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A cross-sectional study on the renal dysfunction in post-menopausal women of Enugu metropolis, Nigeria

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Abstract

Objective: Menopause is the end of a woman's menstrual cycle and fertility. This leads to some hormonal changes which influences metabolic processes and affect many organs of the body including the kidney. Determination of electrolytes, urea and creatinine are biomarkers for renal function. This study assessed the electrolytes, urea and creatinine levels of post-menopausal women living in Enugu metropolis.

Methods: A total of 60 women were recruited for this cross sectional study with 30 post- menopausal women (aged 45-65 years) as test subjects and 30 premenopausal women (aged 20-40 years) as control subjects. The height, weight, waist circumference were measured and body mass index (BMI) calculated, two readings of systolic (SBP) and diastolic (DBP) blood pressure were taken and average recorded. 5mls of blood was collected for the assessment of electrolytes, urea and creatinine by colorimetric methods using cobas c 111 auto analyzer. Data obtained was analyzed using statistical package for social sciences (SPSS) version 25 and results expressed as mean and standard deviation.

Results: The results shows a significant ($p<0.05$) increase in the mean ± standard deviation of SBP (129.43 ± 5.38, 112.67 ± 4.44), DBP (91.03 ± 4.64, 74.57 ± 5.02), WC (90.83 ± 7.14, 73.96 ± 8.33), BMI (28.21 ± 3.56, 24.65 ± 5.39), age (58.80 ± 5.28, 24.93 ± 2.90), Sodium (144.08 ± 2.10, 139.10 ± 2.05), Bicarbonate (25.38 ± 2.06, 23.79 ± 1.41), Urea (4.78 ± 0.78, 2.09 ± 0.28),Creatinine (88.30 ± 23.35, 62.74 ± 8.05) and a decrease in Potassium (3.95 ± 0.30, 4.75 ± 0.50) among the test and control subjects respectively.

Conclusion: This study concludes that post-menopause predisposes a woman to higher blood pressure, WC, BMI, urea, creatinine levels and electrolytes imbalance which might lead to renal dysfunction and cardiovascular diseases.

Keywords: Post-Menopause; Electrolytes; Urea; Creatinine; Kidney; Enugu.

1. Introduction

Menopause is a natural biological process that marks the permanent cessation of menstruation and fertility in a woman's life. It typically occurs between the ages of 45 and 55, with an average age of around 51 [1]. During menopause, a woman's ovaries gradually produce fewer reproductive hormones, such as estrogen and progesterone, leading to the end of monthly menstrual cycles [2]. Postmenopause refers to the stage in a woman's life that follows the menopausal

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transition, characterized by the permanent cessation of menstrual periods and a decline in reproductive hormone levels. This stage typically begins 12 months after the last menstrual period and extends throughout the rest of a woman's life [3].

Menarche occurs at puberty which is the initiation of the menstrual cycle and it happens around the age twelve-thirteen [4]. Also menarche marks the beginning of the adolescence age and here the previous low levels of gonadal hormones; follicular stimulating hormone (FSH) and luteinizing hormone (LH) increases which leads to the enlargement and maturation of the ovarian follicles in the females. The secretion of FSH and LH depends on the stimulatory effect of hypothalamic releasing hormone, GnRH [5]. This hormonal events repeat monthly all through adolescence age and goes further into the reproductive age of the female. As the female begins to approach midlife towards the age of 40- 45years there is follicular depletion and atrophy which results in irregularities in hormonal secretion (reduced estrogen and progesterone secretion by the ovaries which also result to the increase in FSH and LH secretion by the pituitary gland in feedback response) and thus will lead to irregular menstruation, hot flushes and other clinical symptoms seen at menopause [1- 4]. In spite of the fact that menopause is not a disease, it is a significant cause of morbidity and acts as a risk factor for early mortality from ensuing chronic diseases, like osteoporosis, heart disease, stroke, dementia, and cancer [5, 6]. Estrogen plays a protective role in maintaining cardiovascular health, and its decline during menopause may contribute to adverse cardiovascular changes [7].

As a result of menopause transition, and due to estrogen depletion, the serum levels of some biochemical parameters like electrolytes, urea and creatinine are affected. Electrolytes are essential minerals that carry an electric charge and play a crucial role in maintaining various physiological functions within the body [8]. These minerals, including sodium, potassium, calcium, magnesium, chloride, bicarbonate, and phosphate, are dissolved in bodily fluids such as blood and help regulate fluid balance, nerve function, muscle contraction, and pH levels [9]. Electrolyte imbalance refers to disrupted levels of essential ions like sodium, potassium, and calcium in the body. These imbalances can result from various causes, including medical conditions, medications, and diet. For instance, excessive sweating during exercise can lead to sodium and potassium loss [10], while kidney problems might hinder proper electrolyte regulation [11]. Such imbalances can affect nerve function, muscle contractions, and overall bodily functions [12]. Electrolyte imbalances can also contribute to the onset and severity of common menopausal symptoms. For example, hot flashes and night sweats, two hallmark symptoms of menopause, can be influenced by changes in electrolyte levels. Electrolyte imbalances can also contribute to the mood swings, fatigue, and sleep problems that are common at this stage [13]. Electrolytes like potassium and sodium are crucial for maintaining proper heart rhythm [14], imbalances in these electrolytes can lead to arrhythmias, palpitations, and other cardiovascular complications, which can be particularly concerning in postmenopausal women who already face an increased risk of cardiovascular issues due to hormonal changes.

Urea and creatinine levels are vital markers for renal function and metabolic status in postmenopausal women [15]. Monitoring urea and creatinine levels in postmenopausal women is crucial for assessing renal function and metabolic health, with high levels indicating potential risks for kidney dysfunction [16]. Urea is a naturally occurring metabolite in the human body, it is a key nitrogenous waste product in the body, is primarily produced in the liver through the urea cycle, involving the conversion of ammonia and carbon dioxide into urea [17]. This process is crucial for eliminating nitrogenous waste and maintaining acid-base balance.

Creatinine is a waste product formed in the body through the dehydration of creatine, a compound crucial for energy production in muscles [18]. Creatine is synthesized in the kidneys, liver, and pancreas from amino acids like arginine, glycine, and methionine, and is then transported in the blood to various organs, including muscles [5]. Approximately 2% of the body's creatine is naturally converted to creatinine daily, which is then filtered by the kidneys and excreted in urine [19]. The levels of creatinine in the blood are relatively stable and reflect muscle mass, making it a valuable indicator of kidney function. High urea and creatinine levels can signify kidney impairment or failure, emphasizing the diagnostic importance of urea and creatinine in assessing renal health [16]. Determining the renal function status can predict kidney state and prevent any disease progression.

Renal insufficiency is a risk factor for osteoporosis and can increase risk of fracture. It may be a result of an age-related decline in renal function or chronic kidney disease [5]. Also, a study by [20] suggests a possible association between age-related physiological changes in the kidney and decreased bone marrow density, which results in decreased activity of renal 1α-hydroxylase, along with diminished calcium absorption ability in the intestine, resulting in bone loss.

Renal impairment increases cardiovascular risk, atherosclerosis burden in post-menopausal women [15]. However, reduced renal function is indicated by a decreased estimated glomerular filtration rate (eGFR), and closely associated with cardiovascular risk factors such as hypertension, cardiac adverse remodeling, arterial stiffness, and coronary atherosclerosis [21].

Therefore, monitoring electrolytes, urea and creatinine levels in postmenopausal women are essential for evaluating kidney health and potentially predicting associated health risks.

2. Materials and methods

2.1. Study Design/Selection

This cross sectional study involved a total number of sixty (60) women from Enugu metropolis. The study comprised of thirty (30) post-menopausal women (aged 45-65 years) as test subjects and thirty (30) premenopausal women (aged 20- 40) as control subjects. Informed consent was obtained from each participant. Questionnaires were distributed and duly filled by the participants before commencement of the study.

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion criteria for test group

Apparently healthy post-menopausal women, ages 45 - 65 years old

2.2.2. Inclusion criteria for control group

Apparently healthy pre-menopausal women, ages 20 - 40 years old

2.2.3. Exclusion Criteria for both test and control groups

Pregnant women, women with metrorrhagia, HIV positive, dehydration or over hydration. Those on diuretic therapy, and confirmed diabetic subjects.

2.3. Ethical Considerations and Informed Consents

Ethical approval was duly obtained from the ethics committee of the University of Nigeria Teaching Hospital Ituku-Ozalla Enugu (UNTH/HREC/2024/03/870). Written consent of willingness to participate in the study as subject was obtained from all the participants.

2.4. Anthropometric Measurements

2.4.1. Measurements of Body Mass Index (BMI)

The weight, height and BMI of the respondents were recorded. A digital weighing scale (Egole 1112) was used to measure the body weight (kg). A stadiometer was used to measure height (m); and the BMI was calculated by dividing the weight (kg) by the square of height (m^2).

2.4.2. Measurements of Blood Pressure (BP)

A standardized automatic BP monitor (ANDON MODEL KD-595) was used to take the blood pressure measurements in two readings after the participants have been sat undisturbed for a minimum of five minutes and the average record was used.

2.5. Sampling Techniques

Venous blood was collected into appropriately labelled five millilitres (5mls) plain tube. Sample was allowed to clot and retract, centrifuged at 5,000 rpm and the supernatant (serum) was separated into another labelled vial and stored at -20^0C until analysed, and the analyses were carried out within 48 hours of collection. All analysis of the samples was done by the researchers at the laboratory of University of Nigeria Teaching Hospital Ituku-Ozalla Enugu.

2.6. Biochemical Analysis

Serum electrolytes: Sodium, Potassium, Chloride, Bicarbonate, Urea and Creatinine were all estimated on each collected sample.

2.6.1. Serum electrolyte, Urea and Creatinine estimation

Estimation was done by colorimetric methods using cobas c 111 system analyzer, with the manufacturer's instructions duly followed.

2.7. Data Analysis

Data obtained from this study were analysed using the statistical package for social sciences (SPSS) for Windows Inc. Chicago, IL, USA. Student's independent T-test was used to calculate the difference between means. Results were recorded as mean ± standard deviation. P-value < 0.05 was considered statistically significant.

3. Results

Table 1: Shows the anthropometric parameters of postmenopausal and premenopausal women. The result from the table shows a significant increase (P < 0.05) in the mean ± standard deviation of SBP ((129.43 ± 5.38, 112.67 ± 4.44), DBP (91.03 ± 4.64, 74.57 ± 5.02), WC (90.83 ± 7.14, 73.96 ± 8.33), BMI (28.21 ± 3.56, 24.65 ± 5.39), Age (58.80 ± 5.28, 24.93 ± 2.90) in post-menopausal women and premenopausal women respectively.

Table 1 Anthropometric parameters measurements of post-menopausal and premenopausal women

Group	Systolic Blood Pressure (SBP) (mmHg)	Diastolic Blood Pressure (DBP) (mmHg)	Waist circumference (WC) (cm)	Body Mass Index (BMI) (kg/m^2)	Age (years)
Post-menopausal women N= 30	129.43 ± 5.38	91.03 ± 4.64	90.83 ± 7.14	28.21 ± 3.56	58.80 ± 5.28
Premenopausal women N=30	112.67 ± 4.44	74.57 ± 5.02	73.96 ± 8.33	24.65 ± 5.39	24.93 ± 2.90
T-statistic	13.161	13.198	8.420	3.017	30.759
P-value	0.000*	0.000*	0.000*	0.004*	0.000*

Values are given as mean ± standard deviation; *= Significant value (p<0.05)

Table 2: shows the electrolyte levels in postmenopausal and premenopausal women. The result presented in the table shows a significant difference (p < 0.05) in the mean ± SD of Na^+ (144.08± 2.10, 139.10 ± 2.05), K^+ (3.95 ± 0.30, 4.75 ± 0.50), HCO_3^- (25.38 ± 2.06, 23.79 ± 1.41) and a non-significant difference (p > 0.05) in Cl^- (110.46 ± 10.97, 108.57 ± 10.29) in post-menopausal and premenopausal women respectively.

Table 2 Serum Electrolytes levels in Post-menopausal and Premenopausal women.

Groups	Sodium (Na^+) (mmol/l)	Potassium (K^+) (mmol/l)	Chloride (Cl^-) (mmol/l)	Bicarbonate (HCO_3^-) (mmol/l)
Post-menopausal women N=30	144.08± 2.10,	3.95 ± 0.30	110.46 ± 10.97	25.38 ± 2.06,
Premenopausal women N= 30	139.10 ± 2.05	4.75 ± 0.50	108.57 ± 10.29	23.79 ± 1.41
T-statistics	4.599	7.070	0.687	3.480
P-value	0.000*	0.000*	0.495	0.000*

Values are given as mean ± standard deviation; * = significant values

Table 3: shows the urea and creatinine levels of post-menopausal and premenopausal women. This result shows a significant increase ($p < 0.05$) in the mean ± standard deviation of urea (4.78 ± 0.78, 2.09 ± 0.28) and creatinine (88.30 ± 23.35, 62.74 ± 8.05) of post-menopausal and premenopausal women respectively.

Table 3 The serum Urea and Creatinine levels in post-menopausal and premenopausal women.

Groups	Urea (mmol/L)	Creatinine (mmol/L)
Post-menopausal women N= 30	4.78 ± 0.78	88.30 ± 23.35
Premenopausal women N =30	2.09 ± 0.28	62.74 ± 8.05
T-statistics	17.738	5.668
P- value	0.000*	0.000*

Values are given as mean ± standard deviation; * = significant values

4. Discussion

Post-menopause is associated with numerous physiological, hormonal and biochemical changes affecting the general well-being of women. The result presented in this study in table 1 shows that postmenopausal women have significantly higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to the premenopausal women. This rise in blood pressure among the postmenopausal women could be as a result of endothelial deterioration in aging leading to destruction in the release of nitric oxide within the vessel wall, decreasing the excretion of sodium and water by the renal distal tubule promoting cardiac output [3].

Moreover, aging leads to arterial stiffness, increased pulse pressure, decrease in sex hormones (estrogen) and increase in the sensitivity to the dietary sodium chloride. Estrogen affects the expression of the renin-angiotensin aldosterone system (RAAS) and the level of plasma catecholamines which plays significant roles in the pathogenesis of hypertension [22]. This finding agrees with the previous works [3, 23, 24] who reported significant increases in both SBP and DBP in menopausal transition women compared to premenopausal women.

Furthermore, a significant increase in the body mass index and waist circumference of post-menopausal women was observed. This was attributed to decreased physical activity, natural aging, and hormonal changes leading to abnormal fat redistribution. Decreased estrogen levels seen in postmenopausal women can affect insulin sensitivity thereby altering the glucose metabolism leading to abnormal fat distribution. This study is consistent with the finding of a previous study [25] who observed a higher obesity risk among postmenopausal women living in Canada.

The study also evaluated the electrolyte levels of postmenopausal and premenopausal women and the result shows a notable increase in sodium and bicarbonate levels while a decrease in chloride levels exist among the postmenopausal women compared to their premenopausal counterparts. The elevated sodium and bicarbonate levels observed in postmenopausal women of this study might be influenced by various factors. It could be related to hormonal changes associated with menopause. Estrogen, which declines significantly after menopause, has been implicated in the regulation of renal acid-base handling also estrogen receptors are expressed in various tissues involved in electrolyte homeostasis, such as kidney, intestine and bone cells [13, 26], decreased estrogen levels can affect these target tissues and contribute to altered electrolyte processing. This finding agrees with the previous studies by [27,28].

Table 3 of this study evaluated the urea and creatinine levels of postmenopausal and premenopausal women. The result shows a significant increase ($p<0.05$) in the mean and standard deviation of urea and creatinine. The elevated urea and creatinine levels of the postmenopausal women could be linked to decreased estrogen levels which are associated with postmenopause and ageing. Estrogen exerts renoprotective effects by modulating T lymphocytes activated by connexin 43 (Cx 43) against renal ischemia-reperfusion injury, showcasing its inflammatory properties in kidney protection [29]. Estrogen also has been found to preserve renal function in conditions like chronic kidney disease by impacting split renal function, particularly in cases of chronic unilateral ureteral obstruction (UUO) where estrogen administration helped maintain renal function and reduce renal interstitial fibrosis [30]. This observation is in agreement with a study by Siti *et al*, [31] who reported higher creatinine and urea levels in postmenopausal women when compared to premenopausal women in Indonesia.

5. Conclusion

This study observed an increase in blood pressure (SBP and DBP), WC, and BMI in postmenopausal women when compared to their premenopausal counterpart.

The study shows electrolytes imbalance, that is higher Sodium, Bicarbonate and lower Potassium as well as higher Urea and Creatinine levels among the postmenopausal women.

This study suggests that postmenopause could predispose women to electrolytes imbalance and higher Urea and Creatinine levels leading to renal dysfunction and cardiovascular complications.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest, financial or otherwise.

Statement of ethical approval

Ethical approval was duly obtained from the ethics committee of the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu with Ref no: UNTH/HREC/2024/03/870

Statement of informed consent

Informed consent was obtained from all participants in this study before commencement.

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