

Original Research Article

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Epidemiological, Clinical and Therapeutic Profile of Graves' Disease At The National Reference University Hospital of N'Djamena

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ABSTRACT

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Graves' disease is an autoimmune disorder of the thyroid gland. Its diagnosis is straightforward, based on a clinical triad: thyrotoxicosis, diffuse goiter, and orbitopathy. The objective of our study was to describe the epidemiological, clinical, paraclinical, and therapeutic aspects of Graves' disease. This was a descriptive cross-sectional study conducted over a six-month period, from January 1, 2023, to June 30, 2023, including 45 patients with Graves' disease seen in consultation and/or hospitalized in the Endocrinology Department of the University Hospital of the National Reference Center. Patients underwent an interview, a complete clinical examination, and thyroid function tests, including thyroid ultrasound. The hospitalization rate was 39%. The mean age was 33.6 years, and the female-to-male ratio was 6.5: 1. The main reasons for consultation were palpitations, weight loss, and an anterior cervical mass in 80%, 57.6%, and 44.4% of cases, respectively. TSH levels were low in all patients (100%), and thyroid ultrasound revealed a diffuse and hypervascularized goiter in 72% of cases. First-line treatment included an antithyroid drug (ATD), combined with beta-blockers and anxiolytics. Graves' disease is the most common cause of hyperthyroidism, primarily affecting young women. The clinical presentation typically involves a triad of symptoms: thyrotoxicosis, a diffuse goiter, and orbitopathy. First-line treatment was medical, with thyroidectomy considered in the event of recurrence.

Introduction

Graves' disease is an autoimmune disease that is the most frequent and expressive cause of thyroid overactivity. It typically involves a goiter, signs of thyrotoxicosis, and extrathyroidal manifestations, the most frequent of which is ophthalmopathy (1, 2).

It affects approximately 1-2% of the world's population with a female predominance (3, 4). Its prevalence in Europe and the United States is estimated to be between 0.5-2% of the adult population (5, 6). In France, Graves' disease accounts for 70% of hyperthyroidism cases (7). In sub-Saharan Africa, the overall prevalence of hyperthyroidism remains unknown. However, hospital series have been reported with varying frequencies from one country to another (8, 9, 10).

The diagnosis is made based on a highly suggestive clinical picture, most often including the clinical triad: goiter, thyrotoxicosis, and exophthalmos.

Hyperthyroidism is confirmed by a collapse of thyroid-stimulating hormone (TSH) and an elevation of tetraiodothyronine (T4). Imaging reveals a diffuse, homogeneous, hypervascularized goiter on thyroid ultrasound (11). Treatment of Graves' disease involves three therapeutic approaches: synthetic antithyroid drugs (ATDs), with or without beta-blockers, and... Anxiolytics, in our context medical treatment remains the first-line treatment (12).

In Chad, we have little data concerning hyperthyroidism and not exclusively on Graves' disease. However, a study conducted in Chad in 2016 showed a hospital prevalence of Graves' disease of 38.4% (13). Hence the interest of our study, the aim of which is to contribute to the improvement of the management of Graves' disease in Chad.

Materials and Methods

Study framework

The study took place in the Endocrinology department of the National Reference University Hospital Center (CHU-RN) in Ndjamena.

Type and duration of studies

This was a cross-sectional study with a descriptive aim.

Which lasted 6 months from January to June 2023.

Study population

The study population consisted of patients with Graves' disease.

Eligibility criteria

Inclusion criteria

All patients presenting with thyrotoxicosis syndrome with a goiter and the mandatory presence of exophthalmos who were received in outpatient consultation and/or hospitalized in the endocrinology-diabetology department during the study period and who consented.

Exclusion criteria

Patients with thyrotoxicosis syndrome and goiter but without exophthalmos and who did not consent were excluded from this study.

Sampling

The sampling was random, consecutive, and non-exhaustive. The above criteria allowed us to select 45 patients with exophthalmos.

Data collection

Data collection was carried out on a pre-established form containing specific elements (socio-demographic, clinical, paraclinical and therapeutic information) for patients seen for Graves' disease. The diagnosis of Graves' disease was made based on the following criteria: a thyrotoxicosis syndrome, a diffuse goiter, these two criteria had to be associated with exophthalmos and a decrease in TSH levels with an increase in T4L.

Technical equipment

The following materials were used to collect the data: a sphygmomanometer, a scale, a waist gauge, and a measuring tape.

Biology Materials

The biological material consisted of blood serum.

Methodology

Clinical orientation

The presence of exophthalmos is the clinical sign that allowed us to confirm the diagnosis of Graves' disease.

Hormone dosage

The Mini Vidas analyzer (BioMérieux) in the immunology unit of the CH-RN laboratory was used to measure TSH and T4L hormone levels. The software provided with the Vidas system includes data analysis and management programs. A bidirectional computer interface automatically transfers results to the user's laboratory information system (LIS) and to various product and patient reports. A quality control system is available to validate a Vidas system test kit.

In our study, Vidas TSH and T4L cartridges were used for the detection of TSH and T4L hormones. The Vidas has five compartments (A, B, C, D, and E). After collecting whole blood in a dry tube or lithium tube and centrifuging it, 150 µL of serum was collected and transferred to the first well of the Vidas HBcT and HBsAg cartridge. The cartridge is then inserted into one of the Vidas compartments. The analyzer is started by clicking on the appropriate compartment, and the test result is expected within 1 hour and 21 minutes (BioMérieux). The analyses were carried out according to the manufacturer's instructions.

Detection of MB by ultrasound

Ultrasound Thyroid function tests were performed on suspected patients using the automated system (Mindray DC 70) for initial assessment. in the diagnosis of Graves' disease. The presence of hypervascularization observable in medical imaging indicates the presence of Graves' disease.

Data analysis

The data were entered into Microsoft Word and Excel 2010 and analyzed using SPSS.22 statistical software. Qualitative variables were expressed as percentages and quantitative variables as mean $\pm$ standard deviation.

Results and Discussion

Sociodemographic characteristics of the studied population

During the study period, we received 115 patients being

monitored for hyperthyroidism. At the Endocrinology department of the National University Reference Hospital (CHU-RN) of N'Djamena, including 45 patients presented signs in favor of Graves' disease, representing a hospital frequency of 39% (Figure 1).

By age group, the most represented patients were between 28 and 34 years old (15 cases, or 33.3%). The mean age was 33.6 ± 14 years. Our sample consisted of 86.7% women and 13.3% men. The female-to-male ratio was 6.5. 42.2% of patients came from N'Djamena (the capital of Chad). 75.6% of patients were housewives (Table 1).

Distribution of patients according to triggering factors and reason for consultation at the MB

In our sample, divorce was the most frequently found triggering factor (46.7%) followed by marital stress (23.9 %).

Regarding the reason for consultation, 80% of patients presented with palpitations (Table 2).

Distribution of patients according to the Clinical and paraclinical signs of MB

Our study showed that the diagnosis of Graves' disease was based on the triad of exophthalmos, thyrotoxicosis syndrome, and diffuse goiter, all of these clinical signs being correlated with thyroid function tests, namely suppressed TSH and thyroid ultrasound, suggestive of a hypervascularized goiter. Regarding treatment, all patients were receiving synthetic antithyroid drugs (Table 3).

In summary, the following question needs to be answered: did the triggering factors (divorce and marital stress), female sex, the presence of hypervascularization observable in medical imaging, Graves' orbitopathy, or more generally, social and hormonal disorders contribute to an autoimmune condition of the thyroid gland or Graves' disease?

The answer to this question would certainly require comparing the results of this study with those of previous work, however very little up-to-date data exists on this subject in Chad.

Among the 115 hyperthyroidism cases collected during

the study period, 45 patients were identified as having Graves' disease, representing a prevalence of 39%. The frequency of Graves' disease found in our study was comparable to that reported by Dionadji *et al.*, in 2016. At Chad, which was 38.4% (13). This frequency was lower than that reported by other authors: Diagne *et al.*, in 2016 in Senegal, which was 72% (8). Nouedoui *et al.*, in 1999 in Cameroon which was 82% (9), This prevalence observed in our study could be explained by the absence of measurement of anti-TSH receptor antibodies and that the diagnosis is based essentially on clinical arguments.

The average age of the patients was 33.6 ± 14 years, with a range from 14 to 55 years. This result is similar to that found by Seydou Dembélé in Mali 2021 which reported $31.7 \text{ years} \pm 14 \text{ years}$ (14), it is close to that of Diagne *et al.*, in 2016 in Senegal in Dakar, which reported 34.6 years and extremes ranging from 13 to 69 years (8), and it is also close to that of Bilosi *et al.*, in 2002 in France who had found 34 years (15).

The female sex was 86.7% with a sex ratio of 6.5 F/M. This female predominance was comparable with other authors: Mbadinga *et al.*, in 1997 in Congo reported a sex ratio of 7.7 F/M (10). Lokrou *et al.*, in 1988 in Ivory Coast had found a sex ratio of 8 F/M (16) and Bilosi *et al.*, in 2002 in France had found a female predominance in 82% (15). The role of sex hormones on the immune system appears to be the cause of this difference. Estrogens, the main female hormones, could thus decrease immune tolerance, thereby increasing autoimmune diseases. Incidence peaks are also observed that correspond to periods in women's lives when hormones are "disrupted": pregnancy, postpartum, and menopause .

The most affected population was that living in N'Djamena (the capital), at 42.2%. This result was similar to that of Diagne *et al.*, in 2016 in Senegal, where 80.6% came from Dakar (8). In our context, this could be explained by the presence of specialists only in the capital and the availability of thyroid tests only in major cities in Chad.

Housewives represented 75.6%. Sissoko in 2022 in Mali had observed this in 54% (17), as did Seydou Dembélé in Mali in 2021 had recovered 56.7 % (14).

The reason for consultation was dominated mainly by palpitations in 80%, followed by weight loss in 57.8%.

This result was comparable to that of Diagne *et al.*, in 2016 in Senegal who found palpitations followed by weight loss in 46.3% and 39.8% respectively (8), while Yao *et al.*, in 2020 in Côte d'Ivoire found weight loss in 87.7%, followed by palpitations in 86.6% (18), whereas Sissoko in 2022 in Mali reported that the association of goiter and exophthalmos represented the most frequent reason for consultation in 76% (17).

In our study, we found divorce to be the most frequently cited triggering factor in 46.7%. Ould Isselmou in Mauritania in 2013 made the same observation, with divorce being the most frequently cited triggering factor in 12% (19), while Diagne *et al.*, in Senegal in 2016 found the same. Family conflicts had been reported as the most represented triggering factor in 45.6% (8).

This could confirm the context of stress as a triggering factor for Graves' disease.

Tachycardia was the most frequent sign of thyrotoxicosis in 95.5%. This result was similar to that reported by Diagne *et al.*, in 2016 in Senegal, which identified thyrotoxicosis syndrome in 93.5% of cases (8). Lokrou *et al.*, In 1988 in Ivory Coast it was reported that tachycardia was the most frequent, at 82% (16).

Regarding Graves' orbitopathy, 100% of patients present with exophthalmos.

This result was higher than that of Diagne *et al.*, in 2016 in Senegal, who found 78.7% (8), Sissoko in 2022 in Mali, who found 84% (17), and Yao *et al.*, in 2020 in Côte d'Ivoire. in Côte Ivory Coast had reported in 79.4% (18).

Exophthalmos is considered a pathogonomic sign; we used it in our study to confirm Graves ' disease.

In our study series, WHO stage 2 was present in 82.2% of cases. This result is higher than that of Joseph B. in 2022 in Senegal. Had found grade 2 goiter in 48.99% (20),

In our study series, the Thyroid-Stimulating Hormone (TSH) level was low, with a mean of $0.082 \mu\text{IU/ml} \pm 0.05 \mu\text{IU/ml}$. This result was reported by African authors with low mean TSH levels: Diagne *et al.*, in 2016 in Senegal found a mean level of $0.007 \mu\text{IU/ml}$ (8), Seydou Dembélé in 2021 In Mali, an average rate of $0.03 \mu\text{IU/ml}$ was reported (14), Moro *et al.*, in 2002 in Côte d'Ivoire

reported an average rate of 0.04µui/ml (21) and Yao *et al.*, in 2020 in Côte d'Ivoire reported an average rate of 0.09 µui/ml (18).

The tetraiodothyronine (T4) level was elevated, with an average of 138.44 pmol/l. This result was similar to that of Seydou Dembélé in 2021. in Mali had an average rate of 128.58 pmol /l (14), Yao *et al.*, in 2020 in Côte d'Ivoire had found an average rate of 120 pmol/l (18).

The contribution of ultrasound in the diagnosis of Graves' disease was 88.8%, with a diffuse, homogeneous, and hypervascularized goiter. This result was comparable to that reported by several authors: Diagne *et al.*, in 2016 in Senegal reported a hypervascularized appearance in 86.4% (8), and Bennis Oum-Keltoum in 2017 in Morocco reported a homogeneous and hypervascularized appearance in 82.85% (22).

Figure.1 Sociodemographic characteristics of the studied population.

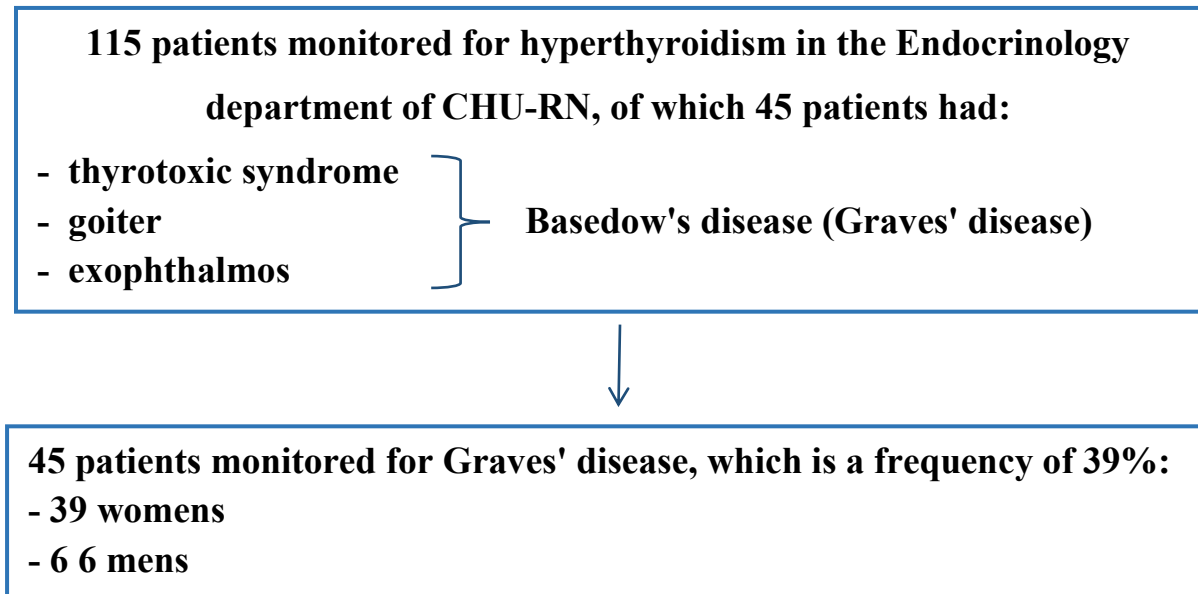


Table.1 Sociodemographic characteristics of the studied population.

Features Epidemiological	n	%
Age range (years)		
28 to 34	15	33.3
35 to 41	10	22.2
Sex		
Female	39	86.7
Male	6	13.3
Origin		
Ndjamena	19	42.2
Bahr-El-Ghazel	9	20
Kanem	6	13.3
Occupation		
Housewife	34	75.6
Student/Pupil	4	8.9

Table.2 Distribution of patients according to triggering factors and reason for consultation

Features	n	%
Triggering factors		
Divorce	21	46.7
Marital stress	13	23.9
Death	10	22.2
Reason for consultation		
Palpitation	36	80
Weight loss	26	57.8
Anterior cervical mass	20	44.4
Exophthalmos	14	31.1
Tremors of the extremities	7	15.6

Table.3 Distribution of patients according to clinical and paraclinical signs

Characteristics	n	%
Orbitopathy		
Bilateral exophthalmos	45	100
Thyrotoxicosis syndrome		
Tachycardia	43	95.5
Weight loss	37	82.2
Insomnia	25	55.6
Fine tremors of the extremities	25	55.6
Motor diarrhea	22	48.9
Nervousness	15	33.3
Goitre		
Stage 1	5	11
Stage 2	37	82.2
Stage 3	3	6.7
TSH (µui/ml)	Low	
Less than 0.01	34	75.6
From 0.1 to 0.2	8	17.8
From 0.3 to 0.4	3	6.6
T4L (pmol/l)	Raised	
Greater than 25	15	33.3
From 25 to 99	6	13.3
100 to 149	6	13.3
150 to 199	2	11.1
200 to 249	5	4.4
250 and more	11	24.4
Thyroid ultrasound		
Diffuse, homogeneous, hypervascularized goiter	18	72
Diffuse homogeneous goiter	5	20
Nodular, heterogeneous goiter	2	8
Treatments		
ATS	45	100
Beta blocker	41	91.1
Anxiolytic	30	66.7

All our patients were receiving medical treatment based on antithyroid drugs (ATDs) in 100%, as well as non-cardioselective beta-blockers in 91.1% and anxiolytics in 66.7%. This result was reported by other authors (18) (8) (22)

Graves' disease is an autoimmune disorder of the thyroid with a predominance in young women.

In this study, the diagnosis of Graves' disease is based on clinical elements, in view of the existence of a thyrotoxicosis syndrome, a diffuse hypervascularized goiter and the obligatory presence of exophthalmos.

This study also helped to determine the triggering factor for Graves' disease (divorce, marital stress),

In view of these results, we recommend conducting expanded studies with anti-TSH receptor antibodies to confirm and determine a high prevalence of Graves' disease in Chad.

Limitations of the study

We wish to conduct specific research on Graves' disease, including Our diagnosis is based on the clinical triad: thyrotoxicosis, goiter, and orbitopathy. It should be noted that Chad is a poor, developing country where the analysis of anti- TSH receptor antibodies (anti -TRAK), which confirms the diagnosis, is unavailable, and Graves' disease is responsible for numerous complications that are often difficult to treat.

We would like to perform a blood test and imaging. This procedure generally involves analyzing biological parameters (TSH; T4L) in the blood to detect hyperthyroidism. A thyroid ultrasound reveals a hypervascularized goiter associated with a pathognomonic clinical sign: exophthalmos. The results obtained have allowed us to confirm the diagnosis and will enable us to contribute to the management of Graves' disease.

Author Contributions

Daboulaye Allah-Sayim Désiré: Conceptualization, Resources. Oumar Abba: Conceptualization, Resources. Batrami Moussa Saleh: Data Preservation, Methodology. Ali Mahamat Moussa: Data Preservation, Methodology. Houba Dallah Tchimy: Methodology. Medila Moussa Ali: Data Preservation. Mouandilmadji Djikoldinguem

Marschall: Resources. Zakaria Abdel-Madjid Zakaria: Resources. Naibe Dangwe Temoua: Resources. Bessimbaye Nadlaou: Conceptualization, Resources

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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