

Progression Profile of Graves' Disease after Treatment with Antithyroid Medications in the Initial Phase with a Loading Dose at the University Teaching Hospital of Brazzaville

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How to cite this paper: Elilié Mawa Ongoth, F., Andzouana Mbamognoua, N.G., Myanda Ohouana, R.L., Okoumou-Moko, A., Dinghat, O.M.Y., Ekoundzola, J.R., Nkoua Eloi, S., Louzolo Kimbembe, R., Sala Apendi, S.S. and Bouénizabila, E. (2026) Progression Profile of Graves' Disease after Treatment with Antithyroid Medications in the Initial Phase with a Loading Dose at the University Teaching Hospital of Brazzaville. *Open Journal of Endocrine and Metabolic Diseases*, 16, 16-25.

<https://doi.org/10.4236/ojemd.2026.161003>

Received: November 26, 2025

Accepted: January 17, 2026

Published: January 20, 2026

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Abstract

Introduction: Graves' disease is an autoimmune thyroid disorder and the leading cause of hyperthyroidism. Initial management involves treatment with antithyroid drugs (ATD) for an initial period of 3 to 6 weeks, with the aim of normalizing thyroid function and stabilizing the patient's clinical condition. However, individual patient characteristics and the response of thyroid function to treatment can influence the progression of the disease. The objective of this study was to investigate the progression profile of Graves' disease after treatment with ATD in the initial phase at the University Teaching Hospital of Brazzaville. **Patients and Methods:** This was an observational, retrospective, and descriptive study conducted from January 1, 2022, to September 30, 2025, in the Metabolic and Endocrine Diseases Department of the University Teaching Hospital of Brazzaville. The study included patients aged 18 years or older with Graves' disease who received ATD treatment organized into an initial and a maintenance phase. The duration of the initial ATD loading dose phase in our study was 4 weeks. **Results:** We collected data from 76 patients with a median age of 35 years (20; 58), with a clear predominance of females (72.4%). Patients consulted on average 11.6 ± 4.55 months after the onset of symptoms, for goiter (86.8%), exophthalmos (78.9%), or weight loss with palpitations (39.5%). Thyrotoxicosis syndrome was found in 92.1% of cases. Specific signs of Graves' disease found were vascular goiter (86.8%), bilateral exophthalmos (78.9%), and pretibial myxedema (2.6%). Thyroid hormone levels showed overt hyperthyroidism (decreased TSH and elevated fT4) in 92.1% of

cases. In 7.9% of cases, hormone tests revealed subclinical hyperthyroidism (decreased TSH and normal fT4). Immunological testing revealed the presence of thyrotropin receptor antibodies (TSH-R-Abs) in 42.1% of cases. All patients received ATD medication. A non-cardioselective beta-blocker was prescribed in 81.6% of cases and an anxiolytic in 52.6% of cases. After the initial phase with a loading dose of ATD, the progression was marked by clinical improvement with biological euthyroidism (67.1%), biological hypothyroidism (13.2%), and persistence of thyrotoxicosis syndrome with biological hyperthyroidism (19.7%). **Conclusion:** Our study shows that antithyroid medications are effective in achieving biological euthyroidism. However, the persistence of hyperthyroidism and the onset of hypothyroidism in some patients demonstrate the need for rigorous serum and clinical monitoring of patients treated for Graves' disease.

Keywords

Graves' Disease, Antithyroid Medications, Progression, Brazzaville

1. Introduction

Graves' disease is an autoimmune disorder affecting the thyroid gland. It is the most common cause of hyperthyroidism and thyrotoxicosis syndrome worldwide [1] [2]. Its clinical, biological, and immunological progression remains highly heterogeneous due to the influence of genetic, environmental, and therapeutic factors [1] [3] [4]. Its management is based on three main therapeutic modalities, namely drug treatment with antithyroid drugs (ATD), surgery, and radioactive iodine. Among these therapeutic options, ATD is the first-line treatment in many medical practice settings due to its accessibility, ease of administration, and ability to induce functional remission of the thyroid gland [1] [5] [6].

The first stage of this ATD drug treatment, the initial phase, lasting between 3 and 6 weeks, aims to rapidly normalize thyroid function (FT4 and fT3) and stabilize the patient's clinical condition [2] [5] [7].

However, the response to this initial therapeutic phase seems to vary from one patient to another.

Depending on individual characteristics, socio-economic factors, the quality of follow-up, and the initial ATD dose chosen [2] [8].

At University Teaching Hospital of Brazzaville, Graves' disease is one of the most common endocrine disorders and the leading cause of hyperthyroidism. Local clinical practice and the various clinical presentations of Graves' disease provide a relevant context for evaluating patient outcomes after the initial phase of ATD treatment [9] [10].

A good understanding of this progression will help optimize treatment protocols with personalized adaptation and anticipation of the risks of relapse or complications.

The objective of this study is to examine the clinical and biological progression of patients treated for disease at University Teaching Hospital of Brazzaville after an initial phase of treatment with ATD at a loading dose.

2. Patients and Methods

This is an observational, retrospective, descriptive study conducted in the metabolic and endocrine diseases department of the University Teaching Hospital of Brazzaville. The study period ran from January 1, 2022, to September 30, 2025, *i.e.*, 3 years and 9 months.

We included patients aged 18 years or older who had been diagnosed with Graves' disease, were being treated at the Brazzaville University Hospital Center, and were receiving ATD treatment in the initial phase with a loading dose for 4 weeks, after which a clinical and biological evaluation was performed.

Patients with other causes of hyperthyroidism (toxic adenoma, thyroiditis, or toxic multinodular goiter), those who received radical treatment after emergency medical preparation, pregnant women, and those who were lost to follow-up before evaluation at the end of the initial phase or who had incomplete medical records were not included.

The study population was determined through exhaustive non-probabilistic sampling, including all cases recorded during the study period that met the inclusion criteria.

Diagnosis of Graves' disease was made in accordance with the French Society of Endocrinology consensus statement on the management of Graves' disease and the European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism. These recommendations include the following for the diagnosis of Graves' disease: presence of a clinical thyrotoxicosis syndrome, specific signs of Graves' disease (exophthalmos, vascular goiter, etc.), a biological hormonal profile of peripheral hyperthyroidism (decreased TSH, elevated or normal free tetraiodothyronine or fT4), and positive autoantibodies directed against the TSH receptor (TRAK) in the immunological assessment [2] [7].

The initial phase, which lasted four weeks in our study, consisted of administering a sufficient dose of ATD, specifically 10 to 30 mg/day of thiamazole or 15 to 40 mg/day of carbimazole, depending on the severity of the hyperthyroidism.

Data were collected from the medical records of patients treated at the center for Graves' disease.

Socio-demographic, clinical, biological, therapeutic, and evolutionary variables were collected.

Therapeutic variables concerned the type of ATD used and its dosage, as well as associated treatments (non-cardioselective beta-blockers, anxiolytics).

Evolutionary data studied included clinical and biological evolution after the attack phase, the occurrence of adverse drug reactions, and status at the end of the attack phase (euthyroidism, persistent hyperthyroidism, iatrogenic hypothyroidism).

Data were entered and analyzed using SPSS (Statistical Package for the Social Sciences) version 25 software. Nominal and ordinal qualitative variables were expressed as frequencies and percentages, while continuous and discrete numerical variables were expressed as means $\pm$ standard deviations or medians with interquartile ranges.

The study was conducted in strict compliance with the confidentiality and anonymity requirements for all participants.

3. Results

During the study period, 130 patients were admitted to our department for consultation or hospitalization for hyperthyroidism.

Graves' disease was the main cause of hyperthyroidism, affecting 94 patients, or 72.3% of cases. The study included 76 patients who met the inclusion criteria. The median age of the patients was 35 years (range: 20 - 58). The study population consisted of 55 women (72.4%) and 21 men (27.6%). The majority of patients came from the city of Brazzaville (85.5%). The different socio-professional categories of the patients are shown in **Figure 1**.

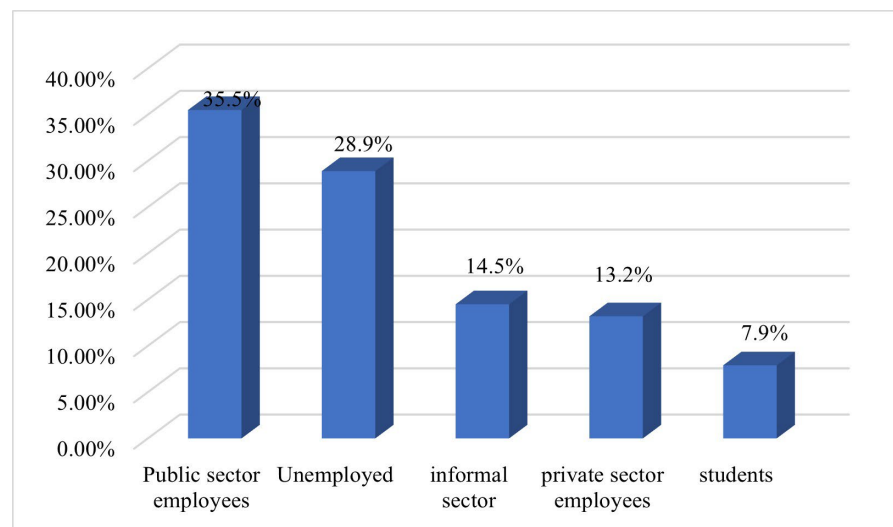


Figure 1. Socio-professional categories of patients.

Average time between the onset of symptoms and consultation was 11.6 ± 4.55 months. The reasons for consultation were goiter (86.8%), exophthalmos (78.9%), or weight loss with palpitations (39.5%). An emotional trigger for the symptoms was found in 47.4% of cases.

Thyrotoxicosis syndrome was found in 92.1% of cases. The specific signs of Graves' disease noted in the study were vascular goiter (86.8%), bilateral exophthalmos (78.9%), and pretibial myxedema (2.6%).

Ultrasound scans performed on all patients showed a generally hypoechoic thyroid gland with hypervascularization in 84.2% of cases.

Hormone testing showed decreased thyroid-stimulating hormone (TSH) in all

patients. Free tetraiodothyronine (fT4) testing led to a diagnosis of peripheral hyperthyroidism in 92.1% of cases and subclinical hyperthyroidism (normal free T4) in 7.9% of cases.

Ultrasound scans performed on all patients showed a generally hypoechoic thyroid gland with hypervascularization in 84.2% of cases.

Immunological testing revealed the presence of thyrotropin receptor antibodies (TRAK) in 42.1% of cases. Graves' disease was associated with other autoimmune diseases in 5 cases (6.57%). These included type 1 diabetes mellitus (4 cases) and rheumatoid arthritis (1 case).

Cardiothyreosis, the serious heart complications arising from excess thyroid hormone, was observed in 17.1% of cases among patients referred by cardiologists to specialized endocrinology consultations.

No patients presented with malignant orbitopathy or acute thyrotoxic crisis.

In terms of treatment, all patients received synthetic antithyroid medication during the attack phase. The different types of ATS used in drug treatment are shown in **Figure 2**.

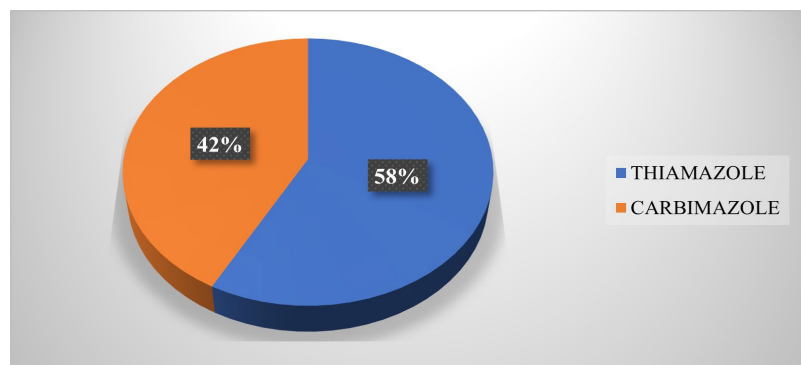


Figure 2. Types of synthetic antithyroid drugs used in initial drug treatment.

Adverse effects of ATD were found in 18.4% of cases. These included mild leukopenia (8 cases), moderate hepatic cytolysis (transaminases less than twice the normal level) in 4 cases, and skin allergy in 2 cases.

The non-specific treatment associated with the management of Graves' disease consisted of medical rest for all patients, a non-cardioselective beta-blocker in 81.6% of cases, and an anxiolytic in 52.6% of cases.

Progression profiles after drug treatment in the attack phase are shown in **Table 1**.

Table 1. Evolving profile after ATS treatment in the initial phase with loading dose.

Evolving profile	N	%
Clinical improvement and euthyroidism	51	67.1
Biological hypothyroidism	10	13.2
Persistent clinical thyrotoxicosis syndrome with biological hyperthyroidism	15	19.7

4. Discussion

Graves' disease is a thyroid disorder first described in 1835 by an Irish physician named Robert James Graves and by a German physician named Karl Von Basedow. It is one of the most common autoimmune thyroid disorders. Its global prevalence is 2% in women and 0.5% in men. It is the most common cause of peripheral hyperthyroidism [1] [11] [12].

During our study period, Graves' disease accounted for 72.3% of all cases of hyperthyroidism recorded in our department. This result is similar to that reported by Diagne *et al.* [6] in Senegal and Abbara *et al.* [13] in the United Kingdom, who reported in their series that Graves' disease accounted for 72% and 83.2% of all cases of hyperthyroidism, respectively.

Data from the literature show that Graves' disease predominantly affects young adults, most commonly between the ages of 30 and 60. This age group is characterized by intense activity and exposure to psychosocial stress [6] [14] [15].

This finding was also observed in our series, where patients with Graves' disease had a median age of 35, with an emotional event preceding the clinical picture in 47.4% of cases.

The clear predominance of women (72.4%) found in our study is consistent with the classic findings of many authors who report that Graves' disease affects women 5 to 10 times more than men, due to the involvement of hormonal and immunogenetic factors that promote autoimmunity [14] [15] [16].

Diagnostic delay reflected in the long average consultation time of 11.6 ± 4.55 months found in our series is consistent with the findings of Diagne *et al.* [6] in Dakar, who found in a retrospective, descriptive study devoted to the epidemiological, clinical, therapeutic, and progressive aspects of Graves' disease in Internal Medicine at the Ledantec University Hospital Center in Dakar that patients consulted on average 12.3 months after the onset of symptoms, with extremes ranging from 5 to 26 months.

Yao *et al.* [15] in Côte d'Ivoire, describing the therapeutic and progressive aspects of Graves' disease at the Military Hospital in Abidjan, found that patients consulted their doctor after an average of 9.3 months.

This delay in diagnosis, resulting from a delay in patients seeking consultation, appears to be due to a lack of awareness of the disease's symptoms among patients, initial self-medication in our contexts, and a delay in seeking specialist consultation in an endocrinology setting [10].

Graves' disease generally presents with a wide range of clinical manifestations, including a variety of symptoms and physical signs that fall within the scope of thyrotoxicosis syndrome, which has been found in a high proportion of cases in multiple studies [6] [13] [17], as in our series, where it was found in 92.1% of cases. This thyrotoxicosis syndrome, associated with manifestations of varying frequency, including vascular goiter, ophthalmopathy, and pretibial myxedema, helps to guide the diagnosis of Graves' disease [6] [18] [19].

In our study, reasons for consultation, represented by goiter (86.8%), bilateral

exophthalmos (78.94%), and weight loss with palpitations (39.5%), were consistent with the classic presentation of Graves' disease [7] [19].

Presence of pretibial myxedema, found in a small proportion (2.6%) of cases, is consistent with the results of several African series, where this specific sign is rare and often observed in less than 5% of cases [6] [9] [15].

Graves' disease is characterized by the infiltration of thyroid-specific T lymphocytes into the thyroid gland and tissues expressing the TSH receptor (TSH-R). This infiltration leads to the production of autoantibodies directed against the TSH receptor (TRAK). These stimulating autoantibodies are evidence of the autoimmune origin of the disease and are responsible for the activation of TSH-R, leading to thyroid hyperplasia and the uncontrolled production and secretion of thyroid hormones, which are responsible for the clinical picture [2] [3] [16].

The positivity of TRAK in 42.1% of cases in our series confirms the autoimmune nature of the disease. This result is similar to that of El Feleh *et al.* [17] in Tunisia, who found TRAK positivity in 45.7% of cases in their series. However, our results differ from those of Koffi Dago *et al.* [20] in Côte d'Ivoire, who found antibody positivity in only 16.18% of cases.

However, our result is lower than that reported by Abbara *et al.* [13] in the United Kingdom, who found TRAK positivity in 99.1% of their series. This difference in results can be explained by methodological variations in TRAK dosage, the duration of the disease prior to diagnosis, genetic factors specific to the population studied, and also the high cost of immunological testing, which limits its availability to all patients in the African context [6] [9].

From a therapeutic standpoint, all of our patients received synthetic antithyroid medication throughout the initial phase, in accordance with the recommendations of several international learned societies [2] [5] [7].

Choice of ATD (carbimazole or thiamazole) and its dose during this initial phase is in line with several international recommendations [2] [7], which recommend the preferential use of thiamazole or carbimazole at doses of 10 to 30 mg/day or 15 to 40 mg/day, respectively, depending on the severity of hyperthyroidism, during this initial phase of drug treatment for Graves' disease.

Addition of a non-cardioselective beta-blocker in 81.6% of cases in our series helped to control the adrenergic manifestations of thyroid disease, as recommended in numerous treatment protocols [1] [2] [4].

Prescription of anxiolytics in 52.6% of cases in our study shows the frequent presence of anxiety disorders in Graves' disease, often exacerbated by metabolic hyperactivity and the psychosocial impact of the disease [3] [21].

In a cross-sectional, descriptive study, Yao *et al.* [15] in Côte d'Ivoire reported the use of three types of ATD in the drug treatment of Graves' disease, namely carbimazole (59.8%), thiamazole (36.6%), and benzylthio-uracil (3.6%). Beta-blockers were used in 87% of cases and anxiolytics in 79.4%.

Close monitoring of ATD treatment throughout the initial phase resulted in clinical improvement and normalization of free tetraiodothyronine (fT4) in 67.1% of cases in our series. This biological euthyroidism reflects a good initial therapeutic

response of thyroid function.

Kahaly *et al.* [2] reported that a significant proportion of patients achieve euthyroidism within 3 to 4 weeks of the initial phase of high-dose synthetic antithyroid drug treatment for Graves' disease.

Progression after this phase was also marked by biological hypothyroidism in 13.2% of cases, reflecting a marked inhibition of the thyrotropic axis by synthetic antithyroid drugs. This could be explained by the marked efficacy of ATS in relation to high dosages or be linked to the possibility of interindividual variability in therapeutic response, prompting the need for careful clinical and biological monitoring after the initial phase [1] [2] [22].

Persistence of clinical and biological hyperthyroidism in 19.7% of cases after the initial phase, as observed in our study, may reflect either resistance to treatment due to a dosage that is inappropriate for the severity of the thyrotoxicosis syndrome, insufficient therapeutic compliance in some patients, or significant and sustained autoimmune activity [1] [6] [8].

Some authors in the literature [1] [4] [22] report that the persistence of hyperthyroidism after initiation of ATD treatment for Graves' disease points to the existence of unfavorable prognostic factors for thyroid function response, such as a large goiter, high titers of anti-TSH receptor autoantibodies, or smoking. These various factors are associated with a marked possibility of recurrence or persistence of hyperthyroidism.

These different types of progression after the initial phase of drug treatment in the management strategy for Graves' disease, as observed in our study, strongly encourage us to analyze patient adherence to treatment and the adjustment of ATD dosages, as well as to search for predictive factors of resistance, such as high TRAK titers, the duration of the disease before treatment, and the size of the goiter [1] [8] [23].

5. Conclusion

Our work on the evolutionary profile of Graves' disease after initial treatment with ATD medication highlights the overall satisfactory efficacy of antithyroid treatment. Indeed, the achievement of euthyroidism in 67.1% of patients demonstrates its efficacy as a first-line treatment. However, the persistence of hyperthyroidism and the onset of hypothyroidism in some cases justify the need for rigorous and prolonged monitoring and personalized care to improve control of the disease and prevent relapses. All of our data highlight the importance of early diagnosis of Graves' disease and appropriate management aimed at optimizing the progression of thyroid disease in the Congolese context.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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