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Assessment of the Effect of Menopause on Thyroid Function in South East, Nigeria

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ABSTRACT: Menopause marks the end of a woman's reproductive life and is associated with significant physiological changes. The thyroid gland plays an important role in regulating overall body metabolism including sexual development and reproductive function. Worldwide, thyroid gland diseases are among the most common endocrine disorders in females, especially those in menopause. This study evaluated the effect of menopause on thyroid function.

Methodology: It was a case-control study among post-menopausal women in Nnewi, Anambra, Nigeria with pre-menopausal women serving as controls. Sampling was by simple random method and comprised 45 post-menopausal women matched with 45 premenopausal women in a ratio of 1:1. Data was obtained with the use of a semi-structured questionnaire. The subjects' blood samples were taken and assayed for thyroid stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) by ELISA technique. Their body mass index (BMI) and blood pressure were obtained using standard procedures.

Result: The mean serum levels of free T4 and TSH in the menopausal individuals were significantly higher compared to the pre-menopausal group. Following linear regression analyses with adjustment for age and BMI, the the average level of TSH and free T4 were higher in the study group, while free T3 level was lower. Also, systolic and diastolic blood pressure was significantly higher in the study group than in the control group.

Conclusion: The findings suggest that menopause is associated with reduced thyroid function and could as a result play a role in cardiovascular disease play a role in cardiovascular dysfunction among women.

KEYWORDS: Estrogen, Menopause, Thyroid function, Thyroxine, TSH

INTRODUCTION

Menopause is a natural phenomenon of permanent discontinuation of menstrual flow due to significantly reduced ovarian activity.[1] Menopause sets in at about 50 years of age but may commence earlier or later.[2] The risk for earlier occurrence increases with tobacco smoking, some forms of chemotherapy, and interventions that may cause ovarian insufficiency.[3],[4] Many changes during the perimenopausal period are influenced by changes in ovarian hormones including estrogen. Follicle-stimulating hormone (FSH) facilitates ovarian follicle maturation in the follicular phase of the menstrual cycle. As menopause approaches, the remaining follicles become more resistant to FSH, and ovarian estrogen production declines. In addition to estrogen, progesterone and testosterone levels also change during midlife years.[5] In post-menopause, ovarian estrogen is markedly reduced. Estrogen affects thyroid function by increasing the level of thyroid-binding globulin thereby reducing the effective circulating level of free thyroid hormones - thyroxine (T_4) and triiodothyronine (T_3).[6] T_4 is converted in the tissues to the more potent T_3.[7]Thyroid function is controlled by the thyroid stimulating hormone (TSH) of the anterior pituitary gland which is regulated by the thyrotropin-releasing hormone (TRH) of the hypothalamus. Under this regulation, the gland secretes thyroid hormones which function primarily to influence many physiological processes in the body including growth and development, increased metabolism, body temperature, and heart rate.[7]-[9]Thyroid hormones interact with other hormones including estrogen and progesterone. They also have similarities with certain metabolites of estrogen and progesterone and can modify thyroid uptake at the receptor sites. [10] Estrogen dominance mimics hypothyroidism by interfering with thyroid hormones and decreasing sensitivity to them.[10] This inhibits thyroid action and lowers the rate of metabolism in the body. Studies on the effect of menopause on thyroid function are commonly associated with reduced effective thyroid hormones,[11]-[13] and the fall in estrogen levels at menopause is linked to some disorders including cardiovascular diseases and the clinical presentation of pre-existing thyroid diseases, and other comorbidities.[14],[15] Increase in age and BMI has also been implicated

in the changes in thyroid function.[15],[16] This study was focused on the assessment and effects of menopause on thyroid function.

2. METHODOLOGY

Study Setting

The study was carried out at Nnamdi Azikiwe University Teaching Hospital which is a tertiary hospital, and in its host community - Nnewi North local government area, Anambra, Nigeria.

Study Design

It was a matched case-control study design carried out between 1st April to 30th June 2017 using the simple random sampling method. Cases were identified as self-reported post-menopausal females between the ages of 18-65 years who had no significant co-morbidities or chronic diseases. They presented to the hospital for other reasons like skin rashes, acute pain, and urinary tract infections. Menopause was defined as the cessation of menstrual flow for at least 12 months prior to the study. The cases were matched to apparently healthy females in the community who self-reported as premenopausal with no significant co-morbidities or past medical history. There were 45 cases and 45 controls matched by socio-demographic factors with a matching ratio of 1:1.

Inclusion criteria: Women within the age range of 18-65 years of age.

Exclusion criteria

1. Women outside the age range of 18-65, and females with thyroid diseases or significant gynecological disorders.
2. Pregnant women or women on significant medications such as dopamine agonists, iodine supplements, rexinoids, hormonal contraceptives, and hormone replacement therapy.
3. Subjects with acute febrile illness within the previous 30 days, or significant chronic diseases such as Diabetes mellitus, Hepatitis B virus, Human Immunodeficiency Virus (HIV), and Sickle Cell Disease.

Informed consent

Informed consent of each subject for the study was verbally obtained.

Method

An interviewer-administered, semi-structured questionnaire was used to obtain the subjects' sociodemographic data and medical history. 5ml of venous blood was collected aseptically from each subject who met the inclusion criteria and consented to the study among the cases and the controls. The serum free T3 and T4, and TSH were analyzed using the ELISA technique.The body mass index (BMI) and blood pressure of the subjects were also evaluated using standard procedures.Statistical analysis

Results

were expressed as mean ± SD. The difference in mean between the cases and the controls was performed using the student's t-test. With adjustment for BMI, multiple linear regression analysis was used to analyze the relationship between menopause on the serum levels of T3, T4, and TSH, as well as on the systolic and diastolic blood pressure. The level of significance was set at $p \leq 0.05$.

3. RESULTS

Table 3.1 shows the mean difference in levels of Thyroid stimulating hormone (TSH), free T4, and free T3 between the cases and the control groups (mean ± SD).

PARAMETERS	Post-menopausal	Premenopausal	t-value	p-value
Thyroid Stimulating Hormone (TSH) (µIU/ml)	3.00±1.84	1.83±0.84	3.903	0.0001
Thyroxine(T4) (µg/dl)	9.31±3.21	6.22±2.58	5.053	0.0001
Triiodothyronine (T3) (ng/ml)	0.90±0.22	0.93±0.27	-0.591	0.556

The mean serum levels of T4 and TSH in the post-menopausal subjects were significantly higher than those of the pre-menopausal group ($p<0.05$). However, no significant difference was observed between the mean serum levels of T3 of the post-menopausal subjects and that of the control group ($p>0.05$). Table 3.2 shows the multiple linear regression analyses on the relationship between menopause on the serum levels of TSH, free T4, and free T3, as well as on systolic and diastolic blood pressure with reference to the control group and with adjustment f

BMI.	Regression coefficient	p-value
TSH	1.180	<0.001
T4	4.754	0.010
T3	-0.031	0.547
Diastolic BP	9.990	<0.001
Systolic BP	26.853	<0.001

On average, serum TSH level in the post-menopausal group was 1.180μIU/ml higher than those of the control group ($p<0.05$), free T4 was 4.754μg/dl higher ($p<0.05$), and free T3 was 0.031ng/ml lesser ($p>0.05$) than those of the control group. Also, diastolic and systolic blood pressure are on average 9.99mmHg and 26.85mmHg respectively higher in the post-menopausal subjects than in the controls ($p<0.05$).

4. DISCUSSION

The mean serum levels of T4 and TSH in post-menopausal women were significantly higher compared to the control group. Mean serum levels of T3 showed no significant difference between the two groups. With adjustment for BMI, serum TSH and free T4 were averagely higher among post-menopausal women than the pre-menopausal. The level of free T3 was averagely lower in the post-menopausal women than in the controls, although this was not statistically significant. These findings suggest that thyroid function does not relatively increase among post-menopausal women in spite of estrogen withdrawal. The higher average serum TSH and slight reduction of free T3 indicate a lesser thyroid function among post-menopausal women. A higher average free T4 level highlights the role of the withdrawal of estrogen in reducing the level of thyroid-binding globulin. This increase in T4 did not translate to a corresponding increase in the level of the more potent T3 producing the effects of the hormones. This corroborates the works of Patwa et al and Rojas et al who reported that the mean serum TSH level in postmenopausal women was comparatively higher than in premenopausal women.[9],[10] It also partly agrees with the work of Farasat et al which reported higher serum TSH levels and low serum T3 and T4 levels were observed in postmenopausal females.[11]Significant average higher systolic and diastolic blood pressure finding may not be directly linked to the activity of the thyroid gland. It could be due to degenerative changes associated with age like arteriosclerosis. However, the resultant relatively reduced thyroid function in this study can be implicated in cardiovascular diseases linked to menopause.[14]

5. CONCLUSION

The discoveries of this study align with the findings that menopause is associated with a reduction in thyroid function and could be linked to other effects like the increase in cardiovascular diseases.

Limitations and strengths

Although this study considers potential sources of interaction with the findings, it is limited by the self-report nature of the category identification and medical history. With the introduction of the sampling age limit, the analysis may be used to make inferences for the earlier years of menopause but not later. The data analysis considers the confounding effect of BMI on thyroid function.

Ethical approval

The ethical approval for this research was obtained from the Nnamdi Azikiwe University Teaching Hospital ethics committee.

Conflict of Interest

The authors declare no conflict of interest

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