Original Article

Prevalence and Pattern of Thyroid Disorders among Patients Attending University of Nigeria Teaching Hospital, Enugu, Southeastern Nigeria

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Abstract

Introduction: Thyroid disorders (TDs) remain the second-most common endocrine disease after diabetes worldwide. Recently, there has been increased interest in the prevalence and pattern of TD based on the fact that it accelerates cardiovascular complications. However, there are limited data on the prevalence and pattern of TDs in the University of Nigeria Teaching Hospital (UNTH) Enugu, Southeast Nigeria. **Objectives:** We studied prevalence and pattern of TDs as seen in patients attending UNTH, Enugu, Nigeria. **Methods:** This study was conducted in the Outpatient Department of UNTH Enugu from January 2016 to January 2019. Demographic and clinical data collected include age, gender, anthropometrics, clinical features, and associated complications of TDs. The patients were grouped as hyperthyroidism, hypothyroidism, and euthyroid sick syndrome (ESS) according to symptoms, signs, thyroid function test, liver function test, fasting blood sugar, and cholesterol. **Results:** A total of 260 patients (210 females and 50 males) with a mean age of 49.22 ± 9.79 years reflected overall prevalence rate of 2.4%. The prevalence of hyperthyroidism 150 (58%), hypothyroidism 100 (39%), and (ESS) 10 (3.9%) was 1.4%, 0.9%, and 0.09%, respectively. Hypertension 34.3%, heart failure 26.7%, and atrial fibrillation 20% seen in Grave's disease were the most common cause of hospitalization and death. **Conclusion:** Grave's disease is the most common cause of TDs and occurs more in females than males in this study. We observed that hypertension, heart failure, and atrial fibrillation are promoters of complication in TDs. Health system facilities need to be strengthened in this area to improve the detection and management of TDs.

Keywords: Complications, Graves' disease, hypothyroidism, prevalence, thyroid disorders

Introduction

In 1960s, thyroid disorders (TDs) were considered to be rare medical condition among Nigerians; however, 1970s witnessed an upsurge in reported cases of TDs.[1] The disease is commonly encountered in clinical practice and the second-most common endocrine disease after diabetes worldwide.[2] Recently, there has been increased interest in the prevalence data of thyroid disease based on the fact that it accelerates cardiovascular complications.[3] Cardiovascular disease (CVD) mortality rate is higher among low- and middle-income countries, including Nigeria, compared to higher income countries.[4] It was observed that excessive mortality is a feature of TDs in most low-income countries, the reported relative survivals after 5 years of diagnosis was 12.5% and this is in contrast to what is obtainable in the United State of America, where the cure rate for thyroid disease is very high.[5] Attempts at lowering the scenario require information on prevalence studies, thyroid registries, and funding of healthcare facilities. Diagnostic facilities are lacking in some rural health centers and these disorders are not commonly reported.

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The population health cannot improve if parts of the population do not benefit from improvements in diagnosis, prevention, and treatment. Although no study has been conducted in Nigeria to determine the National prevalence of TDs, Olurin *et al*.[6] reported that thyrotoxicosis occurred in 53% of cases of TDs in 874 southwestern Nigerians, whereas Edino *et al*.[7] reported thyroid gland disease in Kano northwestern Nigeria. Jaja and Yarhere[8] documented clinical characteristics of children and adolescents with thyroid diseases in Port Harcourt Southsouth Nigeria. However, to the best of our knowledge, few reports have been documented in Southeastern Nigeria.[9] People with TDs may present with thyroid enlargement, which may be diffused or nodular; symptoms of hypothyroidism, symptoms of hyperthyroidism/Graves' disease which may present with prominence of the eye/exophthalmos and rarely the thickening of the skin over the lower leg.[10] TDs may be associated with cardiovascular complications.[3] Ogbera *et al*.[11] had noted the occurrence of heart failure in 42% of patients with thyrotoxicosis in Lagos, Southwestern Nigeria. Considering the treatment cost of CVD, prevention is more vital in Nigeria. It is imperative that there should be health response strategies (diagnostic facilities distribution, manpower development) and healthcare planning to meet population need. Unfortunately, there is no up-to-date information; this creates challenges for identifying strategies to prevent TDs and its cardiovascular complications, strategic resource allocation, and healthcare planning. We, therefore, estimated the prevalence and pattern of thyroid gland disorders among adult patients attending the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria, which has not been updated for quite a long time in our environment.

Methods

Study population and design

This was a study conducted from January 2016 to January 2019 in outpatient department of UNTH, Enugu, Nigeria. The Health Ethics Committee of UNTH approved the protocols, and all participants provided informed consent with the assurance of confidentiality. The study was conducted in accordance with the guidelines in the Declaration of Helsinki. The target population was on adult patient living in rural and urban setting of Southeastern Nigeria attending UNTH Enugu.

The inclusion criteria were prior diagnosis of TD, no clinical or laboratory evidence of any other chronic disease such as liver diseases, renal disease, metabolic syndrome, and active malignancy. Exclusion criteria include patients on certain medication that can cause thyroid dysfunction such as lithium, amiodarone, immunomodulating drugs like interferon alpha, etc., and medications that can interfere with thyroid laboratory measurements such as heparin and furosemide.

A total of 10,725 patients were seen within the period of the study and of which 260 patients aged ≥20 years were identified as having TDs. The patient were grouped as hyperthyroidism, hypothyroidism, and ESS according to signs, symptoms, thyroid function test, liver function test, renal function test, cholesterol, and fasting blood sugar. Demographic and clinical data collected include age, gender, anthropometrics, clinical features, electrocardiogram findings, diagnostic and therapeutic procedures, and complications. Available investigative results were recorded. Graves' ophthalmopathy was diagnosed using the American Thyroid Association Grading System.[12] While goiter size was estimated using the World Health Organization grading system.[13] The diagnosis of heart failure was made according to the Framingham criteria.[14] Weight and height of the participants measured to the nearest 1 kg and 0.1 m using a wall mounted stadiometer (Seca, United State American) and human weighing scale (Precision Hana, India), respectively. The body mass index (BMI) was calculated in kilograms divided by squared height in meters. Patients were considered overweight or obese if they had a BMI of 25–29.9 or ≥30 kg/m^2, respectively. Waist circumference was measured with a nonstretchable measuring tape at the level of the umbilicus. The blood pressure was taken when the subject had rested for 5 min. Systolic and diastolic pressure were taken at the appearance and disappearance of Korotkoff Sounds (Phase I and V), respectively, and the reading taken in 1 mmHg. The process repeated three times at 5 min interval and average measurement recorded. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg (taken on three different occasions) or current use of anti-hypertensive medications.

Left ventricular hypertrophy by electrocardiography was diagnosed in this study using Araoye's criteria[15] which have been validated as the best option for Nigerian patients.

Laboratory investigations were performed by collecting 5 mm of venous blood sample from each participant by venupuncture and was dispensed into dry plain bottles and allowed to clot, retracted, and centrifuged. The serum was separated from the clot immediately and transferred into the well labeled container for liver function test, renal function test, and serum cholesterol; fasting blood sugar was collected in fluoride oxalate bottle. Total triiodothyronine (tT_3), total thyroxine (tT_4), free thyroxine (fT_4), free triiodothyronine (fT_3), and thyroid stimulating hormone (TSH) were determined using a commercially available "second generation" enzyme-linked immunosorbent assay kit (Glory Science Co. Ltd., USA) as described by Chopra *et al*.[16] All the biochemical parameters and hormones were measured within the same period in the Department of Chemical Pathology Laboratory University of Nigeria Teaching Enugu. Intra-assay and inter-assay coefficients of variation were <6% and <10%, respectively. The manufactures references limits of hormones are tT3 (0.6–1.6 ng/ml), tT4 (2.5–12.5 μ/dl), fT3 (1.4–4.2 ρg/ml), fT4 (0.7–2.2 ng/dl), and TSH (0.5–4.8 μU/ml).

Statistical analyses

Data cleaning and editing were done manually and with computer. Patients demographic and baseline characteristics were presented as means and standard deviation (SD).

Categorical data were presented as percentages. The means of hyperthyroidism and hypothyroidism patients were compared using an independence *t*-test. Data were analyzed using the statistical software (SPSS version 21 Inc., Chicago, Illinois, USA). Results were presented as Mean and SD. The test statistics used was Student's *t*-test for quantitative data. Values of $P < 0.05$ were considered statistically significant.

Results

Study characteristics of participants

The distribution and characteristics of variables among the three groups as summarized in Table 1. In all the three study groups, the number of female participants was higher than male counterpart. The mean age among participants was 44.22 ± 9.78, 47.53 ± 9.40, and 54.94 ± 0.63 for hyperthyroidism, hypothyroidism, and ESS respectively. Among all the patients who had an echocardiograph, a normal left ventricular ejection fraction was seen in ESS and hypothyroidism, while 40 (26.6%) of those with hyperthyroidism (Graves' disease) had mild impairment of left ventricular ejection fraction (40%–50%).

A total of 260 patients identified with TDs had a mean age of 49.22 ± 9.79. The overall prevalence rate was 2.4%. The female: male ratio of TDs was 4:2. Among the patients, Graves' disease recorded 150 patients, (58%), prevalence was 1.4%. The female: male ratio in Grave disease was 6.5:1. Patients with hypothyroidism recorded 100 (39%), the prevalence rate was 0.9% and the female:male ratio was 3:1. ESS was present in 10 patients (3.9%) prevalence rate 0.09%.

Most ESS had normal thyroid profile: TSH 1.9 μU/ml ± 0.13, T3 0.51 ng/ml ± 0.15, fT3 1.4 ρg/ml ± 0.7, and fT4 0.85 ng/dl ± 0.25. Subsequently, a follow-up, the patients have remained euthyroid state after discharge. Subclinical hypothyroidism was observed in a male ESS patient with high TSH 5.2 μU/ml ± 0.15, normal T3 0.8 ng/ml ± 0.5 and T4 2.7 μg/dl ± 1.8. The mean comparism of thyroid hormone between hyperthyroidism and hypothyroid was shown in Table 2.

The symptoms in Graves' disease include weight loss, heat intolerance, exophthalmos, tremor, palpitations, and tiredness. The percentage of these symptoms include heat intolerance 86 (57%), tiredness 80 (53%), and menstrual irregularities 30 (19.7%); infertility 7 (4.7%) was one of the presenting clinical features [Table 3].

Table 1: Study population characteristics

Variables	Hypothyroidism (*n*=100)	Hyperthyroidism (*n*=150)	ESS (*n*=10)	CL
Age (year)	47.53±9.40	44.22±9.78	54.94±0.63	
Sex (male/female)	25/75	20/130	5/5	
BMI (kg/m^2)	26±2.1	30.5±1.4	27.71±0.41	25-29.5
Waist (cm)	86±2.7	87±3.7	85±0.9	70-118
SBP (mmHg)	134±15.1	139.5±17.6	130.2±2.75	
DBP (mmHg)	86±8.2	87±10.6	70.9±3.1	
Creatinine (mol/L)	72.3±9.5	68.2±12.5	58.25±8.1	45-195
Urea (mmol/L)	5.43±0.8	5.96±0.81	5.8±0.9	2.5-8.0
ALT (U/L)	9.6±2.4	9.9±4.7	8.5±2.3	3-15
AST (U/L)	5.4±3.1	9.5±3.5	9.2±1.5	5-18
FBS (mmol/L)	6.5±0.9	5.6±0.8	5.2±1.1	3.5-5.6
Cholesterol (mmol/L)	5.9±1.7	7.1±2.5	4.3±1.5	3.5-6.0
Chest X-ray	Clear	Chest X-ray showed slight changes in lung fields in 50 (33%) of hyperthyroidism (Graves' disease)		
ECG	Normal	40 (26.6%) (mild impairment) LVEF (40-50)		

ALT – Alanine aminotransferase; AST – Asparatate aminotransferase; BMI – Body mass index; CL – Confidence limit; DBP – Diastolic blood pressure; FBS – Fasting blood sugar; ECG – Electrocardiogram; LVEF – Left ventricular ejection fraction; SBP – Systolic blood pressure; ESS – Euthyroid sick syndrome

Table 2: Comparison of parameters between hyperthyroidism and hypothyroidism

Variables	Hypothyroidism (*n*=100)	Hyperthyroid/grave disease (*n*=150)	*P*
Age (years)	41.8±3.2	43±7.8	<0.0001*
BMI (kg/m^2)	26±2.1	30.5±1.4	<0.0001*
T3 (ng/ml)	0.74±0.25	3.45±2.88	<0.0001*
T4 (μg/dl)	2.21±2.53	12.68±5.86	<0.0001*
fT3 (pg/ml)	1.87±1.15	3.38±1.93	<0.0001*
fT4 (ng/ml)	0.52±0.26	2.17±1.56	<0.0001*
TSH (μn/ml)	11.82±5.76	0.31±0.21	<0.0001*

*Significant. Variables are presented in mean±SD. BMI – Body mass index; TSH – Thyroid-stimulating hormone; fT4 – Free thyroxine; fT3 – Free triiodothyronine; SD – Standard deviation

The most common signs were that of a palpable thyroid gland, which was present in 122 (81%) of the patients. Cardiovascular complications such as atrial fibrillation 40 (26.7%) and heart failure 30 (20%) were reported and were the reason for chronic morbidity and mortality.

Hypertension was seen 70 (39.4%) of all the TDs patients studied, of which 60 (34.3%) had Grave's disease. Systolic hypertension was seen in patients with Grave's disease except for in those who had hypertension prior to the diagnosis of thyroid disease. The mean age of the patients with hypertension was 41 years. Eye sign of Graves' disease was seen in 48 (32%), among which 12 (25%) had infiltrative disease that involved orbital tissues [Table 4].

The management of patients with Graves' disease was mainly pharmacological with anti-thyroid drugs like carbimazole given at doses needed to maintain euthyroid states in the patients. Only a few of the patients had thyroidectomy and those were often lost to follow-up, and four of the patients had radio-iodine therapy. Of the eight cases of hypothyroidism, three were postthyroidectomy and five were congenital. The patients with hypothyroidism had thyroxine replacement. 24 (20%) of all the patients with palpable gland had Grade 1, 58 (48%) had Grade 2, and 40 (33%) had Grade 3 goiters. Obstructive symptoms were seen in some of the patients with palpable goiters.

Table 3: Frequency of presenting symptoms in patients with graves' disease (*n*=150)

Symptoms	Frequency (%)
Palpitations	74 (49)
Tiredness	80 (53)
Heat intolerance	86 (57)
Excessive sweating	72 (48)
Weight loss	80 (53)
Increased appetite	68 (45)
Oligomenorrhea	22 (14.7)
Menorrhagia	8 (5)
Infertility	74.(7)
Nervousness	52 (35)
Dyspnea on effort	54 (36)
Sweaty palms	54 (36)
Exophthalmos	75 (50)

Data are presented as percentage

Table 4: Frequency of presenting clinical signs in patients with grave's disease (*n*=150)

Signs	Frequency (%)
Palpable thyroid	122 (81.3)
Hypertension	60 (34.3)
Hyper pigmentation	52 (34.7)
Alopecia	40 (26.7)
Heart failure	40 (26.7)
Atrial fibrillation	30 (20)
Eye signs	48 (32)

Data are presented as percentage

Discussion

The current study demonstrates the prevalence of 2.4%, exceeding the rate of 1.6% reported by Ogbera *et al*.[1] in Southwestern Nigeria. It also exceeded that reported in Wickham, United Kingdom and Tayside, Scotland with 0.4%,[17] and 0.15%[18] done 8 and 42 years ago, respectively, but lower compared to prevalence of 5.1% reported in Pakistan.[19] These differences might be attributable to the specific cause of TDs, genetic, diet, and environmental influences on the various studies. It has been reported that youth of Western Cameroun were at high risk of developing iodine deficiency disorder due to low iodine and high dietary thiocyanates,[20] since thiocyanate is a competitive inhibitor of human thyroid sodium/iodide symporter.[21] The percentage of patients with hyperthyroidism (Graves' disease) is similar to the rates of 27.8%–66.7% reported in previous Nigerian studies,[8,22] but higher than the rate of 2% documented by Desai[23] in India. More than 95% of the cause of hyperthyroidism are due to Graves' disease,[24] the predominantly reported autoimmune disease of thyroid in Africa,[1] with a strong female predisposition,[24] as was observed in the index study. The ophthalmopathy characteristics of Graves' disease seen in the current study as well as earlier Nigerian studies,[8,22] had significant exophthalmos at presentation. It has not been concluded whether this observation is attributed to long during of symptoms and late presentation or genetic preposition. Further studies are needed to investigate this observation. In spite of the differences in the data from other zones of the country, the essential point is that TD occur in the Nigeria population and provision for cure is essential at all level of society. This calls for tailored programs to reduce the burden. However, strategies to improve the detection and management of TDs are hampered by not only lack of diagnostic facilities but also economic consideration.

As age of the patients differ, it indicates that prevalence was not solely explained by age factor, since it was not stratified by age. However, the prevalence ratio of TDs was more in female 4:2 than males. This study is in agreement with the report documented in Pakistan where the prevalence of hyperthyroidism was higher in females 3.85% than males 1.2%.[19]

Ten patients had ESS in the present study which is associated with chronic illnesses. It has been documented that this can cause alteration in thyroid hormone pattern in the absence of intrinsic thyroid disease.[25] It has been documented that during prolonged infection, the blood levels of selenium, T3, T4 and TSH may decrease and the conversion of T4 to T3 slows down, thus inducing a hypothyroid state.[26] This contributes to medical practice as awareness of these alterations will help in interpretation of thyroid function test in chronic infection.

Cardiovascular complications were reported in Grave's disease and were the major reason for mortality in this study. Cardiac complications of this disorder have been documented in earlier studies.[1,3,11] About 17.5 million people die each year from cardiovascular diseases globally, 75% of these deaths

occur in low-income and middle-income countries including Nigeria.[27] The current study reported that heart failure was present in 26.7% and atrial fibrillation was present in 20% of patients with Grave's disease. This report is in contrast to 42% obtained by Ogbera *et al*.[11] in Lagos Southwestern Nigeria. However, thyroid hormones affect the cardiovascular system both directly and indirectly,[28] resulting in increased cardiac contractility, increase cardiac output, and reduce systemic vascular resistance. Although hypertension was noted in 34.3% with Grave's disease, but some reported hypertension before the onset of this disorder. However, Grave's disease as cause of hypertension should be suspected, especially when the hypertension in Africa <40 years of age.[1] Another study in Southeastern Nigeria supports this finding where they noted high prevalence of hypertension and obesity among the middle-aged group.[29] The strong association between hypertension and TDs highlights the central role of endothelial dysfunction, which is contributory to the initiation and progression of cardiovascular disease. This gives an idea of the significant individual risk to which many of our patients were subjected. It points to the importance of early diagnosis and intervention against TDs and complications, especially in low income countries like Nigeria. Menstrual irregularities were seen in Grave's disease. Hyperthyroidism may lead to premature menstruation, whereas hypothyroidism may lead to delayed menstruation or pregnancy loss.[30] This has been linked to the connection between thyroid hormone levels and the menstrual cycle which is mediated by thyrotropin-releasing hormone, which has an effect on the ovary.

Although hyperthyroidism is a common endocrine disorder, frequency, and symptoms vary from one patient to another. Report has been documented that clinical management of this disorder is largely rooted in expert opinion and personal experience.[14]

Hypothyroidism is a disorder of diverse origins, in which most cases are due to primary thyroid gland failure arising from chronic autoimmune thyroiditis, radioactive iodine therapy, or surgery. The study reported that post-thyroidectomy and underlying congenital pathology were the main cause of hypothyroidism. Hypothyroidism features are usually nonspecific, and as in hyperthyroidism, there may be cardiovascular complications. Cold intolerance, mental sluggishness, and constipation were prominent features in the patients seen with hypothyroidism in this study. However, reduced mental functioning, lack of physical energy and reduced work output, all contributing to poor quality of life in patients with hypothyroidism.

Patients with chronic disorders frequently delay seeking treatment in this part of the world because of the poor health seeking behavior, lack of diagnostic facilities and financial limitations leading to sociomedical problems. In Nigeria, the belief of not seeking health checks when ill or when apparently healthy is one of the issues that are impacting negatively on the effective health planning. Consequently, we were not surprised to find that approximately half of the patients with palpable thyroid glands presented with Grade 2 goiters. The frequency of occurrence of obstructive features in patients with palpable thyroid glands in this study was also noted. These features included hoarseness and difficulty swallowing.

Limitations

Although we were able to estimate the number of patients with TDs attending UNTH Enugu, we were not able to ascertain the number of thyroid patients resident in Southeastern Nigeria. The results should be considered as a guide for further studies.

Conclusion

The Graves' disease is the most common of TDs and occurs more in females than males. We observed hypertension, heart failure, and atrial fibrillation as promoters of complication and hospitalization. It is recommended that in our patients' hypertension should be managed to lower blood pressure and slow down complications. Health system facilities need to be strengthened in this area to improve the detection and management of TDs.

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Conflicts of interest

There are no conflicts of interest.

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