Biochemical Pattern of Thyroid Function Test and Clinical Impression of Thyroid Disorder in a Rural Tertiary Health Institution in Nigeria

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Abstract

Background: Thyroid disorders are one of the most common endocrine disorders seen globally. Diagnostic challenge may arise both clinically and biochemically because of the multiple function of thyroid hormones (THs). Request for thyroid function test (TFTs) may be based on clinical impression that may suggest thyroid dysfunction or obvious symptoms and signs that are diagnostic of hyperthyroidism or hypothyroidism.

Materials and Methods: This retrospective study looks at the biochemical patterns of TFTs and the clinical impression of thyroid disorders in a rural tertiary institution. Information extracted from the laboratory register includes indication for the test, the hospital number, the gender, the age, and the THs assayed. The corresponding biochemical pattern of the TFT result was established.

Results: A total of 297 requests were submitted for TH assay; 34 were excluded from the present study because there were no clinical information. There were 239 females and 24 males giving a female-to-male ratio of 9.9:1. Majority of the requests (36.5%) were for goiters, followed by gynecological disorders (20.9%) and clinical thyroid disorders (17.9%). About 46% (45.8%) of the goiter cases were biochemically euthyroid, whereas 13.5% were biochemically primary hyperthyroid. Among the 47 cases of thyroid disorders by the physician’s clinical impression, 27.7% were euthyroid, 17% were biochemically hyperthyroid, and 10.6% were hypothyroid. Of the 55 gynecological disorders assessed, only 7.3% show biochemical evidence of TH alteration with 56.4% being euthyroid. About 47% (46.6%) of those that did routine medical examination had altered TH level that includes hyperthyroidism and hypothyroidism.

Conclusion: Goiter is the most prevalent thyroid disorder in this environment. Biochemical pattern of thyroid function test in our environment was mostly euthyroid despite clinical features suggestive of thyroid disorders.

Keywords: Clinical impression, euthyroid, goiter, thyroid disorder, thyroid function test

Résumé

Contexte: Les troubles thyroïdiens sont l’un des troubles endocriniens les plus courants dans le monde. Un défi diagnostique peut survenir à la fois cliniquement et biochimiquement en raison de la fonction multiple des hormones thyroïdiennes (TH). La demande de test de la fonction thyroïdienne (TFT) peut être basée sur impression qui peut suggérer un dysfonctionnement thyroïdien ou des symptômes et signes évidents diagnostiquant une hyperthyroïdie ou une hypothyroïdie. Matériaux et Méthodes: Cette étude rétrospective examine les schémas biochimiques des TFT et l'impression clinique des troubles thyroïdiens dans un institution tertiaire rurale. Les informations extraites du registre de laboratoire comprennent l’indication du test, le numéro de l’hôpital, le sexe, l’âge, et les TH analysés. Le schéma biochimique correspondant du résultat TFT a été établi. Résultats: Un total de 297 demandes ont été soumises pour le
INTRODUCTION

Thyroid disorders are one of the most common endocrine disorders seen globally.\(^1\,^2\) It is a common endocrine disease in Nigeria, second to diabetes mellitus in prevalence in the country.\(^3\,^4\) Presentation may include thyroid gland enlargement, symptoms of reduced or increased hormone production, or complication of the disease itself. Diagnostic challenge may arise both clinically and biochemically because of the multiple function of thyroid hormones (THs) including control of the basal metabolic rate, essential for normal growth, mental development, and sexual maturation and also increase the sensitivity of the cardiovascular and central nervous systems to catecholamines, thereby influencing cardiac output and heart rate. Request for thyroid function tests (TFTs) may be based on clinical impression that may suggest thyroid dysfunction or obvious symptoms and signs that are diagnostic of hyperthyroidism or hypothyroidism. TFT as with all laboratories may be used for screening for thyroid diseases, confirmation/diagnosis, monitoring as well as evaluation of treatment. The analytes commonly assayed in TFT are thyroid-stimulating hormone (TSH), total triiodothyronine (TT3) and/or free triiodothyronine (FT3), and total thyroxine and/or free thyroxine (FT4). Over time, the diagnostic sensitivity and specificity of TH assay has been improving with the fourth generation of assay already available for TSH. Various guidelines are also published on the use of laboratory investigation of thyroid disorders by various professional organizations such as the American Thyroid Association, the National Academy of Clinical Biochemistry, and the Royal College of Physicians in London.\(^5\) Emphasis has been on TSH as the first line of test for the presence of thyroid disorder.\(^6\,^7\) Pituitary TSH secretion regulates T4 (thyroxine) and T3 (triiodothyronine) secretion, which exert log-linear negative feedback on pituitary thyrotrophs.\(^8\,^9\) Due to this relationship, small changes in the concentration of free TH result in large changes in the serum concentration of TSH; therefore, TSH is the best indicator of subtle changes in thyroid function.\(^1\,^0\) T4 is the primary hormone secreted by the thyroid gland. Approximately 80% of serum T3 results from the peripheral conversion of T4 through 5’-mono-deiodination in various tissues. Nearly all THs circulate in the bloodstream bound to plasma proteins, and only 0.02% of T4 and 0.2% of T3 circulate in the free form.\(^1\,^1\) FT4 and FT3 levels are more relevant than total hormone levels. The free hormone is the biologically active form of the hormone. Furthermore, various acquired or inherited changes in transporter proteins alter T4 and TT3 serum levels, regardless of thyroid status.\(^1\,^2\,^3\)

Federal Teaching Hospital is a tertiary health institution established by the Government of Nigeria to the rural community of Ekiti State. It was affiliated to Afe Babalola University, Ado-Ekiti to serve as the teaching hospital for the training of its medical and allied health professional students in 2014. The institution located in Ido/Osi local government of Ekiti State and is manned by specialists in various fields of medicine to provide tertiary specialist services. Laboratory request for thyroid function test usually comes from the Endocrinology, Surgery, and General Outpatient Departments as well as from neighboring hospital from the state and its environments. This retrospective study looks at the biochemical patterns of TFTs and the clinical impression of thyroid disorders in a rural tertiary institution from June 2013 to September 2018.

MATERIALS AND METHODS

This is a retrospective review of laboratory data for TH analysis from June 2013 to September 2018 at the Department of Chemical Pathology, Federal Teaching Hospital, Ido-Ekiti. The Federal Teaching Hospital is one of the two tertiary health facilities in Ekiti State with a bed space of about 350. The hospital is located in Ido-Ekiti, a rural town in the Ido/Osi local government area of the state. Request for TH function test comes from the clinics and in patient wards of the hospital as well as from neighboring hospitals; such samples are submitted at the reception of the Chemical Pathology Laboratory of the hospital. Samples are usually spun at 3000 g/min for 5 min and serum collected and stored deep frozen at \(-20^\circ\)C until analysis which is usually done twice a week. Analyses of hormones (TSH, FT4, and FT3) were estimated using enzyme-linked immunoassorbent assay (ELISA) (Accubind ELISA Microwells kits produced...
by Monobind Inc., 100 North Pointe Drive, Lake Forest, CA 92630, USA, website: www.monobind.com). The limit of detection for TSH is 0.078 µIU/ml, for FT3 is 0.835 pg/ml, and for FT4 is 0.314 ng/dl, defined as 2 standard deviation in the measurement of zero doses with this method in our laboratory.

Detail information extracted from the laboratory register includes indication for the test, the hospital number, the gender, the age, and the THs assayed. The corresponding biochemical pattern of the TFT result was established using the standard method by Dayan[14] and recommendations by Carvalho et al.[15] as follows:

- Primary (overt) hyperthyroidism: Elevated FT3 and or FT4 with suppressed TSH
- Subclinical hyperthyroidism: Normal FT3 and or FT4 with suppressed TSH
- Primary (overt) hypothyroidism: Suppressed FT3 and or FT4 with elevated TSH
- Subclinical hypothyroidism: Normal FT3 and or FT4 with elevated TSH
- Euthyroid sick syndrome (ESS): Low or normal FT3 and or FT4 in the presence of normal or low TSH
- Euthyroid: TSH, FT3, and FT4 within normal reference level.

The statistical analysis was done using SPSS version 20 statistical computer package. The mean, standard deviation, frequencies, and proportions were used as the descriptive statistics.

**RESULTS**

A total of 297 requests for thyroid hormone function test (TFT) were submitted between June 2013 and September 2018. Thirty-four (11.5%) of these requests did not contain any clinical impression and were therefore excluded. TSH was analyzed for 288 samples, FT4 was analyzed for 277, whereas FT3 was analyzed for 275 samples for this same period. A detail of the laboratory audit of the TH request pattern had been previously published.[16] For this study, those that did not include clinical impression were excluded, leaving only 263 TFT results.

Table 1 shows the distribution of the clinical impression for TFT request. Majority of the requests (36.5%) were for goiter-related disorders, followed by gynecological disorders (20.9%) and clinical thyroid disorders (17.9%). There were 239 females and 24 males giving a female-to-male ratio of 9.9:1.

Table 2 shows the age distribution of the studied population, the 40–49 years’ age range was the highest with 25.5%, and 3.8% of the patients’ age was not indicated in the register.
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Table 3 shows the percentage distribution of the biochemical findings of the TFT with the various clinical impression. About 45.8% of the goiter cases were biochemically euthyroid, whereas 13.5% were biochemically primary hyperthyroid goiter. Among the 47 cases of thyroid disorders by the physician’s clinical impression, 17% were biochemically hyperthyroid, 10.6% were hypothyroid, and 27.7% were euthyroid. Of the 55 gynecological disorders assessed, only 7.3% show biochemical evidence of TH alteration with 56.4% being euthyroid. Almost 46.6% of those that did routine medical examination had altered TH level. Fifty percent of the postthyroidectomy cases were in the hypothyroid level. Overall 43% of the 263 TFT results analyzed were euthyroid, and 36.5% had biochemical result findings of nonthyroidal illness with the remaining showing biochemical disorder of the thyroid function.

Figure 1 shows the bar chart distribution of the biochemical findings of the TFT with the clinical impressions.

**DISCUSSION**

Thyroid dysfunction can result in a wide range of symptoms, and thyroid function tests (TFT) are, therefore, one of the most common endocrine tests ordered in general practice. The clinical status of the patient is the most important factor that needs to be considered before deciding on treatment. The symptoms and signs of thyroid diseases may be group as neuropsychiatric, neuromuscular, physical appearance (weight changes), cardiovascular, thyroid gland enlargement, thermoregulation, ophthalmologic, gastrointestinal, and pituitary function (infertility and abnormal uterine bleeding). These are usually used by clinicians to arrive at a diagnostic impression about thyroid dysfunction before requesting for TFTs.

In this study, 94.3% of the requests for TFT had the clinical impression for thyroid disease's symptoms and/or signs; routine medical examination constituted the remaining 5.7% of the clinical impression in this study. The major reason for routine medical test is to reduce the burden of suffering for the major preventable diseases; however, TFT is not one of those screening tests recommended by the US Preventive Services Task Force.

The requesting pattern shows that goiter is the most frequent thyroid disorder in this environment. This is consistent with other findings in the southwest region of the country. Ogbera in Lagos found 97%, whereas Salami in Ogun State found 58.9%. Mshelia in Maiduguri, Northeast Nigeria, also found a prevalence of 63%. The female gender was more affected with thyroid diseases with a female-to-male ratio of 9.9:1. This is similar to studies in Ile-Ife, Maiduguri, Sagamu, and Karachi. Globally, the Total Goiter Prevalence in the general population is estimated to be 15.8%, varying between 4.7% in America and 28.3% in Africa. In Nigeria, a national goiter rate of 20% was reported and 20 million Nigerians were estimated to be affected by iodine deficiency disorders. Worldwide, the most common cause of goiter is...
iodine deficiency.\textsuperscript{[29]} It is estimated that goiters affect as many as 200 million of the 800 million people who have a diet deficient in iodine. In the Wickham study from the United Kingdom, 16\% of the population had a goiter.\textsuperscript{[29]} Goiter occurs in geographical areas where the soil, water, and food supply contains only low level of iodine; it is said to be endemic when goiters are present in >10\% of the population in a given region. Variation in the occurrence of endemic goiter in regions with similar levels of iodine deficiency point to the existence of causative influences, particularly dietary substances that are referred to as goitrogens. Cassava, a very popular staple food in southwest Nigeria, consumed in various meal forms contains thiocyanate that inhibits iodide transport within the thyroid, worsening any possible concurrent iodine deficiency.\textsuperscript{[30]}

The most frequent biochemical pattern among the various clinical impressions is euthyroidism followed by nonthyroidal illness and hyperthyroidism. Euthyroidism is the state of normal thyroid function; in this study, 43\% of the requests showed euthyroid pattern. Mshellia found 67.2\% in their study in Maiduguri. The enlargement of the thyroid gland is a well-known sign of iodine deficiency; with 45.8\% of the 96 goiter cases in our study being euthyroid, this euthyroid goiter may as well be due to iodine deficiency. Nonthyroidal illness also known as ESS can be described as abnormal findings on TFTs that occur in the setting of a nonthyroidic systemic illness without preexisting hypothalamic–pituitary and thyroid gland dysfunction.\textsuperscript{[31,32]} It constitutes only 36.5\% of the biochemical patterns; Udenze found a prevalence of 33\% among metabolic syndrome patients,\textsuperscript{[33]} whereas in India, a prevalence of 32.6\% and 20.6\% was found among acute and chronic nonthyroidal illnesses, respectively, in hospitalized patients.\textsuperscript{[34]} Okpara\textsuperscript{[35]} in Calabar, Nigeria, found a low prevalence of 2.1\%; he adduced that the sample size, study design, and the outpatients status of the patients studied may cause the low prevalence. Alteration in thyroid function test may reflect changes in the production of TH by the effects on thyroid itself, hypothalamic–pituitary–thyroid axis, on peripheral tissue metabolism of the hormones, or combination of these effects. Mechanisms that have been proposed to explain abnormal TFTs in ESS include accuracy of test assay, inhibition TH binding to thyroid-binding proteins or tissue, productions of cytokines, impairment of peripheral deiodination, inhibition of thyroid-releasing hormone and thyroid-stimulating hormone secretion, inhibition of plasma membrane transport of iodothyronines, and thyroxine-binding globulin decrease and desialation.\textsuperscript{[36]}

Actual thyroid dysfunction was observed in this study with primary hyperthyroidism of 12.6\% and primary hypothyroidism of 4.6\%. Okpara\textsuperscript{[35]} in Calabar, Cross River State, found 13.7\% and 4.9\% of primary hyperthyroidism and primary hypothyroidism, respectively; however, values found in Ogun State by Amballi\textsuperscript{[37]} were twice our findings, i.e., primary hyperthyroidism and primary hypothyroidism were 25.5\% and 8.4\%, respectively, in their study. In the northern part of the country, Mshellia\textsuperscript{[31]} found 22.0\% of primary hyperthyroidism and 3.3\% of hypothyroidism. In a study by Ogbera\textsuperscript{[33]} in Lagos, the prevalence of hyperthyroidism was 1.3\% and of hypothyroidism was 0.1\%; 80\% of the thyroid disorder was caused by Graves’ disease. In an endocrine clinic in Ethiopia, 41.7\% of causes of thyrotoxicosis were by Graves’ disease.\textsuperscript{[38]} The global prevalence of Graves’ disease is not known; however, a prevalence of 0.4\% was reported in the United Kingdom.\textsuperscript{[29]} The most common causes of hyperthyroidism are diffused hyperplasia of the thyroid associated with Graves’ disease, the ingestion of excess exogenous THs, hyperfunctional multinodular goiter, and hyperfunction adenoma of the thyroid. Other causes but less common include other forms of thyroiditis, TSH-secreting pituitary adenoma, and secretion of excessive amount of THs by ectopic thyroid arising in ovarian teratomas.\textsuperscript{[30]} Half of the hypothyroidism biochemical findings were from postthyroidectomy cases. Hypothyroidism may also be due to primary gland failure from autoimmune thyroiditis, radioactive therapy, or infiltrative diseases such as bacterial or viral infection, or defect in TH synthesis such as endemic iodine deficiency and antithyroid agents.\textsuperscript{[30]}

Other biochemical patterns of thyroid function test found in this study include subclinical hyperthyroidism (1.9\%) and subclinical hypothyroidism (1.5\%). This finding is low compared to that of Okpara\textsuperscript{[35]} in Calabar with a prevalence of 4.1\% and 6.3\%, respectively, and Eteudo\textsuperscript{[39]} in Abakaliki with a prevalence of 14.3\% and 4.4\%, respectively. The prevalence of subclinical hypothyroidism varies substantially from nation to nation.\textsuperscript{[40]} Previous studies have shown a prevalence range from 1\% to 10\% or as high as 20\%.\textsuperscript{[29,41]} Various causes of subclinical thyroid disease are well established; however, unlike many clinical conditions, subclinical thyroid disease can only be defined biochemically; it is more common in women, and prevalence increases with aging.\textsuperscript{[42]} In epidemiological data from population studies from Europe and the USA, it was stated that an increased risk of progression to overt hypothyroidism or hyperthyroidism occurs with subclinical thyroid disease, and thus, the treatment of mild thyroid failure is important.\textsuperscript{[43]}

**Conclusion**

Thyroid dysfunction can result in a wide range of symptoms and signs. Thyroid function tests (TFT) are, therefore, one of the most common endocrine tests ordered in general practice. It may be used for screening, confirmation/diagnosis, monitoring as well as evaluation of treatment for thyroid disorders. Goiter is the most prevalent thyroid disorder in this environment. Biochemical pattern of thyroid function test in our environment was mostly euthyroid despite clinical features suggestive of thyroid disorders.

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Confl icts of interest
There are no confl icts of interest.

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