-menopausal women ($p < 0.001$), with a strong negative correlation with the age of the post-menopausal women ($p = 0.002$). Furthermore, post-menopausal women had significantly higher insulin levels and body weights than the pre-menopausal women ($p < 0.001$ for each). Both insulin levels and body weights showed strong positive correlations with the age of the post-menopausal women ($p = 0.029$ and 0.015 , respectively). However, no significant correlations were observed between any of the parameters and age of the pre-menopausal women. **Conclusion:** These findings denote a possible high prevalence of metabolic diseases, especially cardiovascular disease, during post-menopausal age, and emphasize the need for targeted interventions focusing on hormonal balance and lifestyle modifications to take care of metabolic health and mitigate cardiovascular risks in post-menopausal women.

1. Introduction

Menopause is the cessation of the menstrual period for twelve months or more without an obvious pathological cause. This usually occurs between ages 45 and 55 in apparently normal, reproducing women, with a median age of 51 years [1]. Menopause is preceded by a peri-menopausal period, characterized by gradual loss of oocytes, altered responsiveness to gonadal steroid feedback, marked hormonal fluctuations, and irregular menstrual patterns [2]. The period after menopause is called the post-menopause, during which the menstrual period ceases completely. Many women spend roughly 40% of their lives in the post-menopausal years [3], barring other illnesses. Menopausal transition is a period when the endocrine, biological and clinical features of menopause begin, including estrogen and progesterone deficiencies and some other physiological changes inherent with menopause [4]. Estrogen deficiency, seen in menopause and post-menopause [5], has been implicated in obesity and increased waist circumference due to fat deposition around the waist [6]. The hormonal deficiency is linked to other physiological changes, including changes in appetite and a decline in insulin sensitivity, which in turn disrupts glucose and lipid metabolism [7]. With reduced estrogen, the body's cells become less responsive to insulin, leading to higher insulin production to maintain normal blood glucose levels [8], contributing to fat accumulation, particularly around the abdomen, a pattern strongly associated with metabolic syndrome and other obesity-related health risks. Insulin resistance causes insulin deficiency inside the cells and further causes the body to produce more insulin, causing hyperinsulinemia. This condition is often associated with weight gain, high risk for type 2 diabetes and cardiovascular disease [9]. Likewise, insulin resistance caused by hyperlipidemia can also lead to hyperinsulinemia.

Lipid profile is an indicator of cardiovascular health [10]. Though data on the metabolism of lipoproteins during the menopausal transition and their relationship with the sex hormones and body fat distribution are still limited and under review [11], it has earlier been posited that estrogen deficiency disrupts lipid metabolism because of its effect on insulin production and sensitivity [6]. Therefore, it is expected that post-menopausal women face increased risk of cardiovascular disease due to changes in lipid profiles and vascular function associated with lower estrogen levels. Triglycerides are a single risk factor for cardiovascular disease [12, 13] and are also involved in the causation of metabolic syndrome [14]. Likewise, very low-density lipoprotein, which transports other lipids from the liver to other tissues [15], has been implicated in atherosclerosis, increasing the risk of cardiovascular disease [16].

Enugu metropolis is a typical urban settlement of a developing country. It is populated by civil servants of different levels and middle-class business people [17]. There is a dearth of information on the metabolic conditions of post-menopausal women in this area. The present study was intended to close this gap and provide possible answers to some unexplained health challenges frequently experienced by post-menopausal women in the area. It will also help clinicians manage and improve the prognosis of the condition.

2. Materials and Methods

Ethical clearance: Ethical clearance was obtained from the Research and Ethical Clearance Committee of the Faculty of Basic Medical Sciences, College of Medicine, Enugu State University of Science and Technology, and individual informed consent was sought and obtained from each subject after detailed explanation of the reasons and procedures for the study.

Study area: Enugu metropolis is the capital city of Enugu State in South-east Nigeria. Its geography, population and growth rate have been described in detail in previous studies [17–19].

Study design: This study was a cross-sectional study and was designed to assess some metabolic changes in post-menopausal women within the metropolis. The study involved 150 post-menopausal women aged between 55 and 70 years, and another 105 pre-menopausal women aged 25 to 40 years, who served as controls. These subjects were recruited from local churches, schools and health centers. An oral on-the-spot interview was held with each subject to assess the onset of menopause or otherwise. Stratified random sampling technique was used to ensure the samples accurately represent different subgroups within the two populations.

Inclusion criteria: Women who have not had their menstrual period for the past one year and aged 55 years and above were included in the study as post-menopausal women. Those used as controls were regularly menstruating women aged 25 to 40 years.

Exclusion criteria: Women who fell within either group but refused to give personal informed consent were excluded. Also excluded were those who had medical conditions that could affect the parameters under study. Such conditions include pregnancy, diabetes mellitus, cardiovascular diseases and those on hormone replacement therapy.

Sample size calculation: The sample size for this study was determined using the Cochran formula [20].

$$N = \frac{Z^2 \times P \times (1 - P)}{E^2}$$

Where:

E: Margin of error tolerated, 5% (0.05).

P: Prevalence of the attribute under study. P is 10% (0.1).

Z: Significance level, usually set at a 95% confidence level (1.96).

N = Minimum sample size.

$$N = \frac{1.96^2 \times 0.1 \times (1 - 0.1)}{0.05^2}$$

$$= \frac{3.84 \times 0.01 \times 0.99}{0.0025}$$

$$= \frac{0.38016}{0.0025}$$

$$= 152.06$$

$$\approx 150$$

Sample collection: A total of 4.0ml of blood sample was collected from each subject through the ante-cubital vein, after overnight fasting (8-12 hours). This was allowed to stand at room temperature to clot and retract. It was then centrifuged at 5,000 rpm for ten minutes; the supernatant was separated into a separation tube and stored frozen at -20°C until needed for analysis. The analyses were done in batches to avoid stress and ensure consistency, and in duplicates to ensure reproducibility.

Biochemical analysis: Lipid profile parameters (Total cholesterol, High-density cholesterol, Low-density cholesterol, Very low-density cholesterol and Triglycerides) were determined as earlier described [21]. Insulin levels were determined using the enzyme-linked immunosorbent assay (ELISA) method with a commercial reagent kit, Calbiotech Insulin ELISA Kit, (Calbiotech, USA), while body weights were measured using digital Weighing Scale (Omron, Vietnam).

Data analysis: Data from this study were analyzed using the Statistical Package for the Social Sciences (SPSS version 23). Descriptive values were presented with standard deviation, while the statistical significance was set at ≤ 0.05 .

3. Results

Table 1 compares plasma lipid profiles, insulin levels and body weights of pre-menopausal and post-menopausal women, highlighting significant differences. Total cholesterol (TC), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) and triglycerides (TG) were significantly higher ($p < 0.001$, each) in post-menopausal women (5.47 ± 0.77 mmol/L; 4.11 ± 0.81 mmol/L; 0.28 ± 0.03 mmol/L and 1.42 ± 0.16 mmol/L; respectively) compared to pre-menopausal women (3.98 ± 0.45 mmol/L; 2.24 ± 0.57 mmol/L; 0.23 ± 0.02 mmol/L and 1.14 ± 0.08 mmol/L, respectively). Likewise, serum insulin levels and body weights were significantly higher ($p < 0.001$ and 0.008 , respectively) in post-menopausal women ($6.57 \pm 1.91 \mu\text{U/mL}$ and $63.98 \pm 11.97\text{kg}$, respectively) compared to pre-menopausal women ($3.24 \pm 0.524 \mu\text{U/mL}$ and $58.45 \pm 6.74\text{kg}$). However, high-density lipoprotein (HDL) was significantly lower ($p < 0.001$) in post-menopausal women (0.72 ± 0.14 mmol/L) than in pre-menopausal women (1.21 ± 0.19 mmol/L). These results suggest that menopause is associated with adverse metabolic changes, potentially increasing cardiovascular risk.

Table 1: Comparison of plasma lipids in Premenopausal and Postmenopausal Women

Variables	Pre-menopausal (n=150)	Post-menopausal (n=105)	t-value	P-Value
TC (mmol/L)	3.98 ± 0.45	5.47 ± 0.77	-11.84	< 0.001
HDL (mmol/L)	1.21 ± 0.19	0.72 ± 0.14	14.66	< 0.001
LDL (mmol/L)	2.24 ± 0.57	4.11 ± 0.81	-13.36	< 0.001
VLDL (mmol/L)	0.23 ± 0.02	0.28 ± 0.03	-9.80	< 0.001
TGL (mmol/L)	1.14 ± 0.08	1.42 ± 0.16	-11.05	< 0.001
Insulin ($\mu\text{U/mL}$)	3.24 ± 0.52	6.57 ± 1.91	11.57	< 0.001
Body weight (kg)	58.45 ± 6.74	63.98 ± 11.97	2.70	0.008

Table 2 shows that the mean values of plasma lipids in post-menopausal women significantly increased across the age groups (55–60 years, 61–65 years, and 66–70 years), signifying positive correlations ($p \leq 0.001$) between age groups and lipid parameters. However, an exception is HDL, which decreased significantly as age increased, signifying a negative correlation ($p = 0.002$) with age. Furthermore, the table shows that both serum insulin and body weight have positive correlations with age ($p = 0.029$ and 0.015 , respectively).

Table 2: Correlation between the variables and age groups of postmenopausal women

Variables	55 - 60 years (n=60)	61 - 65 years (n=57)	66 - 70 years (n=33)	F-value	P-value
TC (mmol/L)	4.50 ± 0.60	5.10 ± 0.70	5.80 ± 0.85	15.24	< 0.001
HDL (mmol/L)	0.85 ± 0.15	0.78 ± 0.12	0.70 ± 0.10	8.52	0.002
LDL (mmol/L)	3.50 ± 0.75	4.20 ± 0.80	4.80 ± 0.85	18.41	< 0.001
VLDL (mmol/L)	0.25 ± 0.02	0.27 ± 0.03	0.30 ± 0.04	9.76	0.001
TGL (mmol/L)	1.20 ± 0.10	1.35 ± 0.12	1.50 ± 0.18	13.67	< 0.001
Insulin ($\mu\text{U/mL}$)	5.76 ± 1.45	6.12 ± 1.62	7.21 ± 1.85	3.86	0.029
Body weight (kg)	56.64 ± 6.38	64.89 ± 7.56	65.17 ± 10.16	4.73	0.015

Table 3 shows the correlation between the lipid profiles, insulin, body weight, and age groups of the controls. Though TC, LDL, VLDL and triglycerides increased relatively as age increased, the changes were not statistically significant. Likewise, insulin levels and body weights increased with age, but the changes were not significant. Conversely, HDL decreased with age, but like other changes, it was not statistically significant. Therefore, there were no correlations between the age group and any of the parameters.

Table 3: Correlation between the variables and age groups in premenopausal women

Variables	20 – 26 years (n=48)	27 – 33 years (n=44)	34 – 40 years (n=13)	F-value	P-value
TC (mmol/L)	3.66 ± 0.61	3.73 ± 0.47	4.01 ± 0.51	1.78	0.207
HDL (mmol/L)	1.22 ± 0.19	1.20 ± 0.15	1.17 ± 0.21	1.22	0.315
LDL (mmol/L)	2.08 ± 0.55	2.22 ± 0.59	2.31 ± 0.47	1.31	0.216
VLDL (mmol/L)	0.23 ± 0.07	0.23 ± 0.05	0.25 ± 0.07	1.09	0.409
TG (mmol/L)	1.09 ± 0.06	1.12 ± 0.08	1.11 ± 0.08	1.21	0.323
Insulin (μIU/mL)	3.15 ± 0.42	3.34 ± 0.48	3.56 ± 0.58	0.89	0.411
Body weight (kg)	56.12 ± 5.34	59.45 ± 6.72	60.78 ± 7.21	1.24	0.302

4. Discussion

The results show a significant increase in lipid profiles in post-menopausal women compared with their pre-menopausal counterparts. These changes are consistent with earlier studies from other areas [22, 23] and indicate increased risk of cardiovascular disease among post-menopausal women. Accumulation of cholesterol and low-density lipoprotein (bad cholesterol) in the blood builds up plaques in the arteries, blocking the arterial lumen and leading to cardiovascular disease. Triglycerides have been recognized as a single risk factor for cardiovascular disease [13]. Hence, hyperlipidemia has generally been associated with cardiovascular disease [24]. This result, therefore, implies a possible higher prevalence of cardiovascular diseases among post-menopausal women than pre-menopausal women. The positive correlation between lipid profile and age in postmenopausal women agrees with earlier studies [25–27] that have shown significant effects of age on lipid metabolism. This also agrees with the findings of another study [28], which insisted that age at menopause alone was not a risk factor for CVD, but that age at menopause and time since menopause started. This implies that age at onset and duration of menopause must be taken into consideration during assessment and management of health complaints of post-menopausal women, requiring individualized assessment in the management of such people. Thus, apart from hormonal intervention, which may not be appropriate for the aging, alternative interventions like dietary management, physical activity, and a plant-based diet, which have shown promise in improving lipid profiles [29, 30], should be given consideration.

Furthermore, this study demonstrated that post-menopausal women had significantly higher insulin levels than pre-menopausal women. This agrees with an earlier study from another area [31], which reported elevated insulin levels and increased risk of metabolic syndrome in post-menopausal women. This significant increase in insulin levels among post-menopausal women may be attributed to estrogen levels, which are known to decline after menopause. Estrogen naturally enhances insulin sensitivity and thus plays a part in glucose uptake into tissues [8]. However, due to hormonal decline during the post-menopausal stage, insulin sensitivity may shift, reducing feedback on insulin production and leading to hyperinsulinemia [31]. Generally, hyperinsulinemia predisposes women to weight gain and aggravates metabolic disturbances like dyslipidemia and hypertension [32]. Reduced glucose uptake causes the body to mobilize fats for energy, leading to visceral fat accumulation, which is prevalent in post-menopausal women and closely linked to increased insulin resistance [33]. Thus, hyperlipidemia will increase insulin resistance, causing less glucose uptake. Reduced glucose uptake further increases mobilization of fats within the body, further increasing insulin resistance. The result will be hyperlipidemia, hyperinsulinemia and increased body weight. This was seen in the present study with a significant increase in mean body weight of post-menopausal women compared to pre-menopausal women. This agrees with an earlier study, which opined that the increase might be due to a combination of hormonal changes, reduced physical activity, and altered fat distribution [34]. On its own, increased body weight can decrease insulin sensitivity and increase circulating insulin in the blood, leading to metabolic dysregulation. Metabolic dysregulation causes adipose tissue to secrete adipokines, like leptin and resistin, which impair insulin signalling, further contributing to insulin resistance [35].

5. Conclusion

The study agrees with previous studies from other areas that menopause can cause hyperlipidemia and hyperinsulinemia, which will lead to increased body weight. The outcome of the correlation studies supports the opinion that age at menopause alone is not a risk factor for cardiovascular disease, but also the age when the health issue is noticed. This emphasizes the need for individualized assessment of postmenopausal women for better management. We suggest that more work involving longitudinal studies as well as large cohorts be undertaken for more precise conclusions.

Article Information

Ethical Approval: The study was approved by the Research and Ethical Clearance Committee, Faculty of Basic Medical Science, College of Medicine, ESUT, (Approval number: ESUCOM/FBMS/ETR/2025/023, Dated 2nd APRIL, 2025).

Informed Consent: Written informed consent was obtained from all participants before their inclusion in the study.

Data Availability statement: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest: The authors declare that there is no conflict of interest in this article.

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Author Contributions: S.O.O. conceptualized the work, supervised it and wrote the manuscript; M.O.A. mobilized the subjects and collected the samples; O.P.O. prepared the reagents and did the laboratory analysis. All authors participated in sourcing the reagents and online materials for the analysis and manuscript development.

AI Use Disclosure: No generative artificial intelligence tools were used in the preparation of this manuscript.

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