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ORIGINAL RESEARCH

The spectrum of thyroid disorders at the Endocrine Clinic of Olabisi Onabanjo University Teaching Hospital, Sagamu, South-west, Nigeria

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Abstract

Background: Thyroid disorders constitute the second most common endocrine disorders worldwide, but they are less commonly researched in this environment due to low cost-effectiveness.
Objective: To study the spectrum of thyroid disorders at the Endocrinology Clinic of a tertiary health facility in Sagamu, South-west, Nigeria, over two years.
Method: This retrospective study was conducted on all new clinic attendees with thyroid disorders between January 2016 and December 2017. The data retrieved included clinical data, results of thyroid function tests and thyroid ultrasonographic scan. The patients were grouped clinically into euthyroid, hypothyroid and thyrotoxic states.
Results: A total of 93 thyroid cases were seen, and this constituted 13.64% of all new endocrine consultations (682 patients). The mean age (±SD; range) of the patients was 37.6 (13.6; 15-78) years. Majority of the patients were females with a female-to-male ratio of 4.5:1. Out of these, 77.4% had Goitrous enlargement. Thyrotoxicosis was the most common form of thyroid dysfunction, (72; 77.40%), mainly due to hyperthyroidism from Graves' disease (50; 69.44%), followed by toxic multinodular goitre (12; 16.67%), toxic solitary nodular goiter (5; 6.94%) and others (5; 6.95 %). Hypothyroidism constituted 10.75% while euthyroid goitre constituted 11.85% of all thyroid cases.
Conclusion: Auto-immune thyroid disease remains the most common thyroid disorder among endocrine clinic attendees. There is a need for further studies to elucidate the likely aetiologies.

Keywords: Auto-immunity, Goitres, Graves' disease, Hypothyroidism, Thyroid disorders, Thyrotoxicosis.

Introduction

Thyroid disorders are common endocrinopathies worldwide and the second most common endocrinopathy in Nigeria; the diseases are most often benign. [1-4] Thyroid disorders could manifest with or without thyroid enlargement, with or without abnormal thyroid function tests. [5] Thyroid enlargement may be diffuse or nodular. [3] In recent times, due to the introduction of iodization program, iodine deficiency associated thyroid

dysfunctions are rarely seen. [6] The aetiology of thyroid disorders varies; may be auto-immune, iodine-induced/deficiency, infective, cancers and drug induced. Thyroid disorders may also result from different levels of abnormality, such as the primary (intrinsic to the thyroid gland), secondary (anterior pituitary) and tertiary (hypothalamus). Thyroid disorders due to secondary or tertiary dysfunctions are rare. Most often, when the latter occurs, it coexists with other endocrine diseases of either pituitary or hypothalamic disorders such as hypopituitarism, or singly as a result of TSH–secreting pituitary tumours. Delayed diagnosis or prolonged uncontrolled thyroid dysfunction is associated with high morbidity and mortality.

Thyroid hormones are necessary for development, growth and the maintenance of metabolic processes in the body. The thyroid gland mainly secretes Thyroxin (3,5,3′,5′-l-tetraiodothyronine or T4), and the circulating level of T4 is approximately fourfold higher than the concentration of the biologically active hormone, 3,5,3′-l-triiodothyronine (T3). [7] A classic endocrine negative feedback loop maintains an inverse relationship between the circulating levels of thyroid hormones and Thyroid Stimulating Hormone (Thyrotropin, TSH) thus, establishing the hypothalamic–pituitary–thyroid (HPT) axis set-point. [8, 9]

While previous studies documented the pattern of thyroid disorders in medical out-patient clinics in Lagos and the spectrum of thyroid disorders in Sagamu [3,5], auto-immunity as a likely etiological factor was not studied. The gap this study sought to fill was the role of auto-immune thyroid disorders in thyroid diseases. Therefore, the study aimed to determine the spectrum, prevalence and complications of thyroid disorders in our Endocrinology Clinic to create awareness among the medical community and to hopefully aid in reducing the burden of this disorder through early diagnosis, prompt treatment and better management outcome.

Methods

This was a retrospective, descriptive study of all new thyroid disorder cases presenting between January 2016 and December 2017 at the Endocrinology, Diabetes and Metabolism (EDM) Unit of the Department of Medicine of the Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Ogun State, south-west Nigeria. This study was carried out in accordance with the principles of the Helsinki Declaration.

The Olabisi Onabanjo University Teaching Hospital, Sagamu, is a state-owned tertiary teaching hospital located in south-west Nigeria. The Endocrinology Clinic in this hospital runs once a week with an average of 5–12 new patients per week; about 1-3 cases of these patients per week constitute thyroid cases.

All the patients with thyroid disorders presenting for the first time at the clinic were recruited into the study. Clinical data including demographics, anthropometric parameters, thyroid examinations, and the results of investigations such as FT3, FT4, TSH, Thyroid auto-antibody to Thyroid Peroxidase (TPO) and TSH, thyroid ultrasonography, and other supportive investigations were retrieved from the patients' hospital records. FT3, FT4 and TSH assays were performed at Majekodunmi Research Laboratory of Olabisi Onabanjo University while the thyroid auto-antibodies were assayed at commercial laboratories. Thyroid scan was performed at the Radiology Department of the hospital. Objective clinical assessment of thyroid dysfunction was done using Wayne's Index, which comprises a constellation of nine symptoms and ten physical signs. A score of more than 19 indicated clinical

thyrotoxicosis. Billewicz score was also used as a diagnostic tool; this comprised eight symptoms and six physical signs with a score of +25 or more diagnosing hypothyroidism [10] in addition to biochemical parameters such as FT4, FT3 and TSH. According to combined results of these two assessments, patients were grouped into euthyroid, hyperthyroid and hypothyroid states. Only a few reports (20%) of Fine Needle Aspiration for Cytology (FNAC) could be retrieved from medical records.

Operational definitions

a) Thyrotoxicosis was defined by clinical and/or biochemical evidence of hyperthyroidism, i.e. elevated thyroid hormones, FT4 >22.0pmol/L, FT3>6.5pmol/L and suppressed TSH <0.5u/U/mL. [10] Overt hyperthyroidism referred to patients with Wayne' Index score > 19 in addition to biochemical features of thyrotoxicosis. [10]
b) Subclinical hyperthyroidism was defined by suppressed TSH <0.5u/U/mL in addition to normal serum thyroid hormones. [10]
c) Subclinical hypothyroidism was characterized by elevated TSH > 0.5u/U/ml [10] in addition to normal serum thyroid hormones. [10]
d) Euthyroidism was defined by Wayne' Index score less than 11 in addition to normal FT3, FT4 and TSH levels. [10]
e) Graves' disease was defined by clinical findings of ophthalmopathy, diffusely enlarged goitre, dermopathy and/or elevated anti-TPO /TSH, in addition to hyperthyroidism. [11]
f) Toxic nodular goitre was defined by ultrasonography findings of heterogenous pattern with the occurrence of nodules, in addition to negative thyroid auto-antibodies.

Data analysis

Statistical analysis was performed using SPSS version 21, and the results were presented as proportions (frequencies, percentages) and mean (±SD) values. The Student's t-test was used to compare mean values. Statistical significance was set at $p < 0.05$.

Results

A total of 93 patients were recruited into the study. The mean age (±SD) of the study participants was 37.6 (±3.6) years. Majority of the patients were female (81.7%) with a female-to-male ratio of 4.5: 1. The mean age of the females was significantly lower than the mean age of the males (36 $\pm$ 4.3 years vs 38 $\pm$ 2.1 years; $p = 0.01$) at presentation. The mean Body Mass Index (BMI) and mean blood pressure of the study participants were 25.40 (±4.43) kg/m^2 and systolic blood pressure (SBP) of 145.25 (15.6) mmHg and diastolic blood pressure (DBP) of 74.23 (10.2) mmHg respectively.

Of the patients with thyroid disorders, 72 (77.4%) had a palpable or visible goitre on clinical examination.

The Spectrum of thyroid dysfunctions (Table I) shows that thyrotoxicosis was the commonest dysfunction with primary hyperthyroidism being the common aetiology of the thyrotoxicosis. Graves' disease was the most frequent cause of thyroid endocrinopathy, and it predominantly affected the females compared to males (female-to-male ratio of 8:1). The mean age (±SD) of the patients with Graves disease (GD), toxic multinodular (TMN) goitre and toxic solitary nodular (TSN) were 33.12 (± 12.8) years, 45.5(±8.8) years and 51.3 (±11) years respectively. The mean age of the patients with nodular goitres was significantly higher than the mean age of patients with diffuse goitres ($p = 0.02$). The predominant cause of hypothyroidism was auto-immune thyroiditis (Hashimoto's

thyroiditis) with a mean age (±SD) of 38.1 (±6.2) years, almost similar to Graves' disease (Table I). Graves' disease constituted a principal aetiological factor of hyperthyroidism in 74% of cases.

Table I: Types and prevalence of thyroid disorders and the mean age of patients

Types of Thyroid Disorders		Frequency (%)	Mean Age (SD) (Years)
1. Thyrotoxicosis			
a. Primary Hyperthyroidism	Graves disease	50 (53.7)	33 (12.8)
	Toxic Multinodular Goitre	12 (12.9)	45.5 (8.8)
	Toxic Solitary nodular Goitre	5 (5.3)	51.3 (11)
	Subclinical hyperthyroidism	1 (1.1)	
b. Drug-induced Thyrotoxicosis (Amiodarone)		1 (1.1)	
c. Postpartum Thyroiditis		1 (1.1)	
d. Iatrogenic: Overdosage of Levo-Thyroxine		2 (2.1)	
2. Hypothyroidism	Autoimmune	4 (4.3)	38.2 (6.8)
	Congenital	1 (1.1)	
	Post-thyroidectomy	1 (1.1)	
	Sub-clinical	4 (4.3)	45.6 (4.1)
3. Euthyroidism (Goitre)		10 (10.8)	48.5 (5.1)
4. Thyroid cancer		1 (1.1)	

Majority of the patients received medical therapy (80; 78.5%); 3 (3.2%) had radio-iodine ablation therapy (performed at an external facility), 3 (3.2%) were referred to the surgical unit while 14 (15.1%) had no treatment and are being monitored on regular bases. The most common Thyroid related complication was hypertension (Table II). More than half of the patients with hypothyroidism had auto-immune thyroiditis.

Table II: Thyroid-related complications among study participants.

Complications	Frequency	Percentage
Hypertension	33	35.5
Diabetes mellitus/ Impaired Glucose Tolerance	12	12.9
Thyroid Storm	3	3.2
Adverse Drug Reaction (Carbimazole-induced)	3	3.2
Skin rash/pruritus/neutropenia with fever	2	2.1%
Compressive Ophthalmopathy with visual impairment	2	2.1%
Cholestatic jaundice	1	1.0%

Discussion

The findings in the present study showed the prevalence of thyroid disorders was 13.74 % over two years of review. Thyroid disorders were leading endocrine diseases in Sagamu, Nigeria, second to Diabetes mellitus. This observation confirmed previous reports that thyroid disorders were common endocrine disorders.[1-3]

A female preponderance was documented in the present study, with a female-to-male ratio of 4.5:1. This agreed with previous studies which reported a predominance of female gender in thyroid disorders. [1-6] Besides, it was observed that thyroid disorders commonly affected the age group of 21-50 years, similar to other studies. [1-6] This pattern of distribution in terms of age and sex can be adduced to the predominance of autoimmune disorders.

More than three-quarters (77.4%) of thyroid disorders were associated with thyrotoxicosis. This confirmed previous reports of a high prevalence of thyrotoxicosis among patients with thyroid disorders. [3,12,13] The most frequent cause of hyperthyroidism in this study was Graves' disease (74%), as suggested by the clinical features of ophthalmopathy, diffuse goiter and biochemical hyperthyroidism, in addition to elevated thyroid autoantibodies, predominantly occurring in the young females with a peak age incidence between the third and fourth decades of life. This agrees with the reports of a high prevalence of Grave's disease from previous studies in Nigeria. [1,3] Toxic nodular goitre plus thyroid negative auto-antibodies comprised toxic multi-nodular goitre and solitary nodular goitre (25%) were common in middle age and above with peak age incidence between the fourth and the fifth decade of life. Other less common forms of thyroid disorders found in this study included post-partum thyroiditis (1.1%), amiodarone-induced thyrotoxicosis (1.1%) (iodine-induced thyrotoxicosis called Jod-Basedow phenomenon caused by the high iodine content of amiodarone), and levothyroxine induced thyrotoxicosis (2.1%); all predominantly occurring in females.

Most of the complications observed were related to hyperthyroidism. The most prevalent was hypertension (33.5%); 36.4% of these had severe systolic hypertension. The diagnosis was based on the American College of Cardiology (ACC)/American Hypertension Association and the Eighth Joint National Committee (JNC-8) criteria.[14] A previous report by Salami *et al*., [5] documented a high prevalence of thyrotoxicosis and heart failure on medical treatment in OOUTH. This finding was higher than the earlier documented report of 8% by Olurin, 17% by Ogbera and 17% by Famuyiwa. [3,12,13] The cardiovascular manifestations of thyrotoxicosis are due to excessive effects of thyroid hormones on the heart via a direct or indirect mechanism, leading to increased heart contractility, cardiac output and increased systemic vascular resistance. [15,- 17]
Thyroid storm is rarely reported in the literature. However, three patients presented with thyroid storm based on the criteria of Burch score greater than 45. [18] Thyroid storm may not be uncommon as previously stated. It is a life-threatening form of severe decompensated thyrotoxicosis that usually has an identifiable precipitating factor and is associated with a high mortality rate, if not treated promptly and appropriately.

Other identified complications included impaired glucose tolerance and Diabetes mellitus (12.9%), compressive features related to goitres (5.4%) which presented with respiratory dysfunction/dyspnea and hoarseness of voice and Graves'ophthalmopathy with retro-orbital compression and visual impairment. Other less commonly reported complications included

carbimazole-induced adverse reactions (2.15%) including urticarial, neutropenia, fever and cholestatic jaundice. Other complications with high prevalence as reported in the literature but not frequently observed in this study include liver, renal dysfunction and metabolic bone diseases with fractures, all reflecting the multi-systemic manifestations of uncontrolled thyrotoxicosis/hyperthyroidism.[19-23] Late presentation was mostly responsible for high morbidity observed, either due to financial constraints, a misconception of cultural beliefs, and ignorance on the part of patients and or the primary care physician.

Hypothyroidism was not commonly reported. This may be due to iodination programme introduced into nutrition guidelines. This may have reduced the prevalence of iodine-induced hypothyroidism. Furthermore, Sagamu is not an area known for endemic goitre. [5] However, very few cases of hypothyroidism were observed in this study, and the cases were due to auto-immune Hashimoto thyroiditis; the latter was the common form of hypothyroidism seen in OOUTH. This is similar to the pattern previously documented by Ogbera *et al*.[3] The common manifestation was subtle and non-specific with complains of tiredness, slowing down and constipation. During the period of study, identified hypothyroid cases were managed with Levothyroxine therapy. Cases of euthyroid goitre were few and they most often presented at the Surgical or General Out-patient Departments either for cosmetic reasons or because of associated obstructive complications.

Thyroid cancers were rarely seen at this study location, and this observation is similar to the incidence of thyroid cancers worldwide, although it remains the most common endocrine malignancy. They frequently present in the surgical department and may probably reflect the rarity of thyroid cancer in our environment. The histopathological pattern of thyroid disorders was not included in the design of the present study; an earlier study in OOUTH by Salami *et al*. [5] reported the histopathological pattern of thyroid disorders. [5]

During the period of the present study, most hyperthyroid patients were managed with anti-thyroid oral medications; however, this was frequently complicated by relapses. Radio-iodine ablation therapy, a mainstay of treatment is not available in Ogun State. There are only three facilities for radio-ablation therapy in Nigeria and where available, the therapy is not readily accessible due to logistic reasons and cost. Therefore, the overall psychological and economic impact on the patients cannot be overemphasized.

In the present study, auto-immune thyroid disorders were principally responsible for presentation in the Endocrinology Clinic compared to the previous report by Salami *et al*. [5] which reported the predominance of simple goitres in a 10-year review of hospital records obtained from the General, Medical and Surgical Out-patient Departments of the hospital.

Limitation of the study: Thyroid uptake scan was not performed due to inaccessibility. Only a few reports of FNAC could be accessed from the hospital's Medical Record Department. In addition, not all the patients in the present study had serological tests.

Conclusion

Thyroid disorders were common endocrinopathies, predominantly due to auto-immune aetiologies. Graves' disease was the most common cause of thyroid disorder. There is a need for radio-ablation therapy, which will improve the burden of relapses.
It is recommended that since OOUTH serves Ogun State and the neighbouring states of the

nation, facilities for radio-iodine therapy for thyrotoxicosis or hyperthyroidism should be procured to reduce the burden of management of hyperthyroidism. Practitioners in resource-limited settings should be encouraged to adopt the use of a clinical scoring system in clinical thyroidology, especially in regions where facilities for Thyroid Function Tests are not readily accessible. This will reduce the burden associated with missed or late diagnosis of thyroid disorders.

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