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Evaluation of Thyroid Hormones, Estrogen, and Progesterone among Pre-Menopausal and Menopausal Women in Awka, Anambra State

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A B S T R A C T

Menopause is associated with significant hormonal and physiological changes that can impact a woman's overall health and well-being. This cross-sectional comparative study evaluated thyroid hormones, estrogen and progesterone levels among pre-menopausal and menopausal women aged 35-65 years residing in Awka, Anambra State, Nigeria. A total of 200 participants, including 100 pre-menopausal and 100 menopausal women, were recruited using purposive sampling from community health centers, women's associations, and religious organizations.. Data were analyzed using SPSS with a significance level of $P < 0.05$. The study found that age, waist-to-hip ratio (WHR), and thyroid-stimulating hormone (TSH) levels were significantly higher in menopausal women, while triiodothyronine (T3), thyroxine (T4), estrogen, and progesterone levels were significantly lower when compared with pre-menopausal women ($P=0.001$). Correlation analysis revealed strong negative relationships between menopause and T3, T4, and estrogen, while TSH showed a positive correlation with menopause. Significant correlations were observed between estrogen and thyroid hormones ($P = 0.004$). These findings underscore the hormonal changes associated with menopause, providing critical insights into the health risks faced by menopausal women in this region. The study highlights the need for targeted healthcare strategies to support women during this transitional phase.

INTRODUCTION

The thyroid gland plays a vital role in regulating metabolism, growth, and overall physiological functions through the secretion of thyroxine (T_4) and triiodothyronine (T_3). These hormones are essential for maintaining homeostasis and are tightly regulated by the hypothalamic-pituitary-thyroid (HPT) axis via the thyroid-stimulating hormone (TSH). However, thyroid function is influenced by various factors, including reproductive hormones such as estrogen and progesterone, which fluctuate across different phases of a woman's life, particularly during the transition from pre-menopause to menopause. [1,10]

Menopause, defined as the permanent cessation of menstruation due to ovarian follicular depletion, is associated with significant hormonal shifts, including a marked decline in estrogen (specifically estrogen) and progesterone. [2,3] These changes impact multiple physiological processes, including cardiovascular function, bone health, and metabolic regulation. Emerging evidence suggests that estrogen influences thyroid hormone metabolism, thyroid receptor sensitivity, and thyroid-binding globulin levels, while progesterone may modulate thyroid activity through its effects on the HPT axis. [3,4,5] In contrast, pre-menopausal women experience a relatively stable hormonal environment, with cyclic variations in estrogen and progesterone that may contribute to different thyroid hormone dynamics compared to their menopausal counterparts.

Understanding the interplay between thyroid hormones, estrogen, and progesterone is particularly important in populations with unique genetic, dietary, and environmental influences. In Nigeria, thyroid disorders are prevalent, yet limited data exist on how reproductive hormonal changes during menopause influence thyroid function, particularly in Anambra State. [3] Given the crucial roles of thyroid hormones, estrogen, and progesterone in metabolic and cardiovascular health, evaluating their levels in different reproductive phases could provide valuable insights into thyroid dysfunction risks and overall hormonal balance.

Despite the growing global interest in women's endocrine health, research on the interrelationship between thyroid hormones, estrogen, and progesterone among Nigerian women remains scarce. As Awka, Anambra State, undergoes demographic and lifestyle transitions, a better understanding of hormonal variations in pre-menopausal and menopausal women is essential for developing targeted diagnostic and therapeutic strategies.

This study aims to assess and compare thyroid hormone levels (T_3, T_4, and TSH) alongside estrogen and progesterone among pre-menopausal and menopausal women in Awka, Anambra State. The findings will enhance the understanding of endocrine changes associated with menopause and provide a foundation for improved clinical interventions and healthcare policies tailored to women's hormonal health

METHODS

Study Site and Design: The study was conducted in Awka, Anambra State, Nigeria, an urban area with a diverse population that included women from various socio-economic backgrounds. This cross-sectional comparative study targeted pre-menopausal and menopausal women aged 35 to 65 years who resided in Awka. The study aimed to evaluate thyroid hormones, estrogen, and progesterone among these women. A purposive sampling method was employed to recruit participants from community health centers, women's associations, and religious organizations within the Awka region.

The study population consisted of women aged 35-65 years, with specific inclusion criteria ensuring the accurate categorization of pre-menopausal women (35-45 years) as those with regular menstrual cycles within the past three months and menopausal women (45-65 years) as those with the absence of menstrual periods for at least 12 consecutive months. The Study was carried out between the months of January and June, 2024. Exclusion criteria were meticulously defined to eliminate confounding factors, such as pre-existing thyroid or adrenal disorders, hormone replacement therapy, pregnancy, lactation, and chronic diseases like diabetes, cardiovascular disease, and cancer.

The sample size for this study was determined using a standard formula for comparative studies, often based on the formula for estimating sample size in two independent groups:

where:

$$n = \frac{(Z\alpha/2+Z\beta)2\times 2\sigma 2}{\Delta 2}$$

- n = Sample size per group
- Zα/2= Standard normal deviate for the desired confidence level (1.96 for 95%)
- Zβ = Standard normal deviate for the desired power (0.84 for 80% power)
- σ= Estimated standard deviation of the outcome variable
- Δ = Minimum detectable difference between the two groups

The sample size for the study was determined using a standard formula for comparative studies, ensuring statistical robustness. The formula was designed to achieve a 95% confidence level and an 80% statistical power, which means the study had a high likelihood of detecting significant differences between the two groups (pre-menopausal and menopausal women) if they existed. A total of 200 participants, equally divided into 100 pre-menopausal and 100 menopausal women, were enrolled to provide adequate power for meaningful comparison while minimizing the risk of false-negative findings.

Ethical Consideration: Ethical approval was obtained from the University on the Niger Research Ethics Committee. Written informed consent was obtained

from all participants before enrollment, and the study was conducted per the principles of the Declaration of Helsinki 1975, as revised in 2013.

Data and Sample Collection: Data collection involved anthropometric measurements, blood sample collection, and hormonal assays. Waist and hip circumferences were measured using a flexible tape measure, and the waist-to-hip ratio (WHR) was calculated.

Blood samples (5ml) were collected from each participant. These samples were stored in plain tubes and centrifuged to obtain serum for biochemical analysis, which was then stored at -20°C until analysis. Hormonal assessments were conducted using enzyme-linked immunosorbent assay (ELISA) to measure serum levels of thyroid hormones (T3, T4, and TSH), progesterone, and estrogen. The analysis was performed using the ACUBIND KIT (Monobind Inc., 100 North Pointe Drive, Lake Forest, California 92630, USA) and measured with the Mindray MR-96A microplate reader (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Mindray Building, Keji 12th Road South, High-tech Industrial Park, Nanshan, Shenzhen 518057, P.R. China).

The serum estradiol level and thyroid hormones were respectively estimated as described by Munro et al. and Bravermann. [7,8]

The study minimized bias by recruiting participants from diverse community sources and applying strict inclusion criteria to ensure accurate classification of menopausal status. Standardized laboratory procedures, including calibrated ELISA kits and controlled sample storage, reduced measurement variability. Additionally, strict exclusion criteria were implemented to eliminate confounding factors from pre-existing health conditions.

Statistical Methods: The collected data were analyzed using Statistical Package for Social Sciences (SPSS) version 23 (IBM Corporation, NY, USA). Descriptive statistics were used to summarize the data, and comparisons between pre-menopausal and menopausal women were made using Mann-Whitney for continuous variables. Spearman correlation analysis assessed the relationships between thyroid hormones, progesterone, and estrogen. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study revealed distinct hormonal and anthropometric differences between pre-menopausal and menopausal women. Notably, pre-menopausal women exhibited significantly lower levels of thyroid-stimulating hormone (TSH) and a reduced waist-to-hip ratio (WHR) compared to their menopausal counterparts (P=0.001). Conversely, menopausal women showed a significant decrease in triiodothyronine (T3), progesterone, and estrogen levels when compared to pre-menopausal women (P=0.001). While thyroxine (T4) levels were observed to be lower in menopausal women, this difference did not reach statistical significance(P=0.202). In essence, the data highlight a clear divergence in hormonal profiles and body composition between these two female life stages,

emphasizing the physiological changes associated with the menopausal transition as shown in Table 1.

Furthermore, the analysis revealed a strong and significant relationship between menopausal status and specific hormone levels. Specifically, levels of triiodothyronine (T3), thyroxine (T4), and estrogen exhibited a robust negative correlation with menopause, indicating a substantial decrease in these hormones during the menopausal transition ($r = -0.674$, $p = 0.001$ for T3; $r = -0.705$, $p = 0.001$ for T4; $r = -0.767$, $p = 0.004$ for estrogen). Conversely, thyroid-stimulating hormone (TSH) displayed a strong positive correlation with menopause ($r = 0.425$, $p = 0.001$), suggesting a significant increase in TSH levels post-menopause as shown in Table 2.

As Estrogen levels decrease, there is a significant positive correlation with T3 ($r = 0.569$, $p = 0.001$), T4 ($r = 0.624$, $p = 0.000$), and Progesterone ($r = 0.777$, $p = 0.002$), indicating that their levels also decline. Conversely, TSH shows a significant negative correlation with Estrogen ($r = -0.399$, $p = 0.004$), suggesting that as Estrogen decreases, TSH levels increase. The data suggest that declining estrogen is associated with decreased T3, T4, progesterone, and increased TSH, as shown in Table 3.

Table 1: Mean Serum Levels of T3, T4, TSH, Estrogen, Progesterone, and anthropometric Parameters in Pre-Menopausal and Menopausal Women Residing in Awka

Parameter	Pre-Menopausal Women Mean ± SD	Menopausal Women Mean ± SD	P-Value
Age (years)	39.5 ± 2.0	56.6 ± 3.2	0.000*
WHR	0.87 ± 0.07	0.97 ± 0.07	0.001*
T3 (nmol/L)	2.8 ± 0.78	1.58 ± 0.58	0.001*
T4(µg/dl)	9.76 ± 2.5	8.8 ± 2.4	0.202
TSH(mIU/L)	1.5 ± 0.53	2.3 ± 1.2	0.005*
Estrogen (pg/mL)	121 ± 35	6.6 ± 2.3	0.001*
Progesterone(ng/mL)	7.25 ± 3.0	0.22 ± 0.13	0.001*

**significant, p<0.05 significant level*

Thyroxine (T4), Thyroid-Stimulating Hormone (TSH), Triiodothyronine (T3), WHR = waist to Hip ratio,

Table 2: Relationship Between Thyroid Hormones, Progesterone, and Estrogen With Pre-Menopausal and Menopausal Women

PARAMETERS	r	P-value
T3 (nmol/L)	- 0.674	0.000*
T4(µg/dl)	- 0.705	0.000*
TSH(mIU/L)	0.425	0.001*
Estrogen (pg/mL)	-767	0.004*
Progesterone(ng/mL)	-678	0.002*

**significant, p<0.05 significant level*

Table 3: Relationship Between Estrogen and Thyroid Hormones in Pre-Menopausal and Menopausal Women

PARAMETERS	ESTROGEN	
	r	**P-value**
T3 (nmol/L)	0.569	0.000*
T4(µg/dl)	0.624	0.000*
TSH(mIU/L)	-0.399	0.004*
Progesterone(ng/mL)	0.777	0.002*

**significant, p<0.05 significant level*

DISCUSSION

The findings of this study highlight significant hormonal and anthropometric differences between pre-menopausal and menopausal women, emphasizing the physiological changes that occur during menopause. The observed decrease in T3, T4, estrogen, and progesterone levels among menopausal women aligns with previous studies that have reported a decline in thyroid and reproductive hormones due to aging and ovarian senescence. [11]

This study observed a significantly higher thyroid-stimulating hormone (TSH) level in menopausal women. This finding aligns with the study by Kumari et al., which reported that mean serum TSH levels were higher in postmenopausal women compared to premenopausal women, though the difference was not statistically significant. [10] Similarly, Rojas et al. recorded higher TSH levels in postmenopausal women (2.80 µIU/mL) than in premenopausal women (2.52 µIU/mL). [11,13] However, while their study demonstrated an age-related increase in TSH levels, the difference between groups was not statistically significant, unlike the findings of the present study.

The lack of significance in their study may be attributed to the absence of baseline TSH evaluations within specific groups and geographic variations.

Additionally, Kolanu et al. reported mean serum TSH levels in older postmenopausal women (3.39 ± 2.45 μIU/mL), which were notably higher than those observed in younger and middle-aged premenopausal women (2.60 ± 1.35 μIU/mL). [12] Conversely, another study reported conflicting results, showing lower serum TSH levels in postmenopausal and older women, whereas premenopausal women exhibited higher TSH activity. [14] These discrepancies suggest that age-related changes in TSH levels may be influenced by physiological variations, including pituitary gland function and hormonal regulation across different age groups.

Several factors have been proposed to explain the increased TSH activity in the elderly, including variations in nutritional iodine intake, sleep disturbances, the presence of anti-thyroid antibodies, and altered sleep patterns. [15] Aging is known to affect the pituitary-thyroid axis, leading to a gradual shift in serum TSH levels with advancing age. [16] Even in the absence of overt thyroid disease, the endocrine system undergoes age-related changes. A decline in T4 levels and a reduced thyroid response to TSH may contribute to elevated TSH secretion. [12] Additionally, increased TSH levels in older individuals could be attributed to occult thyroid disease or an age-related shift in the TSH regulatory set point.

The increased WHR observed in menopausal women aligns with findings by Lovejoy et al. and Greendale at al., who reported that hormonal decline during menopause contributes to altered fat distribution, favoring central adiposity. [17] Differences in lifestyle, diet, and physical activity may contribute to variations in WHR findings across different studies.

In contrast, menopausal women exhibited a significant decline in triiodothyronine (T3), progesterone, and estrogen levels compared to premenopausal women. Although thyroxine (T4) levels were also lower in menopausal women, the difference was not statistically significant. This finding differs from the study by Kolanu et al., which reported no significant variation in T3 and T4 levels between the two groups. [12] Similarly, Kumari et al. observed a reduction in both T3 and T4 levels, though the decrease in T4 was not statistically significant.

The strong negative correlation between menopause and levels of T3, T4, and estrogen aligns with the findings of Kumari et al. who reported a decline in thyroid hormone levels among postmenopausal women. [10] However, other studies, such as that of Duru et al. found no significant difference in T4 levels between premenopausal and menopausal women, which is consistent with the non-significant T4 variation observed in this study. [5] These inconsistencies may

be attributed to variations in sample size, geographic factors, iodine intake, and genetic influences on thyroid function across different populations.

Our findings further suggest that as estrogen levels decline, there is a corresponding decrease in T3, T4, and progesterone levels, while TSH levels increase. This aligns with the study by Duru et al. which highlighted estrogen's role in modulating thyroid function, noting that reduced estrogen levels impair the peripheral conversion of T4 to T3. [5] Additionally, the decline in progesterone during menopause is attributed to the cessation of ovarian function, leading to decreased secretion. Some other studies also reported lower progesterone levels in females with polycystic ovarian. [20,21]

The observed positive correlation between estrogen and thyroid hormones supports the idea that estrogen plays a regulatory role in maintaining thyroid homeostasis. As estrogen levels drop during menopause, lower thyroxine-binding globulin (TBG) levels may disrupt the balance between free and bound thyroid hormones, contributing to the hormonal shifts observed. [22] One widely accepted mechanism by which estrogen influences thyroid dysfunction, particularly in postmenopausal women, involves its binding to thyroglobulin. This interaction restricts thyroxine's cellular entry, increasing bound thyroxine concentrations while reducing the availability of free thyroid hormones. [23] Santin et al. however, did not observe a significant correlation between estrogen and thyroid hormones, and this variation could be attributed to methodological differences, including assay sensitivity, population health status, or dietary factors such as iodine consumption, which influences thyroid hormone synthesis.

Due to declining estrogen levels, menopause is associated with increased inflammatory markers and altered glycemic indices. Reduced estrogen contributes to insulin resistance and a pro-inflammatory state, elevating the risk of metabolic and cardiovascular disorders. [24]

CONCLUSION

This study supports the notion that menopause is associated with significant alterations in thyroid and reproductive hormone levels. The variations observed between our findings and previous research may stem from differences in population demographics, environmental factors, and methodological approaches. Further longitudinal studies with larger sample sizes are necessary to better understand the intricate relationship between menopause, thyroid function, and reproductive hormones.

Ethical Considerations: Ethical approval was obtained from the University on the Niger Research Ethics Committee. Written informed consent was obtained from all participants before enrollment, and the study was conducted per the principles of the Declaration of Helsinki 1975, as revised in 2013.

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

Author contributions
Conceptualization: Authors 1, 3
Methodology: Authors 2, 4
Data analysis: Authors 1, 2
Writing–original draft preparation: 1, 3, 5
Writing – review and editing: Authors: 2, 4, 5
Supervision: Authors 1, 2, 3, 4, 5

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