

## ORIGINAL ARTICLE

## HYPERTHYROIDISM IN A PRIVATE MEDICAL SERVICES CENTER, ADDIS ABABA: A 5-YEAR EXPERIENCE

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### ABSTRACT

**Introduction:** *Hyperthyroidism is a common thyroid disorder especially in women. The disorder manifests predominantly as Graves' disease in iodine-sufficient areas and nodular toxic goiter in iodine-deficient countries. In Ethiopia, the magnitude of the disorder is unknown and its management remains suboptimal.*

**Objective:** *The aim of this study was to analyze the pattern and management of patients with hyperthyroidism at the United Vision Medical Services Center, between August 30, 2013 and February 1, 2018.*

**Methods:** *The study was a retrospective analysis of all patients with hyperthyroidism at the United Vision Medical Services Center. The data was statistically analyzed using the SPSS package. The results were tabulated and discussed with literature review.*

**Results:** *A total of 589 patients were studied. The median age was 40 years; the male to female ratio was 1:7.9; and 93% of patients presented with goiter. Majority presented more than two years after the onset of symptoms, in 91% with a toxic nodular goiter. A low thyroid stimulating hormone was noted in 83% of patients and 94% used propylthiouracil. Among 213 patients, 96% underwent a near-total thyroidectomy, in 92% without incident.*

**Conclusion:** *The incidence and prevalence of hyperthyroidism is apparently on the increase in Addis Ababa. Hyperthyroidism predominantly affects women, and, in surgery, toxic nodular goiter is more common than diffuse goiter and the treatment of choice in experienced hands is near-total thyroidectomy.*

**Keywords:** *Hyperthyroidism, pattern, management, United Vision Medical Services, Addis Ababa.*

### INTRODUCTION

Hyperthyroidism is a common disorder characterized by increased thyroid hormone synthesis and secretion; and if undiagnosed or untreated, it can have profound adverse effects (1-3). Thyroid hormones are essential for growth, neuronal development, reproduction and regulation of energy metabolism.

The prevalence of overt hyperthyroidism ranges from 0.2% to 1.3% in iodine-sufficient parts of the world and its incidence corresponds to population iodine nutrition, with higher rates occurring in iodine-deficient countries, mostly due to longstanding nodular thyroid disease (1). Many cases of hyperthyroidism remain undiagnosed in the community unless routine testing is undertaken (4).

Globally, common causes of hyperthyroidism include Graves' disease, toxic multinodular goiter (TMNG), and toxic thyroid adenoma (2). Toxic adenoma and TMNG are the result of focal or diffuse hyperplasia of thyroid follicular cells whose functional capacity is independent of regulation by the thyroid-stimulating hormone (TSH) (5). In Graves' disease, activating thyrotropin-receptor antibodies induce thyroid hormone overproduction (6).

In iodine-sufficient areas, about 80.0% of patients with hyperthyroidism have Graves' disease, whereas TMNG and toxic adenoma account for 50.0% of all cases of hyperthyroidism in iodine-deficient areas, and more predominantly in elderly people (2,7-10). The total goiter rate of 39.9% reported in a recent national study on children is a clear indication that even Ethiopia's young population is severely affected by iodine deficiency, which necessitated national salt iodation (11).

However, a progressive increase in the prevalence of hyperthyroid and autoimmune thyroid disorders has been reported following iodine fortification showing connection between iodine fortification and iodine-induced hyperthyroidism and autoimmune thyroiditis (7,10,12). The increase in the rate of hyperthyroidism following iodine supplementation in several African countries may reflect the conversion of nonfunctioning nodules to hyperfunctioning state and could represent the transition from iodine-deficient to iodine-sufficient states or autonomous hyperfunctioning nodules to compensate for hypothyroidism (10,12). Anthonia OO, et al. (8) cited the prevalence rate of autoimmune thyroid disorders (AITD) of 1.2%, 3.7% and 9.9% from Ethiopia, Libya and Tunisia respectively.

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In all forms of overt thyrotoxicosis, the serum value of TSH is decreased and the measurements of free thyroxine (fT4) or free tri-iodothyronine (fT3), or both, are raised (13,14). As a result of scarce resources, diagnosis and management of thyroid disorders in the African continent remain suboptimal (8,15).

The purpose of this study was to analyze the pattern and management of hyperthyroidism in a private surgical service to foster the bridging of private-public partnership in making appropriate policies in the control and monitoring of thyroid disorders, iodine intake and salt iodation programs. To our knowledge this is the first study on hyperthyroidism in a private facility within Ethiopia.

## MATERIALS AND METHODS

This study was a retrospective analysis of medical records of patients with hyperthyroidism at the United Vision Medical Services Center (UVMSC), Addis Ababa in the period between August 30, 2013 to February 1, 2018. All patients with hyperthyroidism managed at the surgical unit of the medical services center during the study period, including patients referred from other clinics to the Center for surgical treatment were included. UVMSC, besides other medical services, provides outpatient care including preoperative evaluation of endocrine patients, pathology, imaging and laboratory services as well as follow up care for referred as well as visiting patients from all over the country. The collected data included demographic and clinical features, diagnostic reports, types of medical and surgical treatments and follow up courses of patients. During the study period, there was no radioisotope scanning or pharmacy service at the Center and the supply of thionamides was scarce on the market. Thyroid receptor antibody status was not assessed because of unavailability.

Five patients with thyrotoxicosis without goiter were excluded and 589 patients with hyperthyroidism make the basis of this study. Majority of the patients (428/589, 72.7%) had follow up at the medical services center. The extent of thyroidectomy is termed subtotal when the total estimated thyroid tissue left behind is about 8 grams, and near total when the remnant thyroid tissue is not more than 3 grams on one or both lobes of the thyroid gland.

Documents of 589 patients with hyperthyroidism were retrieved and 213 of these patients with controlled toxic goiters underwent thyroidectomy, 205 of these patients had a near total thyroidectomy (NTT) at the Bethzatha General Hospital, a private hospital in Addis Ababa.

Diagnosis of postoperative complications was based on documents of clinical evaluation and or laboratory confirmation.

A questionnaire was prepared, pretested, and the format was filled out by a senior surgical resident. The data were entered into computer and statistical analysis was done by using the SPSS package and the results were tabulated and discussed with literature review.

As the study was a retrospective analysis of medical records, a written ethical clearance was obtained from the management of the United Vision Medical Services Center.

## RESULTS

As is shown in Table 1, most of the patients (400/589, 67.9%) were under 50 years of age, majority between 30 to 49 years (288/589, 48.9%) and 32.1% (189/589) above 49 years of age. The age range was 15 to 85 years. The overall mean age was 42, and median, 40 years. The median (range) age of patients with goiter type was TMNG, 42 (15-85), diffuse goiter, 35 (20-60), and toxic nodule, 33 (20-60) and thyroid cancer, 48 (19-65) years. Nearly 89.0% (523/589) of patients were females. The male to female ratio was 1.0:7.9. Most of the patients (77.6%) came from Addis Ababa.

The main presenting symptom was goiter or neck swelling in 92.9% (547/589) of patients. Associated symptoms to the most common presenting feature included increased sweating (36.5%), weight loss (24.8%), increased appetite (8.0%), palpitation (7.5%), and irritability (7.1%). Shortness of breath and change in voice were uncommon.

The duration of illness was more than two years in 59.4% of patients. Only 28.2% of patients presented within one year of the onset of their disease. The mean duration at the time of presentation was 28 months.

Goiter was the most common physical finding (582/589, 98.8%), most frequently nodular goiter (534/589, 90.7%) and in majority, a multinodular goiter (504/589, 85.6%). Tachycardia was a common finding (42.4%). But, clinically diffuse goiter (8.3%), retrosternal extension (6.1%), toxic thyroid nodule (5.1%), and exophthalmos (2.9%) were rare clinical features. Hypertension (10.4%), diabetes mellitus (6.1%), and bronchial asthma (0.6%) were noted in 123 patients.

**Table 1:** Demographic and clinical features of 589 patients with hyperthyroidism at United Vision Medical Services Center, Addis Ababa, August 30, 2013 to February 1, 2018.

<b>Variables</b>	<b>Number</b>	<b>Percent</b>
<b>Age groups (n=587)</b>		
<30	112	19.0
30-39	160	27.2
40-49	128	21.7
50-59	116	19.7
>60	73	12.4
Mean/median +SD (range) age	42/40+13.6 (15-85) years	
Sex ratio, M:F	1.0:7.9 [66 (11.2%):523 (88.8%)]	
Address		
Addis Ababa	457	77.6
Outside of Addis Ababa	132	22.4
<b>Main presenting symptoms</b>		
Goiter or neck swelling	547	92.9
Palpitation	9	1.5
Neck pain	28	4.8
Other	5	0.8
Associated symptoms		
Increased appetite	47	8.0
Weight loss	146	24.8
Sweating	215	36.5
Hoarse voice	5	0.8
Fatigue	12	2.0
Palpitation	44	7.5
Shortness of breath	6	1.0
Irritability	42	7.1
Others	72	12.2
Duration of illness		
1-12 months	166	28.2
13-24 months	73	12.4
25-60 months	138	23.4
>61 months	212	36.0
Mean duration +SD (range)	28 +81.3 (1-600) months	
Comorbid disease (n=123)		
Hypertension	61	10.4
Diabetes mellitus	36	6.1
Bronchial asthma	4	0.7
Others	22	3.7
Physical findings		
Multi nodular goiter	504	85.6
Tachycardia	250	42.4
Diffuse goiter	48	8.1
Thyroid nodule	30	5.1
Exophthalmos	17	2.9
Retrosternal extension	36	6.1
Cervical lymphadenopathy	2	0.3
Other	5	0.8

Fine needle aspiration cytology report of 105 patients (Table 2) was consistent with nodular colloid goiter in 67.6% followed by follicular neoplasm (9.5%), thyroid cyst (6.7%), papillary thyroid carcinoma (8.6%), and thyroiditis (2.9%). Histological examination of the 10 follicular neoplasms showed follicular adenoma (50.0%), nodular colloid goiter (30.0%) and follicular carcinoma (20.0%).

Sonography examination on 76 patients revealed multinodular goiter in most of the patients (72.4%) followed by thyroid cyst (15.8%), solitary thyroid nodule (7.9%) and enlarged lymph nodes (1.3%). Chest x-ray evaluation in 102 patients showed tracheal displacement (41.2%), retrosternal extension (25.5%) and calcifications (4.9%).

Thyroid function tests (TFTs) were determined in all patients (Table 2) and the most frequent derangement was a low TSH level (82.7%). The rate of raised T3 or fT3 level plus a low TSH level or a raised T4 or fT4 plus a low TSH level was equivalent. All TFTs were in the toxic level in 16.0% of patients.

The most common final diagnosis was TMNG (79.1%) followed by toxic thyroid nodule (6.5%), diffuse toxic goiter (8.3%), toxic thyroid cancer (1.9%), toxic thyroid cyst (2.0%), and toxic thyroiditis (0.5%). Diffuse toxic goiter with exophthalmos was rare (2.9%).

**Table 2:** Reports of investigations and final diagnosis in 589 patients with hyperthyroidism at United Vision Medical Services Center, Addis Ababa, August 30, 2013 to February 1, 2018.

	Number	Percent
<b>Fine needle aspiration cytology (n=105)</b>		
Nodular colloid goiter (NCG)	71	67.6
Thyroid cyst	7	6.7
Follicular neoplasm	10	9.5
Papillary thyroid carcinoma	9	8.6
Thyroiditis	3	2.9
<b>Histology report (n=10)</b>		
Nodular colloid goiter	3	30.0
Follicular adenoma	5	50.0
Follicular cancer	2	20.0
<b>Neck ultrasound report (n=76)</b>		
Thyroid cyst	12	15.8
Solitary thyroid nodule	6	7.9
Multinodular goiter	55	72.4
Lymphadenopathy	1	1.3
<b>TFT report (n=589)</b>		
Raised T3 or fT3	155	26.3
Raised T4 or fT4	152	25.8
Low TSH	487	82.7
Raised T3 or fT3 + low TSH	51	8.7
Raised T4 or fT4 + low TSH	54	9.2
Raised T3 or fT3 + raised T4 or fT4 + low TSH	95	16.1
<b>Chest X-ray report (n=102)</b>		
Normal	27	26.5
Tracheal deviation	42	41.2
Retrosternal extension	26	25.5
Calcification of goiter	5	4.9
Other	2	2.0
<b>Final diagnosis (n=589)</b>		
Solitary toxic nodule	38	6.5
Toxic multinodular goiter (TMNG)	466	79.1
Diffuse toxic goiter	61	10.3
Toxic thyroid cancer	11	1.9
Toxic thyroid cyst	12	2.0
Toxic thyroiditis	3	0.5

As depicted in Table 3, most of the patients (93.9%) were treated with propylthiouracil (PTU), in 26.1% with beta-blockers. Due to lack of the drugs on the local market, only 10.2% of patients were treated with carbimazole or methimazole. Two hundred patients (34.0%) took antithyroid drug (ATD) therapy for more than 12 months, 16.1% for more than 2 years. Majority of the patients (47.8%) used ATD for six months or less. The mean duration of medical treatment at the time of data collection was 15 months.

Patients that became euthyroid with ATD therapy (213, 36.2%) underwent surgical treatment (Table 3), 205 patients in Bethzatha General Hospital. A 15 years old female underwent NTT because of progressive exophthalmos. The most common surgical procedure was an NTT (205/213; 96.2%).

Postoperatively 196 patients (92.0%) remained euthyroid. Twenty-two (10.3%) patients developed postoperative complications including hypothyroidism (6.6%), hypoparathyroidism, weakness of voice, and hematoma (0.9% each).

The follow up of (Table 3) 428 patients (72.7%) was up to three years with a mean duration of 7.9 months. The average duration from first visit to date of operation was 3.8 months, range 5 days to 56 months. The mean duration of postoperative follow up at the time of last visit was 5.8 months, range 7 days to 37.7 months. Postoperative follow up was low after 3 months probably due to personal preference of follow up venue.

**Table 3:** Medical and surgical treatment and postoperative course of patients with hyperthyroidism at United Vision Medical Services Center, Addis Ababa, August 30, 2013 to February 1, 2018.

	Number	Percent
<b>Medical therapy (n=589)</b>		
Propylthiouracil (PTU)	553	93.9
Beta-blocker	154	26.1
Methimazole or carbimazole	60	10.2
<b>Duration of medical therapy(n=589)</b>		
1-6 months	268	45.5
7-12 months	120	20.4
13-24 months	105	17.8
>24 months	95	16.1
Mean duration + (range) of medical therapy	15.4 ± 18.1 (1-120) months	
<b>Extent of surgical treatment (n=213)</b>		
Lobectomy	1	0.5
Subtotal thyroidectomy (STT)	6	2.8
Near total thyroidectomy (NTT)	205	96.2
Total thyroidectomy (TT)	1	0.5
<b>Post-operative complication (n=22)</b>		
Hypoparathyroidism	2	0.9
Hypothyroidism	14	6.6
Hematoma	2	0.9
Voice weakness	2	0.9
Other	2	0.9
<b>Status at last follow up visit(n=213)</b>		
Euthyroid	196	92.0
Hyperthyroid	1	0.5
Hypothyroid	16	7.5
<b>Duration between 1st &amp; last visits (n=428)</b>		
<3 months	177	41.4
3-6 months	84	19.6
>6 months	167	39.0
Mean + (range)	236.7 (1-1809) days	
<b>First visit to operation date (n=213)</b>		
<3 months	118	55.4
3-6 months	35	16.4
>6 months	60	28.2
Average duration ± SD (range)	114 ± 166.6 (5-1679) days	
<b>Operation date to last visit (n=213)</b>		
<3 months	147	69.0
3-6 months	26	12.2
>6 months	40	18.8
Mean ± (range)	173.8 ± 123.7 (7-1131) days	

## DISCUSSION

Hyperthyroidism is a common disorder especially in women and characterized by excess synthesis and secretion of thyroid hormones leading to thyrotoxicosis, and it commonly includes diffuse toxic goiter, toxic multinodular goiter and toxic adenoma.

A majority of patients in our series were in the age group 30-49 and overall median age was 40 years. Others (16,17) reported median ages of 38 and 49 years. Several studies have reported that patients with Graves' disease are younger than those with nodular hyperthyroidism (18,19). The median age of 42 years in our 61 diffuse toxic goiter patients cannot be compared because of the small population of patients. The male to female ratio, 1:7.9 in this study, is comparable with the 1:5.8 to 1:10.0 in other studies reconfirming a clear female gender predisposition to hyperthyroidism (2,10,13,17,19,20). Osei SK, et al (10) reported the median age and the male to female ratios of patients for the various thyroid disorders as follows: TMNG, 36 and 1:8.3, toxic adenoma, 35 and 1:6.1, and Graves' disease, 37 and 1:4.9. Nearly 78.0% of our patients were from Addis Ababa. C Abuye, et al. reported high prevalence of severe iodine deficiency disorders, even in Addis Ababa (11).

In another study (21), symptoms of thyrotoxicosis were, in decreasing order of frequency, palpitations, weakness, heat intolerance, and disturbed sleep. Signs and symptoms were more frequent in Graves' disease, in young patients, and were partially related to biochemical severity. As was also observed in our study, most patients with symptomatic chronic hyperthyroidism had one or several signs or symptoms of thyrotoxicosis. Similar to 59.1% reported from Nigeria (17), 59.4% of our patients presented more than two years after the onset of their symptoms but presented earlier than patients with euthyroid goiters because of the severity of symptoms of hyperthyroidism (22).

The importance of thyrotoxicosis as secondary cause of hypertension especially in Africa has been emphasized (23). A study on 878 patients with Graves' disease revealed that 6.5% of patients were diabetic and 17.1% were hypertensive (24). Hypertension (10.4%) and diabetes mellitus (6.1%) were uncommon comorbidities in the present study. Literature review of studies worldwide concludes that thyroid dysfunction and diabetes mellitus (DM) may coexist and recommends that patients with DM should be screened for thyroid dysfunction (25).

Correlating well with the physical finding, sonography neck scanning on 76 of our patients revealed multinodular goiter in most of the patients (72.4%). While sonographic thyroid examination is an excellent imaging tool, there are few indications for its use in the initial thyroid evaluation (26).

In iodine replete areas Graves' disease is reported to be more frequent than nodular goiter, whereas in iodine depleted areas secondary hyperthyroidism is predominant (1). In our study, the most common goiter was TMNG (79.1%) followed by diffuse toxic goiter (10.3%) and toxic thyroid nodule (6.5%). The prevalence of toxic nodular goiter increases with increasing age and presence of iodine deficiency and may therefore be more common than Graves' disease in chronic iodine deficient regions (27). Anecdotal studies on thyroid disorders in endocrine clinics at Black Lion Hospital showed preponderance of Graves' disease of 55.7% [19] and 48.2% [16,19]. The disparity from ours is probably due to selective referral of patients with diffuse goiters to internists and nodular goiters to surgeons. In a recent national survey in Ethiopia, severe iodine deficiency has been reported (11). The national salt iodation in Ethiopia, unless iodized salt intake is closely monitored, may lead to iodine-induced hyperthyroidism in patients in areas where goiter is endemic. Nonetheless it would appear that the occurrence of AITD in Africa is much less than that in iodine-replete Western populations. Anthonia OO, et al. (27) cited the prevalence rates of AITD of 1.2%, 3.7% and 9.9% from Ethiopia, Libya and Tunisia respectively.

Pathological examination in our series confirmed thyroid cancer in only 1.9% of 105 patients with suspicious features of neoplasms. In surgery, the reported prevalence of thyroid carcinoma in hyperthyroid patients varies widely, ranging from 1.0% to 21.1%. All histological types of thyroid cancers can be associated with lower incidences of all types of hyperthyroidism, and the most frequently reported type is papillary thyroid carcinoma followed by follicular carcinoma as was also noted in the present series (28). The rate of follicular carcinoma in follicular neoplasms in this series is comparable with that in the literature (29).

Thyroid function tests (TFTs) were determined in all patients and the most frequent derangement was a low TSH level (82.7%). Serum TSH measurement has the highest sensitivity and specificity of any single blood test used in the evaluation of suspected hyperthyroidism and should be used as an initial screening test.

However, when hyperthyroidism is strongly suspected, diagnostic accuracy improves when both a serum TSH and fT4 are assessed at the time of the initial evaluation. Serum TSH may remain suppressed for several months after starting therapy (13,14,30).

Most of our patients (93.9%) were treated with PTU due to scarcity of carbimazole or methimazole, which is the preferred ATD except in first trimester pregnancy where PTU is used (17). In addition, compliance with a once-daily methimazole therapy is superior to multiple daily doses of PTU (30).

The American thyroid association guideline suggests that patients with overtly TMNG or toxic adenoma be treated with either I<sup>131</sup> therapy or thyroidectomy (30). For patients with TMNG, the risk of treatment failure or need for repeat treatment is less than 1.0% following NTT or TT, compared with a 20.0% risk of the need for retreatment following I<sup>131</sup> therapy (30).

In our setup, thyroidectomy is still widely employed in the management of hyperthyroidism as patients often manifest with large goiters and secondary hyperthyroidism. The most common surgical procedure in this series was NTT (96.2%) and only one patient had TT. In high income countries, TT represents the treatment of choice for cancers, Graves' disease and increasingly for benign disease (17,30). In low- and middle-income countries, the risk of hypothyroidism, the risk of limited access to thyroxine and the risk of recurrence after partial resections need to be balanced. Moreover, a STT results in a high risk of recurrence, especially in hyperthyroidism, that often becomes unresectable due to scarring and fixation to the deep structures that complicate re-operations (22,29-31). If surgery is chosen as the initial therapy for Graves' disease and TMNG, the preferred procedure is NTT or TT by a high-volume surgeon [30]. However, TT should be avoided whenever possible, if thyroxine supplies are unreliable and, in a bid, to circumvent the inevitable need for lifelong thyroid hormone replacement (22,31-33).

Postoperatively 92.0% (196/213) of our patients remained euthyroid, which shows that surgery is a very effective treatment option. Twenty-two (10.3%) patients developed postoperative complications including hypothyroidism (6.6%), temporary hypoparathyroidism, weakness of voice, and hematoma (0.9% each), which is lower than a finding of hypocalcemia (4.3%) and voice related changes (3.9%) reported from Nigeria (17). In the hands of high-volume thyroid surgeons, following thyroidectomy for Graves' disease, the rates of permanent recurrent laryngeal nerve damage and hypocalcemia have been documented to be less than 1.0% and 2.0 % respectively (30).

In Nigeria, radioactive iodine is offered to only about 7% of patients with thyroid disorders and doses are mostly administered empirically (17). Similar to the report by Sarr A, et al (24) none of our patients received radioactive iodine therapy service because of unavailability in the country.

In conclusion, this study shows that hyperthyroidism predominantly affects young women and our observations indicate that the incidence and prevalence of hyperthyroidism are apparently on the rise and may be related partly to excess consumption of iodized salt. In our experience, nodular toxic goiter is more common than Graves' disease. Propylthiouracil is the main modality of medical treatment. NTT is the most commonly employed and effective surgical treatment and associated with a low and acceptable rate of mostly temporary complications.

## RECOMMENDATION

To know the magnitude and make appropriate policy on the management, the introduction of national registry of thyroid disorders should be emphasized. To prevent goiter and its subsequent consequences, closely monitored salt iodation should be encouraged, but to prevent secondary (iodine-induced) hyperthyroidism, cautious consumption of iodized salt should be practiced especially in areas where chronic goiter is common.

All patients should be examined to exclude goiter and in all patients with goiter TFTs should be done. Thyroid receptor antibody tests should also be available in laboratories to appropriately diagnose Graves' disease, particularly when exophthalmos is absent in diffuse toxic goiter. Alternative and effective antithyroid drugs, especially carbimazole, should be available in the local pharmaceuticals. Besides, the importance and availability of radioactive iodine for the treatment of small and medium goiters should be underscored.

## ACKNOWLEDGEMENT

This study was partially supported by the Addis Ababa University College of Health Sciences. We gratefully appreciate the cooperation of the UVMSC administration in data collection and all referring clinics and hospitals for participating in the care and follow up of the patients. We also thank Bethzatha General Hospital for the surgical care of patients. Mr. Wondwossen Bekele, AAU Department of Community Health assisted in data entry into computer and analysis.

**Conflict of Interest**

The authors have no conflict of interest to declare.

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