Addis Ababa University

College of Health Sciences

Department of Internal Medicine

Investigator: Rahel Teweldebrhan[1]

Advisor: Tedla Kebede[1]

[1]School of Medicine; College of Health Sciences

Corresponding Author: [1]Rahel Teweldebrhan; email: rahel.tewelde98@yahoo.com; Mobile: 0913287333

Graves' Disease Remission Rate and Associated Factors in Patients with Graves' disease in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

A thesis submitted to Addis Ababa University, College of Health Sciences, School of Medicine, Department of Internal Medicine in partial fulfillment of the requirement for a specialty certificate in Internal Medicine

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Declaration

I, Rahel Teweldebrhan, do hereby declare that this manuscript is a result of the works of my own making except where due is made in a review of previous literature in the content, and by my knowledge, has never been submitted for any prior academic award or qualification in this institution.

Rahel Teweldebrhan: Signed: _____Date: _____

Email: rahel.tewelde98@yahoo.com;

Phone: +251913287333

Approval of Thesis Submission

I hereby certify that I have read this thesis prepared under my direction and recommend that it can be accepted as fulfilling the thesis requirement.

Name of Thesis Advisor	Signature	Date
_____	_____	_____
Name of Head of Department	Signature	Date
_____	_____	_____

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Research Summary Information

Name of the Principal Investigator	Dr. Rahel Teweldebrhan
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Address of the PI	Tel: +251913287333 rahel.tewelde98@yahoo.com

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List of Abbreviations

AOR - Adjusted Odds Ratio

ATD - Antithyroid Drug

CBC - Complete Blood Count

ETB - Ethiopian Birr

FPC - Finite Population Correction

FT3 - Free Triiodothyronine

FT4 - Free Thyroxine

GD - Graves' Disease

GREAT - Graves Recurrent Events After Therapy

HMIS - Health Management Information System

IU/L - International Units Per Liter

LFT - Liver Function Test

MMI - Methimazole

OR - Odds Ratio

PTU - Propylthiouracil

RAI - Radioactive Iodine

SD - Standard Deviation

SPSS - Statistical Package for the Social Sciences

T3 - Triiodothyronine

T4 - Thyroxine

TASH - Tikur Anbessa Specialized Hospital

TRAb - Thyrotropin Receptor Antibodies

TSH - Thyroid-Stimulating Hormone

TSI - Thyroid-Stimulating Immunoglobulins

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Abstract

Background: Graves' disease is an autoimmune disorder. It commonly presents with signs and symptoms of hyperthyroidism. It predominantly affects women in their 3rd to 5th decade. Diagnosis involves clinical evaluation, thyroid function testing and antibody testing. Treatment options include antithyroid drugs, radioactive iodine and thyroidectomy. Limited information is available in sub-Saharan Africa settings.

Objectives: This study aims to assess the rate of remission, the time to remission and determine factors associated with and predicting remission of Graves' disease.

Methods: A hospital-based retrospective cross-sectional study design was used. One hundred seventy-six (176) Graves' hyperthyroidism patients treated and followed up from September 2019 to August 2024 were selected from a teaching referral hospital, Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia. All clinically diagnosed Graves' disease patients who received only medical treatment for a minimum of 12 months were included in the study. The rate of remission and time to remission in Graves' disease patients were analyzed using descriptive statistics. Predictors of remission among independent variables were determined first through bivariate logistic regression, followed by multivariate logistic regression to calculate adjusted odds ratios with a 95% confidence interval and a significance threshold of less than 0.05.

Results: The study included 176 patients diagnosed with Graves' hyperthyroidism, with 83.6% achieving euthyroid status and 45.5% attaining remission after antithyroid drug (ATD) therapy. Symptom improvement was reported in 89.2% of patients, while 79.0% showed improved clinical signs. Predictors of remission were explored, and multivariate logistic regression identified the presence of goiter (AOR: 0.282, $p = 0.001$) and ophthalmopathy (exophthalmos) (AOR: 0.421, $p = 0.019$) as statistically significant factors negatively impacting remission rates. The findings highlight the efficacy of ATD therapy in achieving euthyroid status and remission, while demonstrating the importance of addressing clinical signs such as goiter and exophthalmos in optimizing patient outcomes.

Conclusion: The study identified exophthalmos and goiter as statistically significant predictors leading to non-remission in Graves' hyperthyroidism. This emphasizes the importance of patient-specific management strategies for patients presenting with these clinical features.

Introduction

Background

Thyroid hormones are essential for growth, neuronal development, reproduction and regulation of energy metabolism. The main hormones produced by the thyroid are triiodothyronine (T3) and thyroxine (T4) (1). Hyperthyroidism is a common disorder characterized by increased thyroid hormone synthesis and secretion. Common Symptoms of hyperthyroidism include palpitation, weight loss despite increased appetite, nervousness, irritability, sweating, and difficulty sleeping (2).

Grave's disease is the leading cause of hyperthyroidism in areas with adequate levels of iodine i.e. iodine-sufficient areas (3). The main pathogenesis mechanism is related to unique types of autoantibodies, also called thyroid-stimulating immunoglobulins, that bind to and stimulate the thyrotropin receptor (TSHR) (4). Grave's disease can involve the thyroid gland exclusively or it can present with extrathyroidal manifestations, among which Graves orbitopathy is the commonest (3). It typically presents with symptoms of hyperthyroidism along with unique features like goiter, orbitopathy and occasionally pretibial and localized myxedema (skin thickening on the shins) (5).

Grave's disease is diagnosed through a combination of medical history, physical examination, and blood tests to measure thyroid hormone levels and detect specific antibodies. Additionally, high radioactive iodine uptake test and ultrasonographic imaging can be used in the diagnosis (1,2,6).

Graves' predominantly affects women (female: male ratio 8:1) typically in their 3rd to 5th decades of life (7). In Africa, the epidemiology of thyroid dysfunction has been challenging to monitor due to lack of population-based studies but the few available studies show a prevalence rate of 1.2 to 9.9% among which graves is the commonest (8). A study published more than three decades back in Ethiopia showed that the prevalence of autoimmune thyroid disease was reported to be 1.2% and among these Graves' disease was the commonest at 41.7% (9).

The hyperthyroidism in Graves' is treated by reducing thyroid hormone synthesis, using an antithyroid drug, or reducing the amount of thyroid tissue with radioiodine treatment or by surgical management i.e. thyroidectomy (10). The optimal approach depends on patient preference, geography, clinical factors, availability and affordability.

Statement of the Problem

Even though significant advancements have been made in medical treatments, achieving long term remissions remains a challenge (11). Besides genetic predisposition, environmental triggers and patient adherence to treatment protocols, age, sex, smoking and severity of initial hyperthyroidism influence remission rates as well as relapses once treatment is stopped (12–14). Understanding these factors is crucial for improving patient outcomes and developing effective treatment regimens on a global scale.

In Africa, the burden of Graves' disease is further complicated by limited healthcare resources and varying levels of access to medical care (8). Especially, sub–Saharan Africa faces challenges in disease management due to limited diagnostic and treatment sources which is further complicated by patients' health-seeking behavior and treatment adherence issues. The lack of comprehensive data on thyroid disorders especially Graves' disease in Ethiopia adds a significant challenge for healthcare providers (9).

Rationale of the Study

The remission and relapse rate of Graves' disease has been well documented across the world with a good level of consistency (11,15–21). However there has always been differing views in predictors affecting the outcomes of treatment with antithyroid drugs (15–21). In Ethiopia, there is lack of studies on Graves' disease leaving a gap in understanding the effectiveness of current treatment protocols and factors influencing remission (22–24). This study aims to fill this gap by examining Graves' disease remission rates and identifying predictors.

Significance of the Study

The findings of this study will provide useful insights into the effectiveness of currently available medical treatment options and identify factors influencing remission rates and areas for improvement. This will ultimately lead to better patient outcomes.

On a broader scale, this study has the potential to inform clinical practices not only in Ethiopia but in other developing countries facing similar challenges. By identifying factors associated with remission, more targeted approaches of treatment and follow-up can be devised. This could lead to improved management of Graves' disease with better outcomes.

Literature Review

Epidemiology of Graves' Disease

Graves' disease is the most prevalent cause of hyperthyroidism in iodine repleted geographical areas, with 20–30 annual cases per 100,000 individuals (25). Approximately 3% of women and 0.5% of men develop GD during their lifetime (26). The peak incidence of GD occurs among patients aged 30–60 years, with an increased incidence among African Americans (27). Graves hyperthyroidism (GH) is at least four times more common in women than in men. GH is relatively rare in children. Its incidence starts to increase at the age of 13 years and remains rather stable after the age of 30 years. The average age is 47 years.

The extent of autoimmune thyroid disorders in Africa in general and in Ethiopia in particular remains unknown because of underdiagnosis, underreporting and lack of nationwide studies but the few available studies note a prevalence rate of 1.2% to 9.9% of which Graves diseases is the commonest. Anthonia OO, et al. (8) cited the prevalence rate of autoimmune thyroid disorders (AITD) in Africa ranging from 1.2%, 3.7%, 9.9%, from Ethiopia, Libya and Tunisia respectively.

Clinical Presentation of Graves' Disease

Graves' typically presents with symptoms of hyperthyroidism such as tachycardia, weight loss, and heat intolerance, along with unique features like goiter, orbitopathy and occasionally pretibial and localized myxedema (skin thickening on the shins) (5). Graves' ophthalmopathy occurs in 20-30% of patients while pretibial myxedema is now rarely observed and clinical feature of Graves' disease is becoming milder especially in western countries presumably due to earlier diagnosis and treatment (28). Duration of symptoms until diagnosis is less than 6 months in 61% of patients. A positive family history of autoimmune thyroid disease (AITD) is present in about 50% (29).

Grave's disease is diagnosed through a combination of medical history, physical examination, and blood tests to measure thyroid hormone levels and detect specific antibodies. Low TSH levels, elevated T3 and T4 levels along with elevated thyroid stimulating immunoglobulins (TSI) or thyrotropin receptor antibodies (TRAb) are diagnostic of Graves' disease (30,31). Additionally, high radioactive iodine uptake test and ultrasonographic imaging can be used in the diagnosis (1,2,6).

Treatment of Graves' Disease with Antithyroid Drugs

The major agents for treating thyrotoxicosis are drugs of the thionamide class: carbimazole (CBZ), methimazole (MMI), and propylthiouracil (PTU). CBZ is rapidly decarboxylated in the liver to the active substance MMI. Equivalent doses are 40 mg CBZ, 30 mg MMI, and 400mg PTU (13,32). Each of these agents inhibits the function of thyroid peroxidase, thereby reducing oxidation and organification of thyroidiodide, iodotyrosine coupling, and thyroid hormone biosynthesis. The plasma half-life of MMI is about 6 hours, whereas that of PTU is about 1.5 hours (13,32).

12- to 18-months course of antithyroid drugs leads to remission in approximately 50% of patients. Adverse reactions which could occur in the first 90 days of treatment and relapses in certain group of patients remain a challenge for this approach. (10,11) Treating Graves' disease with RAI and surgery result in gland destruction or removal necessitating life-long levothyroxine replacement (11).

Remission Following Antithyroid Treatment

The majority of patients have a prolonged course of treatment with relapsing and remitting episodes over the years (33). Achieving euthyroid state is a key milestone in the management of Graves' disease and often comes before remission. Euthyroid state, defined as normalization of thyroid hormones and TSH can be achieved through ATD therapy in approximately 70-80% of patients with in the first six months of treatment (34). However, there is variability in time required to achieve euthyroid status depending on adherence to therapy, baseline thyroid levels and disease severity (13).

Remission reflects sustained absence of hyperthyroid symptoms after discontinuation of ATD therapy. Remission rates following ATD therapy range from 30-50% (35). Although hyperthyroidism can almost always be controlled as long as the drug is taken, overall, only

approximately 20-30 percent of patients achieve a permanent remission after one to two years of treatment (31). Studies using long-term antithyroid drugs for 5-10 years of longer have reported remission rate as high 84 percent (36). Relapse rates, which can exceed 50% within the first two years post-therapy, highlight the challenges of achieving stable remission in Graves' disease. Definitive treatments, such as radioactive iodine and thyroidectomy, may offer higher rates of sustained remission but are often reserved for patients with severe disease or persistent relapses.

Methimazole achieves euthyroid state more rapidly than PTU, especially in patients with more severe hyperthyroidism. In one randomized trial, methimazole 30mg daily resulted in a higher percentage of patients with free T4 >7ng/dl having normal free T4 levels at 4, 8, and 12 weeks compared with PTU 300mg daily (37). In a study assessing the effect of long term (36-102 months) versus conventional (18 - 24months) treatments showed 53% relapse in conventional group compared to 15% in the long term group after 48 months of methimazole withdrawal (36).

Factors Predicting Remission and Relapse

While euthyroid status is a prerequisite for remission, not all patients achieve remission even after prolonged euthyroid states. Significance of predictive markers such as TRAb levels, TSI levels, goiter size, ophthalmopathy, gender, age and smoking status (35,38). The absence of exophthalmos and smaller goiter size (19,35), lower baseline levels of TSI below 1.4 IU/L (38) have been strongly linked to better remission rates.

One study showed 97% of patients with TRAb >3.85 IU/L relapsed. It also showed 80% of those patients with TRAb <2 IU/L remained euthyroid for a median follow-up period of 15 months (39). In another study it is showed the frequency of prolonged remission among patients treated with a thionamide for one to two years is usually under 40% (40). And additional two studies mentioned that after 5-10 years of treatment, remission rate have been reported as high as 84% (36,41).

Smoking is a well-established risk factor for Graves' disease and non-remission. The odds ratio for Graves hyperthyroidism is 3.30 (CI 2.09–5.22) in current smokers when compared with never smokers (42). Male gender is considered an adverse prognostic factor for remission of Graves' disease treatment with antithyroid drugs (ATDs), though published data are conflicting, one retrospective study done on 235 patients(64 men and 171 women) showed Men treated with

ATDs have high remission rates 47% vs 58% (*P: 0.14*) and similar recurrence rates (14% vs. 20%; *p: 0.32*) compared to women (43).

GREAT score provides a reasonable prediction of recurrence risk after a course of ATDs based on just four items, age, FT4, TBI, and goiter size (by inspection and palpation), called the GREAT score (Graves Recurrent Events After Therapy. According ot this score younger patients, visible goiter, high free T4 levels and higher TBI levels predict higher recurrence risk after one year treatment with ATD (44).

Objectives

Primary objective

- To assess the rate of remission and associated factors in patients with Graves' Hyperthyroidism in TASH.

Secondary objectives

- To determine the rate of remission of Graves' hyperthyroidism.
- To determine the time to development of graves remission in patients with Graves' hyperthyroidism in TASH.
- To evaluate factors associated with remission in patients with Graves' hyperthyroidism.

Methods

Study Area

The study was conducted at the Tikur Anbessa Specialized Hospital (TASH), one of the largest specialized referral and teaching hospitals located in the nation's capital city, Addis Ababa, Ethiopia.

The hospital's divisions included internal medicine, surgery, gynecology and obstetrics, pediatrics, anesthesiology, radiology, oncology, pathology, dermatology, psychiatry, laboratory, pharmacy, and referral clinics.

Study Design

This study employed a hospital-based retrospective cross-sectional design to analyze data on Graves' disease patients treated at Tikur Anbessa Specialized Hospital (TASH). Data from patient HMIS records is used to assess different thyroid function levels, achievement of remission and predictors of remission.

Inclusion and Exclusion Criteria

Inclusion Criteria

- All clinically diagnosed Graves' hyperthyroidism patients treated at TASH between September 2019 and August 2024 were included in the study.
- Patients who received only medical treatment were considered eligible.
- Patients who underwent antithyroid drug (ATD) therapy for more than 12 months were included.

Exclusion Criteria

- Patients whose hyperthyroidism was caused by conditions other than Graves' disease, such as toxic multinodular goiter (TMNG), toxic adenoma, or iodine-induced hyperthyroidism, were excluded.
- Medical records with incomplete or missing data were excluded.
- Patients who underwent alternative treatments, such as surgery or radioactive iodine (RAI), were excluded from the study.

Source Population

The source population for this study were all clinically diagnosed Graves' hyperthyroidism patients treated at TASH during the five-year period from September 2019 to August 2024.

The study participants for this study were all patients with Graves' hyperthyroidism who fulfilled the inclusion criteria.

Sample Size Calculation

Using a remission rate of 50% for Graves' disease as suggested in global studies, the sample size was calculated using the single population proportion formula. The sampling fraction (n/N) was > 5%; therefore, the estimate of standard error used in the sample size formula was corrected with a finite population correction (FPC), as the n=N. The required sample size, after applying a 95% confidence interval, a remission rate of 50%, and a 10% non-response rate, was determined to be 213 participants.

Sampling Procedure

Participants were selected from TASH HMIS of the endocrine clinic. A total list of Graves' disease patients was prepared as a sampling frame, and a random sampling method was used to determine study participants. However, since there was a limited number of study participants fulfilling the inclusion criteria, all eligible patients were included in the study. And accordingly, 176 patients were found to fulfill the inclusion criteria with a complete set of medical records.

Data Collection Instrument

Secondary data from patients' electronic medical records was used as the data source for this study. A modified data abstraction form was prepared by the investigator, based on tools used in previous studies. Prior to the actual study, a pretest was conducted on 30 participants at TASH one week earlier to identify and address any ambiguities or inconsistencies in the data abstraction process.

Data was collected using both paper-based and digital methods. The data abstraction tool was also designed and implemented using Kobo Collect™.

Study Variables

- **Dependent Variable** – The dependent variable is the occurrence of disease remission.

- **Independent Variables -**
    - Socio-demographic characteristics (baseline age, sex, place of residence,)
    - Baseline TSH, Free T4, Total T3
    - Goiter size
    - Exophthalmos
    - Type of antithyroid medication and dose used
    - Duration of ATD Therapy

Operational Definitions

Remission - Normal TSH and free T4 after 12 months of stopping ATD in patients who took ATD for at least 12 -18 months.

Data Collection Procedure

Data was collected by the investigator using both paper-based and digital methods. The data abstraction tool was implemented using Kobo Collect™.

Data Quality Assurance

To assure the quality of the data, a pre-test was conducted. The steadiness and clarity of the data collection tool were revised following the pre-test. The Kobo online survey tool was configured to administer the prepared questionnaire in the English language. Data collection was done by the investigator for consistency and quality. The collected data was thoroughly examined for completeness, and any incomplete data was excluded from the analysis.

Data Management and Analysis

The collected data was exported to Microsoft Excel, and incomplete entries were cleaned. The cleaned data was coded and entered for analysis using IBM SPSS Statistics, Version 26.0. Continuous were presented as means with standard deviations and ranges. And categorical variables were presented in frequencies and percentages.

Determinants and associated factors were analyzed using logistic regression. Initially, binomial logistic regression was performed on each independent variable ad crude odds ratio and significance value were obtained. Consequently, variables that predicted the dependent variable in a statistically significant manner ($p < 0.05$) during binomial regression were further analyzed through multivariate logistic regression to adjust for any confounding effects. The final adjusted

odds ratios and significance values were reported, with a p-value < 0.05 used to confirm significant associations between independent and dependent variables.

Ethical Considerations

A written ethical approval letter was obtained from the Institutional Review Board. Permission to access the medical charts of the patients was also sought and granted by the hospital administration. All information collected from the patients' medical records was kept confidential to respect patients' rights and to comply with the regulations of the hospital where the study was conducted. Information obtained during the study was handled solely by the investigator. Confidentiality was ensured by excluding study participants' identifiers (such as names and phone numbers), and all data were analyzed in aggregate.

Dissemination of Results

The results of this study will be presented to the department of internal medicine as part of the internal medicine specialty thesis. Attempts will be made to present the results at scientific conferences and to publish the manuscript in local or international journals.

Results

The study screened HMIS records of 296 patients in TASH. 176 patients (24 males, 152 females) who were found to fulfill the study criteria were taken as study participants.

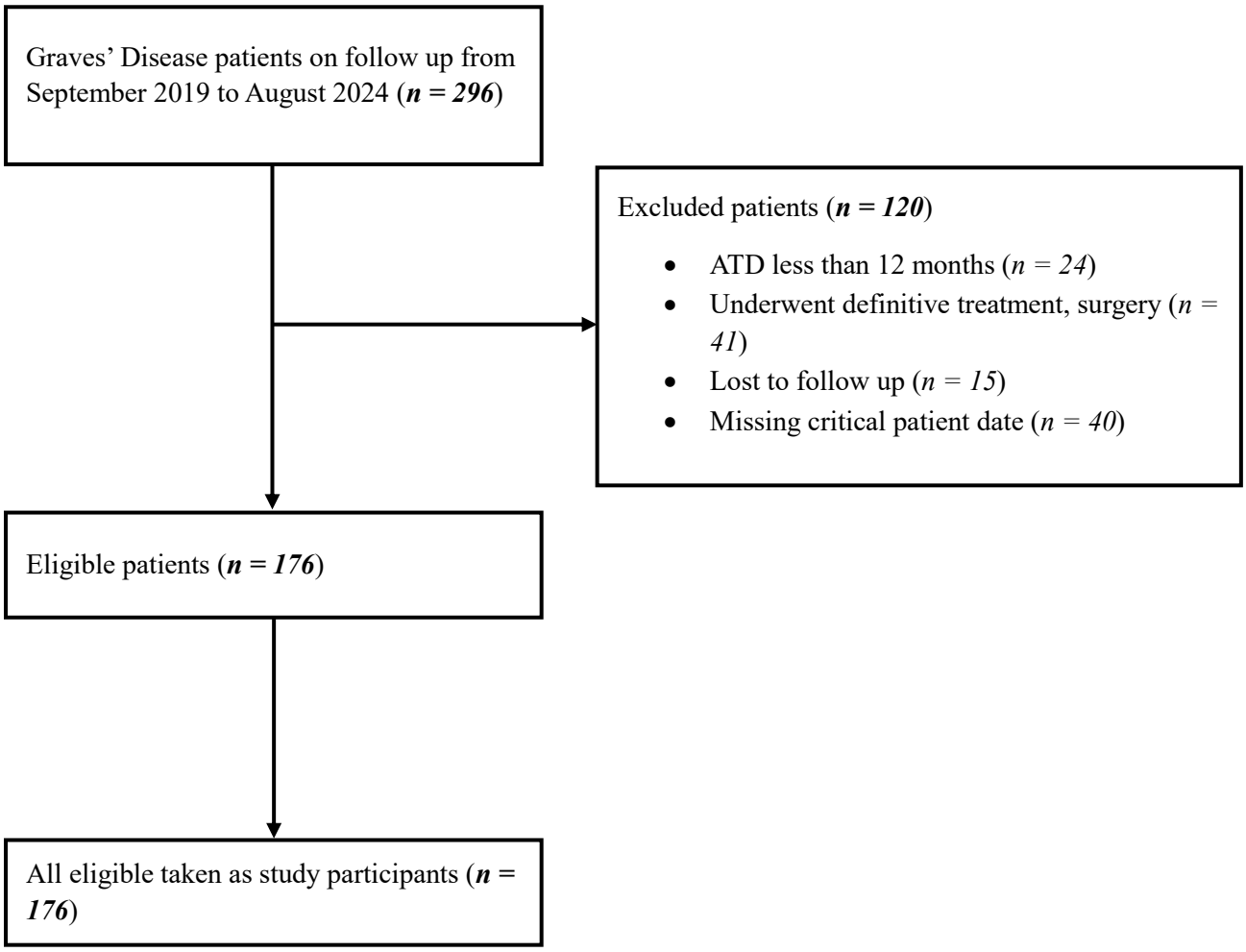

Figure 1. Patient Selection Flowchart

Baseline Characteristics

Out of 176 patients fulfilling the inclusion criteria, 152 (86.4%) were female patients. The mean age at diagnosis was 33.3 ± 9.1 years (range 15 – 62). The mean duration since diagnosis of grave's hyperthyroidism was 44.3 ± 13.6 months (range 12 – 60) at the time of data collection. The mean duration of symptoms before diagnosis of grave's hyperthyroidism was 6.8 ± 4.2 months (range 1 – 36).

175 (99.4%) of the patients have at least one symptom of hyperthyroidism prior to their diagnosis and 136 (77.3%) and 125 (71.0%) patients reported having heat intolerance and

palpitations respectively. 150 (85.2%) had signs of hyperthyroidism at the time of grave's diagnosis and among this tachycardia and goiter were found in 88 (50.0%) and 85 (48.3%) of patients respectively. Ophthalmopathy (exophthalmos) was found in 60 (34.1%) of patients. The mean weight of patients was 55.1 ± 9.9 kgs (range 35 – 100) while their baseline pulse rate was 102 ± 14 (70 – 140). Complications of hyperthyroidism were found in 9 (5.1%) of patients and out of this 6 (3.4%) was heart failure.

Characteristic	No. of Patients	Percent	Mean	Standard Deviation (SD)
Sex				
Male	24	13.6%		
Female	152	86.4%		
Age at Diagnosis			33.3	9.1
Duration Since Diagnosis (Months)			44.3	13.6
Symptom Duration Before Diagnosis (Months)			6.8	4.2
Symptoms of Hyperthyroidism at Diagnosis				
Present	175	99.4%		
Absent	1	0.6%		
Palpitation	125	71.0%		
Tremor	44	25.0%		
Heat Intolerance	136	77.7%		
Weight Loss	72	40.9%		
Other Symptoms	35	19.9%		
Signs of Hyperthyroidism at Diagnosis				
Present	150	85.2%		
Absent	26	14.8%		
Hypertension	19	10.8%		
Tachycardia	88	50.0%		
Exophthalmos	60	34.1%		
Goiter	85	48.3%		
Other Signs	13	7.4%		
Weight of Patients				
Before Treatment			55.1	9.9
After Treatment			60.5	10.2
Pulse Rate of Patients				
Before Treatment			102	14
After Treatment			80	8

Table 1. Baseline Characteristics of Patients until Grave's Diagnosis

Laboratory Results Before and After Treatment

Out of 176 patients, Total T4 was done for 8 patients, Total T3 for 12 patients and Free T3 for 35 patients. On the other hand, Free T4 and TSH were done for all patients. Before initiation of treatment, means of Free T4 and Free T3 levels were found to be 5.2 ± 2.78 (range 0.79 – 9.87) and 7.01 ± 3.39 (range 2.1 – 14.17) respectively. Baseline mean TSH was 0.0097 ± 0.017 (0.0001 – 0.1). Following treatment, for the most recent TFTs, mean of Free T4 and Free T3 were found to be 1.59 ± 1.37 (range 0.1 – 9.7) and 2.98 ± 1.71 (range 0.3 – 8.46). Mean of the recent TSH level was 1.86 ± 4.42 (range 0.001 – 51.2).

175 (99.4%) of patients had high levels of Free T4 (> 1.72) and 176 (100%) of patients had low suppressed levels of TSH (< 0.35) at the baseline. And following treatment, 129 (73.3%%) had normal Free T4 levels (0.8 – 1.72) and 125 (71.0%) had normal TSH levels (0.35 – 4.94).

Lab Parameter	Baseline		Recent	
	Mean	SD	Mean	SD
Total T4*	18.3	6.0 (8.9 – 26.3)	5.82	6.1 (2.0 – 14.88)
Total T3**	4.5	2.3 (1.6 – 10.0)	1.77	0.72 (0.94 – 3.50)
Free T4	5.2	2.78 (0.79 – 9.87)	1.59	1.37 (0.1 – 9.7)
Free T3***	7.01	3.39 (2.1 – 14.17)	2.98	1.71 (0.3 – 8.46)
TSH	0.01	0.017 (0.01 – 0.1)	1.86	4.42 (0.01 – 51.2)
* Total T4 Values were available only for 8 patients. ** Total T3 values were available only for 12 patients. *** Free T3 values were available for 35 patients. Accordingly, Free T4 and TSH levels were found for all 176 patients and used as references to determine thyroid function state of patients.				

Table 2. Thyroid Function Test Results

Treatment of Grave's Hyperthyroidism

All 176 patients were given antithyroid drugs after diagnosis of Grave's hyperthyroidism. 160 (90.9%) were put on Propylthiouracil (PTU), 15 (8.5%) were put on Carbimazole and 1 (0.6%) was put on Methimazole. Side effects were reported in only 9 (5.1%) of patients and among this agranulocytosis was reported in 7 (4.0%) patients. The initial dose for PTU was mostly in the range 250 – 400 mg with 135 (84.4%) patients. From this group 131 (81.9%) took 300 mg daily dose of PTU. For carbimazole most patients were started on 5 – 10 mg with 11 (73.3%) of patients and from these 8 (53.3%) were started on 10 mg. 167 (94.9%) of patients took ATD for 18 or more months.

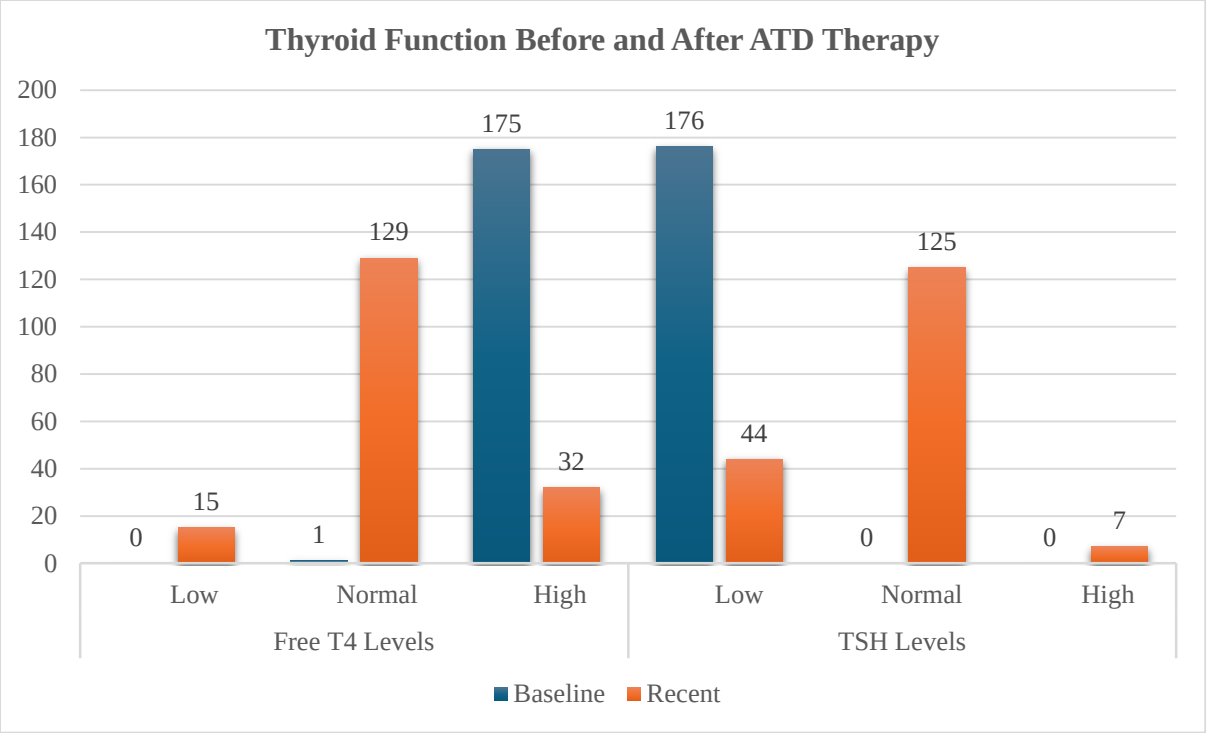

Figure 2. Thyroid Function at Baseline and Following ATD Therapy

Beta adrenergic blockers were administered for 93 (52.8%) of patients and Propranolol was used commonly in 81 (46.0%) of patients followed by Atenolol for 7 (4.0%) patients and Metoprolol for 2 (1.1%) of patients.

	No. of Patients Percent	Achieved Euthyroid	Achieved Remission
Anti-Thyroid Dugs			
Carbimazole	15 (8.5%)	12 (80%)	6 (40%)
Methimazole	1 (0.6%)	1 (100%)	1 (100%)
PTU	160 (90.9%)	134 (83.8%)	73 (45.6%)
Administration of Beta-Adrenergic Blocker			
No	83 (47.2%)		
Yes	93 (52.8%)		
Atenolol	7 (4.0%)		
Metoprolol	2 (1.1%)		
Propranolol	81 (46.0%)		
Others	2 (1.1%)		

Table 3. Antithyroid Drug and Beta-Adrenergic Blocker Treatment

Outcome of Treatment

Symptom improvement was reported in 157 (89.2%) of patients. Improved clinical signs were reported in 139 (79.0%) of patients. The mean weight of patients on their last visit was 60.47 ± 10.17 kgs (range 41 - 105) and the mean pulse rate on their last visit was 80 ± 8 bpm (range 54 - 107). Euthyroid status was achieved in 147 (83.6%) patients and of these 12 were taking carbimazole, 1 methimazole and 134 were taking PTU. The mean time of ATD treatment to achieve Euthyroid state was 6.58 ± 7.95 months (range 1 – 52).

For 64 (43.5%) of the patients, ATDs were continued regardless of euthyroid status and out of these 60 (40.8%) took ATD for more than 18 months. ATDs were discontinued in 83 (56.5%) of the patients. Remission was achieved in 80 (45.5%) patients. Out of this, remission was maintained in 62 (77.5%) patients while 18 (22.5%) patients relapsed. The mean time to relapse was 31.33 ± 18.98 months (range 12 - 60).

Parameters	No. of Patients
Symptoms of Hyperthyroidism	
Improved	157 (89.2%)
Not Improved	19 (10.8%)
Signs of Hyperthyroidism	
Improved	139 (79.0%)
Not Improved	37 (21.0%)
Euthyroid State	
Achieved *	147 (83.6%)
Not Achieved	29 (16.4%)
ATD Drugs after Euthyroid (***n = 147***)	
ATD Discontinued	83 (56.5%)
ATD Continued ***	64 (43.5%)
Remission	
Achieved	80 (45.5%)
Not Achieved	96 (54.5%)
Status on Follow-Up	
Remission Maintained****	62 (77.5%)
Relapsed **	18 (22.5%)
* Mean duration to Euthyroid state was 6.58 ± 7.95 months (range 1 – 52) ** Mean time to relapse was 31.33 ± 18.98 months (range 12 - 60) *** Out of these, 60 (40.8%) took ATDs for more than 18 months **** Mean time duration in remission was 39.07 ± 16.2 months (range 12 - 48)	

Table 4. Outcomes after Treatment with ATD

Predictors of Remission

Several variables were explored as predictors of achieving remission in Grave's hyperthyroidism patients. After binary logistic regression, gender (OR: 2.24, 95% CI: 0.88 – 5.72, p value: 0.09), age at diagnosis (OR: 1.002, 95% CI: 0.97 – 1.04, p value: 0.897), baseline free T4 (OR: 0.979, 95% CI: 0.927 – 1.034, p value: 0.445) and duration of ATD therapy (OR: 0.584, 95% CI: 0.141 – 2.415, p value: 0.458) were found to be not statistically significant.

On the other hand, presence of exophthalmos (OR: 0.443, 95% CI: 0.224 – 0.878, p value: 0.02), and presence of goiter (OR: 0.294, 95% CI: 0.149 – 0.578, p value: < 0.001) were found to be statistically significant. And after multivariate logistic regression, both presence of exophthalmos (AOR: 0.421, 95% CI: 0.204 – 0.870, p value: 0.019) and presence of goiter (AOR: 0.282, 95% CI: 0.138 – 0.577, p value: 0.001) remained statistically significant after controlling for effects of other variables.

Predictors	OR (95% CI)	Sig. Value	AOR (95% CI)	Sig. Value
Gender	2.24 (0.88 – 5.72)	0.09	0.452 (0.139 – 1.464)	0.185
Age at Diagnosis	1.002 (0.97 – 1.04)	0.897	0.99 (0.953 – 1.028)	0.6
Exophthalmos	0.443 (0.224 – 0.878)	0.02	0.421 (0.204 – 0.870)	0.019
Goiter	0.294 (0.149 – 0.578)	<0.001	0.282 (0.138 – 0.577)	0.001
Baseline Free T4	0.979 (0.927 – 1.034)	0.445	0.975 (0.916 – 1.038)	0.423
Duration of ATD therapy	0.584 (0.141 – 2.415)	0.458	1.017 (0.206 – 5.028)	0.984

Table 5. Binomial and Multivariate Regression Results of Predictor Variables for Remission

Discussion

This study involved 176 patients with Graves' hyperthyroidism who were diagnosed and were undergoing treatment at TASH. It assessed the baseline characteristics, treatment approach, treatment outcome and predictors of remission. The baseline characteristics showed female predominance (with male to female ratio: 1:6.35). This aligns with the established epidemiology of Graves' disease, where women are affected 5 – 10 times more frequently than men which could be due to a higher likelihood of autoimmune disorders in females (25,28,45). Mean age at diagnosis (33.3 ± 9.1 years) shows higher prevalence of disease among young adults and it is consistent with multiple studies that report disease onset in the third to fifth decades of life (21). Additionally, baseline data showed a long disease duration since diagnosis averaging 44.3 ± 13.6 months with symptoms present for a mean duration of 6.8 ± 4.2 months before diagnosis. These findings strengthen the chronic nature of Graves' and the challenges to early detection and intervention as they support and strengthen findings from other major studies that revealed time to diagnosis to be less than 6 months (29,46).

Majority of the patients (99.4%) presented with at least one hyperthyroid symptom, with symptoms such as heat intolerance (77.3%) and palpitations (71.0%) being the most common. Symptoms reflect the systemic nature of Graves' and coincide with other studies (34). Among clinical signs tachycardia (50.0%), Goiter (48.3%) and Ophthalmopathy (34.1%) were found to be common. This clinical findings in our patients align closely with numerous other studies that characterize them as hallmarks of the disease (25) especially ophthalmopathy which is reported to be 20 – 40% in Graves' patients (28,47). Low rate of complications (5.1%) from hyperthyroidism such as heart failure suggests a relatively better timely diagnosis and intervention in contrast with higher complication rates in other resource-limited settings reaching as high as 22% (48,49).

PTU was used in 90.9% of patients, likely due to local availability, though carbimazole and methimazole are preferred globally due to better safety profiles in terms of hepatotoxicity and agranulocytosis (15,34). The prolonged ATD duration (≥18 months in 94.9% of patients) reflects a cautious approach to achieve remission, though optimal duration remains debated, with studies suggesting 12-18 months suffice for most (38,50).

Baseline laboratory findings confirmed hyperthyroidism with 99.4% of patients having elevated free T4 all patients having suppressed TSH levels. Following treatment, 73.3% achieved normal levels of free T4. This is found comparable to other studies which reported normalization of thyroid function in 60-70% of patients with in the first 12 months (17,34,48,51).

Treatment outcomes were encouraging, with 89.2% reporting symptom improvement, improvement of clinical signs in 79.0% and 83.6% achieving euthyroid status after a mean duration of 6.86 months. 40.8% of patients with euthyroid status continued taking ATDs possibly indicating a cautious approach to discontinuation due to concerns over relapse or persistent hyperthyroidism. These results coincide with studies reporting euthyroid state in 70 – 90% of ATD-treated patients within 6 – 12 months (15,17,38). Remission rate of 45.5% was found consistent with 40 – 50% reports from long term cohorts (13,16,50). Of those who achieved remission, 77.5% maintained remission and 22.5% experienced relapses with mean relapse time of 31.33 months, which underscores the challenges of sustained remission. However, reports from other studies show comparable relapse rates ranging 20 – 30% within 2-5 years post-ATD discontinuation (25,52). This further emphasizes the importance of incorporating predictive biomarkers such as TSI and TRAb, to improve identification of high risk patients (17).

In terms of predictors, logistic regression identified exophthalmos (AOR: 0.421, p=0.019) and goiter (AOR: 0.282, p=0.001) as significant predictors of lower remission likelihood. These findings further support the findings of studies linking extrathyroidal manifestations and thyroid gland size to persistent disease activity (29,47). In addition to persistent disease activity, larger thyroid volume and orbitopathy were linked to increased relapse risk (19). It also supports the notion that presence of ophthalmopathy reflects a more aggressive disease phenotype with higher TRAb levels (35,50). Similarly, increased thyroid volume indicates greater disease burden and elevated TSIs, reducing ATD efficacy (16).

The lack of significance for gender, age, baseline Free T4, and ATD duration contrasts with some reports linking male gender, younger age or high thyroid hormone levels to poorer outcomes (47,52). However, the results were consistent with other studies that did not show significance for these predictors (17). This discrepancy may arise from population-specific factors, such as genetic predispositions or environmental influences like iodine status, which can modulate

disease course (28,43). The absence of a significant association with ATD therapy duration may be influenced by variations in dosing regimens or patient adherence (7).

Strengths and Limitations of the Study

The study used comprehensive clinical data with detailed baseline and follow up data of 176 patients. By examining Graves' disease as TASH, the study addresses critical gap in regional literature and to the knowledge of the author this is the first study focused solely on Graves' hyperthyroidism in the country. Additionally, the study tracked long term outcome assessment over long period of time with statistical rigor to identify predicting factors.

Limitations of this study include the retrospective design, utilization of HMIS records, and incomplete Total T4/T3 and free T3 data, which may introduce bias or limit thyroid function assessment. The absence of TRAb and TSI measurements, an excellent predictors of relapse is a significant gap, particularly given the predictive value of exophthalmos and goiter (50,52). Additionally, predominant utilization of PTU may skew side effect profiles, reducing generalizability to settings using methimazole. Future studies should incorporate prospective designs, TRAb monitoring, and TSI measurements, which influence Graves' disease outcomes (28).

Conclusion

In conclusion, this study highlights favorable treatment responses in Graves' hyperthyroidism at TASH, with high euthyroid states and symptom resolution rates. The remission rates also follow global trends. The association of exophthalmos and goiter with lower remission emphasizes the need for tailored approach, such as prolonged ATD therapy or early consideration of definitive treatments like radioiodine or surgery in high-risk patients (25,34). This study contributes to the understanding of remission predictors in Graves' hyperthyroidism, emphasizing the role of clinical features in guiding treatment decisions as well as long-term follow-up to manage relapses effectively.

References

1. Cleaveland Clinic. Hyperthyroidism [Internet]. 2024. Available from: https://my.clevelandclinic.org/health/diseases/14129-hyperthyroidism
2. Mayo Clinic. Hyperthyroidism - Symptoms and causes [Internet]. Available from: https://www.mayoclinic.org/diseases-conditions/hyperthyroidism/symptoms-causes/syc-20373659
3. Lanzolla G, Marinò M, Menconi F. Graves disease: latest understanding of pathogenesis and treatment options. Nat Rev Endocrinol [Internet]. 2024;20(11):647–60. Available from: https://doi.org/10.1038/s41574-024-01016-5
4. Orgiazzi J. Thyroid autoimmunity. Presse Med [Internet]. 2012;41(12, Part 2):e611–25. Available from: https://www.sciencedirect.com/science/article/pii/S0755498212005556
5. Ross DS. UpToDate. 2024. Overview of the Clinical Manifestations of Hyperthyroidism in Adults. Available from: https://www.uptodate.com/contents/overview-of-the-clinical-manifestations-of-hyperthyroidism-in-adults?topicRef=7872&source=see_link
6. Ross DS. UpToDate. 2024. Diagnosis of Hyperthyroidism. Available from: https://www.uptodate.com/contents/diagnosis-of-hyperthyroidism?topicRef=7872&source=see_link#H1510489691
7. De Leo S, Lee SY, Braverman LE. Hyperthyroidism. Lancet (London, England). 2016 Aug;388(10047):906–18.
8. Ogbera A, Kuku S. Epidemiology of thyroid diseases in Africa. Indian J Endocrinol Metab [Internet]. 2011;15(6):82. Available from: https://doi.org/10.4103/2230-8210.83331
9. Mengistu M. The pattern of thyroid diseases in adult Ethiopians and experience in management. Ethiop Med J. 1993 Jan;31(1):25–36.
10. Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson JL. Hyperthyroidism and Other Causes of Thyrotoxicosis. In: Harrison's Principles of Internal Medicine, 21e [Internet]. New York, NY: McGraw-Hill Education; 2022. Available from: http://accesspharmacy.mhmedical.com/content.aspx?aid=1197729784
11. Burch HB, Cooper DS. Management of Graves Disease: A Review. JAMA. 2015 Dec;314(23):2544–54.

12. Kahaly GJ. Management of Graves Thyroidal and Extrathyroidal Disease: An Update. J Clin Endocrinol Metab [Internet]. 2020 Dec 1;105(12):3704–20. Available from: https://doi.org/10.1210/clinem/dgaa646

13. Cooper DS. Antithyroid Drugs in the Management of Patients with Graves' Disease: An Evidence-Based Approach to Therapeutic Controversies. J Clin Endocrinol Metab [Internet]. 2003 Aug 1;88(8):3474–81. Available from: https://doi.org/10.1210/jc.2003-030185

14. Gigliotti BJ. Age and Sex Predict Severity, Remission, and Recurrence in Graves' Disease. Clin Thyroid [Internet]. 2021 Jun 1;33(6):260–2. Available from: https://doi.org/10.1089/ct.2021

15. Abraham P, Avenell A, McGeoch SC, Clark LF, Bevan JS. Antithyroid drug regimen for treating Graves' hyperthyroidism. Cochrane database Syst Rev. 2010 Jan;2010(1):CD003420.

16. Allannic H, Fauchet R, Orgiazzi J, Madec AM, Genetet B, Lorcy Y, et al. Antithyroid drugs and Graves' disease: a prospective randomized evaluation of the efficacy of treatment duration. J Clin Endocrinol Metab. 1990 Mar;70(3):675–9.

17. Anagnostis P, Adamidou F, Polyzos SA, Katergari S, Karathanasi E, Zouli C, et al. Predictors of long-term remission in patients with Graves' disease: a single center experience. Endocrine [Internet]. 2013 Oct 11;44(2):448–53. Available from: http://link.springer.com/10.1007/s12020-013-9895-0

18. Barnes H V, Blizzard RM. Antithyroid drug therapy for toxic diffuse goiter (Graves disease): thirty years experience in children and adolescents. J Pediatr. 1977 Aug;91(2):313–20.

19. Laurberg P, Wallin G, Tallstedt L, Abraham-Nordling M, Lundell G, Tørring O. TSH-receptor autoimmunity in Graves' disease after therapy with anti-thyroid drugs, surgery, or radioiodine: a 5-year prospective randomized study. Eur J Endocrinol. 2008 Jan;158(1):69–75.

20. Liu J, Fu J, Xu Y, Wang G. Antithyroid Drug Therapy for Graves' Disease and Implications for Recurrence. Int J Endocrinol. 2017;2017:3813540.

21. Wiersinga WM. Graves' Disease: Can It Be Cured? Endocrinol Metab (Seoul, Korea). 2019 Mar;34(1):29–38.

22. Gebreyohannes EA, Ayele EM, Tesfaye SA, Seid MA. Normalization of thyroid function tests among thyrotoxicosis patients attending a University Hospital in North-West Ethiopia. Thyroid Res [Internet]. 2019;12(1):3. Available from: https://doi.org/10.1186/s13044-019-0064-2

23. Kebede D, Abay Z, Feleke Y. Pattern, clinical presentations and management of thyroid diseases in national endocrine referral clinics, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Ethiop Med J. 2012 Oct;50(4):287–95.

24. Gulilat A. Assessment of the diagnosis, follow-up and treatment outcomes in patients with hyperthyroidism at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. Addis Ababa Univ. 2021;(May).

25. Smith TJ, Hegedüs L. Graves' Disease. N Engl J Med. 2016 Oct;375(16):1552–65.

26. Nyström HF, Jansson S, Berg G. Incidence rate and clinical features of hyperthyroidism in a long-term iodine sufficient area of Sweden (Gothenburg) 2003-2005. Clin Endocrinol (Oxf). 2013 May;78(5):768–76.

27. McLeod DSA, Caturegli P, Cooper DS, Matos PG, Hutfless S. Variation in rates of autoimmune thyroid disease by race/ethnicity in US military personnel. JAMA. 2014 Apr;311(15):1563–5.

28. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol [Internet]. 2018;14(5):301–16. Available from: https://doi.org/10.1038/nrendo.2018.18

29. Vos XG, Smit N, Endert E, Tijssen JGP, Wiersinga WM. Variation in phenotypic appearance of Graves' disease: effect of genetic anticipation and duration of complaints. Eur J Endocrinol. 2009 Jul;161(1):113–8.

30. Williamson S, Greene SA. Incidence of thyrotoxicosis in childhood: a national population based study in the UK and Ireland. Clin Endocrinol (Oxf). 2010 Mar;72(3):358–63.

31. Havgaard Kjær R, Smedegård Andersen M, Hansen D. Increasing Incidence of Juvenile Thyrotoxicosis in Denmark: A Nationwide Study, 1998-2012. Horm Res Paediatr. 2015;84(2):102–7.

32. Cooper DS. Antithyroid drugs. N Engl J Med. 2005 Mar;352(9):905–17.

33. Hussain YS, Hookham JC, Allahabadia A, Balasubramanian SP. Epidemiology, management and outcomes of Graves' disease-real life data. Endocrine. 2017 Jun;56(3):568–78.

34. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016 Oct;26(10):1343–421.

35. Bahn RS. Graves' ophthalmopathy. N Engl J Med. 2010 Feb;362(8):726–38.

36. Azizi F, Amouzegar A, Tohidi M, Hedayati M, Khalili D, Cheraghi L, et al. Increased Remission Rates After Long-Term Methimazole Therapy in Patients with Graves' Disease: Results of a Randomized Clinical Trial. Thyroid. 2019 Sep;29(9):1192–200.

37. Nakamura H, Noh JY, Itoh K, Fukata S, Miyauchi A, Hamada N. Comparison of methimazole and propylthiouracil in patients with hyperthyroidism caused by Graves' disease. J Clin Endocrinol Metab. 2007 Jun;92(6):2157–62.

38. Bartalena L. Treatment of hyperthyroidism: block and replace versus titration. Endocr Abstr [Internet]. 2008;16. Available from: https://www.endocrine-abstracts.org/ea/0016/ea0016s1.1

39. Carella C, Mazziotti G, Sorvillo F, Piscopo M, Cioffi M, Pilla P, et al. Serum thyrotropin receptor antibodies concentrations in patients with Graves' disease before, at the end of methimazole treatment, and after drug withdrawal: evidence that the activity of thyrotropin receptor antibody and/or thyroid response modify durin. Thyroid. 2006 Mar;16(3):295–302.

40. Törring O, Tallstedt L, Wallin G, Lundell G, Ljunggren JG, Taube A, et al. Graves' hyperthyroidism: treatment with antithyroid drugs, surgery, or radioiodine--a prospective, randomized study. Thyroid Study Group. J Clin Endocrinol Metab. 1996 Aug;81(8):2986–93.

41. Villagelin D, Romaldini JH, Santos RB, Milkos ABBP, Ward LS. Outcomes in Relapsed Graves' Disease Patients Following Radioiodine or Prolonged Low Dose of Methimazole Treatment. Thyroid. 2015 Dec;25(12):1282–90.

42. Wiersinga WM. Smoking and thyroid. Clin Endocrinol (Oxf). 2013 Aug;79(2):145–51.

43. Diker-Cohen T, Duskin-Bitan H, Shimon I, Hirsch D, Akirov A, Tsvetov G, et al. DISEASE PRESENTATION AND REMISSION RATE IN GRAVES DISEASE TREATED WITH ANTITHYROID DRUGS: IS GENDER REALLY A FACTOR? Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol. 2019 Jan;25(1):43–50.

44. Jansen HI, Heuveling van Beek C, Bisschop PH, Heijboer AC, Bruinstroop E, Boelen A. The need for the GREAT+ score to predict relapse in Graves' disease: a questionnaire among patients and internal medicine specialists. J Endocrinol Invest [Internet]. 2024;47(10):2499–505. Available from: https://doi.org/10.1007/s40618-024-02358-7

45. Bartalena L, Masiello E, Magri F, Veronesi G, Bianconi E, Zerbini F, et al. The phenotype of newly diagnosed Graves' disease in Italy in recent years is milder than in the past: results of a large observational longitudinal study. J Endocrinol Invest. 2016 Dec;39(12):1445–51.

46. Khan A, Khan MMA, Akhtar S. Thyroid Disorders, Etiology and Prevalence. J Med Sci [Internet]. 2002;2(2):89–94. Available from: https://doi.org/10.3923/jms.2002.89.94

47. Tanda ML, Piantanida E, Liparulo L, Veronesi G, Lai A, Sassi L, et al. Prevalence and natural history of Graves' orbitopathy in a large series of patients with newly diagnosed graves' hyperthyroidism seen at a single center. J Clin Endocrinol Metab. 2013 Apr;98(4):1443–9.

48. Karmisholt J, Andersen SL, Bulow-Pedersen I, Carlé A, Krejbjerg A, Nygaard B. Predictors of Initial and Sustained Remission in Patients Treated with Antithyroid Drugs for Graves' Hyperthyroidism: The RISG Study. J Thyroid Res. 2019;2019:5945178.

49. Azeez TA, Adetunji TA, Adio M. Thyrotoxicosis in Africa: a systematic review and meta-analysis of the clinical presentation. Egypt J Intern Med [Internet]. 2022;34(1):57. Available from: https://doi.org/10.1186/s43162-022-00145-5

50. Mohlin E, Filipsson Nyström H, Eliasson M. Long-term prognosis after medical treatment of Graves' disease in a northern Swedish population 2000-2010. Eur J Endocrinol. 2014 Mar;170(3):419–27.

51. Žarković M, Wiersinga W, Perros P, Bartalena L, Donati S, Okosieme O, et al. Antithyroid drugs in Graves' hyperthyroidism: differences between "block and replace" and "titration" regimes in frequency of euthyroidism and Graves' orbitopathy during treatment. J Endocrinol Invest [Internet]. 2021;44(2):371–8. Available from: https://doi.org/10.1007/s40618-020-01320-7

52. Vitti P, Rago T, Chiovato L, Pallini S, Santini F, Fiore E, et al. Clinical features of patients with Graves' disease undergoing remission after antithyroid drug treatment. Thyroid. 1997 Jun;7(3):369–75.

Annex I: Data Abstraction Tool

Section One: Clinical Information of the Patient

Question No.	Questions	Answer
201	Duration Since Graves' hyperthyroidism diagnosis	_____years
	Duration of symptom before diagnosis	
202	Were Symptoms of hyperthyroidism present at diagnosis?	1. Yes 2. No
203	If yes for Q.202	1. Palpitation 2. Tremor 3. Heat intolerance 4. Weight loss 5. Others specify
204	Were signs of hyperthyroidism present at diagnosis?	1.yes 2.No
205	If yes for Q.204	1. Hypertension 2. Tachycardia 3. Exophthalmos 4. Goiter 5. Others Specify
206	Did symptoms of hyperthyroidism improve after treatment?	1.Yes 2.No
207	Did signs of hyperthyroidism improve after treatment?	1.Yes 2.No

208	Initial weight and Pulse rate	Weight _____Kg PR _____/min
209	Recent weight and Pulse rate	Weight _____Kg PR _____/min
210	Any Complications of hyperthyroidism present?	
211	If yes for Q.210	1) AF 2) HF 3) Osteoporosis 4) Stroke 5) Others specify
212	Baseline TFT	1. TT4: _____ 2. TT3: _____ 3. FT4: _____ 4. FT3: _____ 5. TSH: _____
213	Recent TFT	1. TT4: _____ 2. TT3: _____ 3. FT4: _____ 4. FT3: _____ 5. TSH: _____
214	Was TT3/TT4 Ratio done for suspected GD?	1. Yes 2. No
215	If yes for Q.214, the ratio was	1. ≥20 2. <20
216	Were TRAb and TSI levels done for suspected GD?	1. Yes 2. No
217	If yes for Q.216, What was the value?	1. TRAb: _____ 2. TSI: _____
218	Was Baseline CBC done?	1. Yes 2. No

219	If yes for Q.218, ANC was	1. <1000 2. ≥1000
220	Was Baseline LFT done?	1. Yes 2. No
221	If yes for Q.220, Transaminases were	1. ≥3x ULN 2. <3x ULN
222	Was Beta adrenergic blocker used?	1. Yes 2. No
223	If yes for Q.222, Which drug?	1. Propranolol 2. Atenolol 3. Metoprolol 4. Other specify
224	Was he/she on ATD?	1. Yes 2. No
225	If yes for Q.224, Name of ATD?	1. Methimazole 2. Carbimazole 3. PTU
226	If PTU used, what was the initial dosage?	
227	If PTU used, what was the recent maintenance dosage?	
228	If methimazole/carbimazole used, what was the initial dosage?	
229	If methimazole/carbimazole used, what was the recent maintenance dosage?	
230	For how long was he/she on the maintenance dose	
231	Date ATD were Initiated:	

232	How many months after treatment initiation was Euthyroid state achieved?	
233	Was any major Side effect of ATDs occurred?	1. Yes 2. No
234	If yes for Q.233, What was the side effect?	1. Hepatotoxicity 2. Agranulocytosis 3. Vasculitis 4. Others specify
235	What was the duration of ATD therapy?	1. ≥ 18 months 2. < 18 months
236	What was the Outcome of treatment with ATDs?	1. Euthyroid state 2. Hyperthyroid state 3. Hypothyroid state
237	What happened to ATD after outcome of Q.236?	1. continued 2. discontinued 3. discontinued and LT4 initiated
238	If the answer to Q 237 is continued, for how many months the patient is on treatment?	
239	If the answer to Q 237 is discontinued, after how many months of taking was it discontinued?	
240	If the answer to Q 237 is discontinued, after how many months of taking after achieving Euthryoid state was discontinued?	
241	If the answer for Q237 is treatment discontinued, what was the outcome after that	1. remission maintained 2. relapse
242	If the answer to Q 241 is relapse, How many months after drug discontinuation the relapse occurred?	