Patterns of Thyroid Hormone Profile among Women on Hormonal Contraceptives in Kano Metropolis

Abdullahi HL,[1] Mohammad IY,[2] *Taofiki TT[3]

ABSTRACT

The use of hormonal contraceptives is on the increase globally and is widely accepted by women of childbearing age in Nigeria. However, it is associated with certain risk factors related to thyroid dysfunction. This study aimed to determine the patterns of thyroid hormone profile in women on hormonal contraceptives in Kano, Nigeria. The study population included 173 women on hormonal contraceptives, and 100 apparently healthy women as the control group. The thyroid profile of both groups was assayed by Enzyme-Linked Immunosorbent Assay (ELISA) procedure. In the case group, 141(81.50%) were Euthyroid, and 32(18.50%) had abnormal thyroid hormonal profile. 17(9.83%) of these had Sick euthyroid syndrome; 11(6.36%) had Subclinical hypothyroidism; 03(1.73%) had Overt hyperthyroidism while 01(0.58%) had Overt hypothyroidism. The thyroid profiles of the control group showed that 71(71.0%) had Euthyroid, while 29(29.0%) had abnormal thyroid hormonal profile. 10(10.0%) had Sick euthyroid syndrome; 6(6.0%) had Subclinical hypothyroidism; 05(5.0%) had T3 thyrotoxicosis; 04(4.0%) had T4 thyrotoxicosis; 03(3.0%) had Overt hypothyroidism and 01(1.0%) had Overt hyperthyroidism. The percentages of women with abnormal thyroid hormonal profile were significantly higher in the control group than in the case group. There was also a very weak correlation between BMI and serum thyroid hormone levels. This study suggests that hormonal contraceptives do not affect the thyroid profile of women on oral contraceptives.

Keywords: Thyroid hormones, Hormonal Contraceptive, Thyroid dysfunction, Patterns

INTRODUCTION

The thyroid gland is an endocrine gland situated at the root of the neck on either side of the trachea. It has two lobes, which are connected in the middle by an isthmus. The thyroid is the largest single endocrine gland weighting 20-40g depending on the age, sex and other physiological conditions. It is the only endocrine gland that does not store its hormones within the cell, but in follicular cavities surrounded by cells. It produces hormones that regulate metabolism and organ functions.[1]

The thyroid gland maintains the level of metabolism in the tissue that is optimum for their normal function. Thyroid hormones also regulate gene expression, tissue differentiation, and general development. The thyroid gland produces two hormones, 3,5,3 - triiodothyronine (T3) and 3,5,3,5 tetraiodothyronine (T4, Thyroxine) which have long been recognized for their importance in regulating general metabolism.[2]

Hyperthyroidism is a disorder of thyroid gland caused by a number of conditions including diffuse toxic goiter, toxic multinodular goiter, solitary toxic nodule and thyroiditis.[3] Hypothyroidism is a primary disease of the thyroid gland which occurs as a result of damaged thyroid gland (chronic lymphocytic thyroiditis), an inherited condition where thyroid hormone synthesis is inefficient (enzyme abnormalities associated with dyshormonogenesis), after ablation or removal of thyroid tissue with radioactive iodine or surgery leading to a fall in T_4 and T_3 and increase in TSH.[3]

Hormonal contraceptives (HCPs) are synthetic biochemical substances that act on the endocrine system and permit sexual union without resultant pregnancy.[4] In Sub-Saharan Africa, the use of contraceptives among women, increased from about 5 % in 1991 to about 30 % in 2016.[5]

Department of Medical Laboratory Sciences,[1] College of Health Sciences, Bayero University, Kano, Kano State, Nigeria.
Department of Chemical Pathology,[2] Bayero University, Kano, Kano State.
Hospital Service Management Board,[3] Kano State, Nigeria.

*Corresponding author: tijanitaofik04@gmail.com,
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Generally, hormonal contraceptives are used for the prevention of pregnancy, but are also prescribed for the treatment of polycystic ovary syndrome, menstrual disorders such as dysmenorrhea, menorrhagia and hirsutism.[4] The risk associated with hormonal contraceptives includes cardiovascular disease, blood clot (venous thromboembolism and arterial blood clot), cancer (breast cancer and cervical cancer) and thyroid dysfunction.[6] Most of the HCPs are taken daily, increasing the possibility of side effects. However, the estrogen in HCPs can impair the thyroid gland, leading to secretion of more thyroid hormones, which can result in hyperthyroidism and less active or inactive thyroid glands.[7]

STATEMENT OF RESEARCH PROBLEM

There is paucity of data on thyroid profile in women on hormonal contraceptives in Nigeria. Available literature shows that majority of previously published studies focused on the prevalence of hormonal contraceptives use rather than their effects on thyroid function.

Justification of the Study

Hormonal contraceptives are widely accepted by women of childbearing age especially in Nigeria, but it is associated with certain risk factors relating to thyroid dysfunction. Hence, there is a need for research geared towards determining the patterns of thyroid hormone profile among women on hormonal contraceptives and the risk associated with their usage.

Aim and objectives of the Study

The aim of this study was to determine the patterns of thyroid hormone profile in women on hormonal contraceptives.

The specific objectives of the study were as follows:

1. To determine the serum levels of thyroid hormones (T_3, T_4 and TSH) in women on hormonal contraceptives in Kano, Nigeria.
2. To compare the results of serum thyroid hormone levels in women taking hormonal contraceptives with those of control subjects not on hormonal contraceptives.
3. To determine the patterns of thyroid dysfunction among the women on hormonal contraceptives.
4. To determine the relationship between the duration of use of hormonal contraceptives and thyroid hormone levels.
5. To determine the relationship between the body mass index (BMI) and thyroid hormone levels.

MATERIALS AND METHODS

Study Design

The study was a Case-Control study carried out between May and October, 2018, comprising of 173 age-matched women on hormonal contraceptives (The case group) and 100 apparently healthy women not on any form of hormonal contraceptives (The control group) at the family planning units of Murtala Muhammad Specialist Hospital (MMSH), Bamali Nuhu Maternity Hospital (BNMH) and Sabo Baki Zuwo Maternity Hospital (SBZMH) in Kano State, Nigeria.

All women with unstable menstrual cycles, smokers, high BP, infections, renal diseases, diabetes, cardiovascular diseases and history of thyroid diseases and those who declined consent were excluded from this study. The sample size was calculated using a prevalence rate of 13%[8] and an allowable error of 5% at 95% confidence interval.

Ethical Considerations

Ethical approval was obtained from The Ethical Committee on Research Planning of the Kano State Ministry of Health. Further approval was obtained from all the various hospitals, and informed consent was obtained from all participants through consent forms and questionnaires.

Sample Collection and Analysis

Five (5) milliliters of blood sample was collected by antecubital venipuncture using standard procedures between 8:00am and 10:00am. Serum was obtained and used for assays for Serum T3, T4 and TSH using

Enzyme-Linked Immunosorbent Assay (ELISA) procedure with diagnosis-related group (DRG) International (USA) reagents.

Statistical Analysis

Data was analyzed with the Statistical package for social science (SPSS) software package version 20.0. (IBM Corporation, Armonk, NY, USA). The student t-test was used to test for significant differences between groups. Pearson's correlation was performed between the variables, and statistical significance was set at $p < 0.05$ for all tests.

RESULTS

General Characteristics

In the case group, the age of the participants had a Mean ± S.D of 25.50 ± 0.710 years while the control group had a Mean ± S.D of 26.38 ± 8.620 years. The Mean ± S.D of the Body Mass Index of the case group was 25.308 ± 4.584 kg/m^2, and the control group recorded a value of 21.958 ± 2.651 kg/m^2

Table 1 shows the distribution of the case group by the type of contraceptives used. Table 2 shows the duration of use of hormonal contraceptives among the case group.

The Thyroid Profile

Of the 173 women on hormonal contraceptives, 141(81.50%) had normal serum T3, T4 and TSH concentration (euthyroid), and 32(18.50 %) had abnormal thyroid hormonal profile. Out of the 32 abnormal cases, 17(9.83%) had decreased serum T3 levels with normal T4 and TSH concentration (Sick euthyroid syndrome); 11(6.36%) had raised serum TSH levels with normal T3 and T4 levels (Subclinical hypothyroidism); 03(1.73%) had raised serum T3 and T4, with normal TSH levels (Overt hyperthyroidism) and 01(0.58%) had decreased serum T3 and T4 levels with normal TSH (Overt hypothyroidism).

Among the 100 control subjects, 71(71.0%) had normal serum T3, T4 and TSH concentration (euthyroid), and 29(29.0%) had abnormal thyroid hormonal profile. Of the 29 abnormal controls, 10(10.0%) had decreased serum T3, with normal T4 and TSH concentration (sick euthyroid syndrome); 06(6.0%) had raised serum TSH with normal T3 and T4 concentration (Subclinical hypothyroidism); 05(5.%) had raised serum T3 with normal T4 and TSH concentration (T3thyrotoxicosis); 04(4.0%) had raised serum T4 with normal T3 and TSH concentration (T4thyrotoxicosis); 03(3.0%) had decreased serum T3 and T4 and raised TSH concentration (overt hypothyroidism) and 01(1.0%) had raised serum T3 and T4 and suppressed TSH (Overt hyperthyroidism).

In the case group, the Mean ± SD value for serum T3 was 1.199 ± 0.609ng/ml when compared with the T3 of the control group which was 1.066 ± 0.614 ng/ml. A student t-test showed no statistically significant difference in the mean T3 levels between both groups. Also, the mean value of T4 for the case group was 6.595 ± 1.94µg/dl which showed no statistically significant different when compared with the mean value of T4 for the control group (7.496 ± 2.50µg/dl). The mean ± SD value of TSH for women on hormonal contraceptives was 3.81 ± 1.94IU/ml which showed no significant difference with the value of 3.83 ± 1.92IU/ml gotten for the control group. The values are presented in Table 3 below.

The confidence interval for all the parameters (for both groups) were within their standard reference ranges. The control cases of T3(0.944-1.188), T4(6.999-7.993) had wider confidence interval when compared with their test cases - T3(1.108-1.291), T4(6.304-6.886). The confidence interval of TSH showed no significant difference between the lower boundary and upper boundary of the control cases (3.453-4.215) and the test cases (3.517- 4.010).

Correlation between BMI and Thyroid Hormone

Correlation coefficient (r) values showed a very weak positive correlation for the T3 and TSH, and BMI pair while the correlation coefficient (r) was weakly negative for the T4 and BMI pair. The correlation analysis is presented in Table 4 below.

Table 1: Types of Contraceptives used

Contraceptive	Frequency (%)
Noristat (P type)	97(56.07%)
Depoprovera (P type)	50(28.90%)
Implanon (Implantable)	21(12.14%)
Combined types & Pills	5(2.89%)

Table 2: Duration of Contraceptive Use

Duration of Use (in months)	Frequency (%)
0 -12	88(50.87%)
13 -24	38(21.97%)
25 - 36	14(8.09%)
37 - 48	16(9.24%)
49 - 60	5(2.89%)
61 - 72	0(0%)
> 72	12(6.94%)
Total	173(100%)

Table 3: Comparison of Serum T3, T4 and TSH levels in Women on Hormonal Contraceptives and the Control group

Parameter Examined	N	Mean	SD	t-value	df	P-value	Comment
T3(Case group)	173	1.199	±0.609	1.739	271	0.676	NS
T3(Controls)	100	1.066	±0.614				
T4(Case group)	173	6.595	±1.940	-3.316	271	0.067	NS
T4(Controls)	100	7.496	±2.504				
TSH(Case group)	173	3.809	±1.941	-0.105	271	0.808	NS
Controls	100	3.834	±1.919				

Values are mean ± standard deviation; $P < 0.05$ is considered significant
Key: NS = not statistically significant

Table 4: Correlation between the Body Mass Index (BMI) and Thyroid Hormone (T3, T4 and TSH) level in Women on Hormonal Contraceptives

Variable	Test parameter	T3(ng/ml)	T4(µg/dl)	TSH(IU/m
BMI(kg/m^2)	R	0.191	-0.016	0.078
	P	0.012	0.836	0.309
	N	173	173	173

DISCUSSION

The results obtained from the study showed patterns of thyroid hormone profile in women on hormonal contraceptives as well as the controls. The percentage of women with abnormal thyroid hormonal profile was significantly higher in the control group (29.0%) than the case group (18.50%). This suggests that the use of hormonal contraceptives does not alter the patterns of thyroid hormonal profile. This is similar to an earlier report by Rapport and Chazenbalk[9]

who found no difference between women on hormonal contraceptive use and non-users of contraceptives.

The confidence interval of T3 and T4 of the control cases were slightly increased when compared with the confidence interval of the test cases. The TSH showed a narrow confidence interval between the test cases and control cases. The lower boundary of the case group (3.517) was higher than the lower boundary of the control cases (3.453) and the upper boundary of the test cases (4.010) was lower than the upper boundary of the control group (4.215). This indicates that the TSH test is a sensitive assay of thyroid evaluation, as a patient with a value higher than the upper boundary of the control group will be readily picked up (sub clinical thyroid disorder), even when T3 and T4 values are within their respective reference (physiological) ranges.

Also, the correlation between the body mass index (BMI) and thyroid hormone levels shows that correlation coefficient (r) values was weakly positive for the T3 and TSH and BMI pair while the correlation coefficient (r) was weakly negative for the T4 and BMI pair. This implies that there is no linear relationship between BMI and thyroid hormone levels. This agrees with earlier findings.[10]

However, a report[11] found a relationship between the BMI and Total T3 TT3), fT3, Total T4(TT4) and TSH in morbid obese subjects. An earlier report[12] also theorized that an increase in body weight can contribute to diverse thyroid function (as expressed by TSH concentration) even in euthyroid subjects.

Most women with thyroid disorders are diagnosed with the condition for the first time during a family planning evaluation. Majority of those with subclinical hypothyroidism have very few symptoms and routine population screening has been advocated.[13] Based on recent evidence of significant intellectual impairment in the offspring of women who were even mildly in hypothyroidism early in pregnancy, testing of thyroid function should be recommended as standard practice for women who intend to become pregnant.[14] However, population screening has not been endorsed unanimously, because the benefits of subsequent therapy have not been established in prospective clinical trials.[15]

However, due to the grave consequences of underlying thyroid diseases on reproductive outcome, and because it has been established that greater percentage of cases of infertility associated with abnormal thyroid function are in subclinical class (they have few symptoms or not at all), it is suggested that thyroid function screening (using the "initial test model" by measuring serum TSH) be incorporated in women on hormonal contraceptives.

CONCLUSION

This study suggests that there is no definitive link between hormonal contraceptive use and thyroid dysfunction. Also, there is very little evidence of correlation between BMI and duration of hormonal contraceptive use. We however found more links to support the use of Serum TSH as an early marker of thyroid dysfunction.

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