Scientific Research Publishing

Journal of Biosciences and Medicines, 2024, 12, 155-166
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Association of Basedow's Disease and Comorbidities at the Abass Ndao Hospital Center (Senegal)

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How to cite this paper: Sow, P.G., Sow, D., Diouf, H., Diouf, L.D., Dramé, A. and M'baye, G. (2024) Association of Basedow's Disease and Comorbidities at the Abass Ndao Hospital Center (Senegal). *Journal of Biosciences and Medicines*, **12**, 155-166.
https://doi.org/10.4236/jbm.2024.1212013

Received: September 15, 2024
Accepted: December 3, 2024
Published: December 6, 2024

Abstract

Introduction: Graves' disease associated with comorbidities can increase morbidity and mortality. Our objective was to describe the epidemiological, clinical, therapeutic and evolutionary aspects of comorbidities associated with Graves' disease at the Abass hospital center, Ndao. **Methods:** This was a cross-sectional and descriptive study conducted from January 2020 to December 2020. It focused on patients followed for Graves' disease at Abass hospital, Ndao de Dakar. Epidemiological, clinical, therapeutic and evolutionary data were evaluated. **Results:** Three hundred and three eighteen (318) cases were collected, 70 of which had comorbidities (51.15%). The average age was 38.45 years with extremes ranging from 15 to 71 years. Women represented 91.42% of patients. A consultation delay of more than one year was noted in 24.29%. Cardiovascular comorbidities were dominated by hypertension with 30%. Graves' disease was associated with an evolving pregnancy in 10 women. Endocrine comorbidities were dominated by type 1 diabetes noted in 8.57% each. Biermer's disease was noted in 2 patients. Female gender was the most common etiological factor of Graves' disease noted in 64 patients (91.42%). A hereditary predisposition existed in 4 patients (5.71%), stress was noted in 7 patients (10%). 43 patients were under thyrozol (61.42%), 41 patients were on propranolol (58.57%), 14 patients were on carbimazole (20%). A good balance was noted in 44 cases (68.75%) after 9 months of treatment. **Conclusion**: Graves' disease is a public health problem with nonspecific signs. It requires screening and treating comorbidities to reduce morbidity and mortality.

Keywords

Epidemiology, Basedow, Comorbidities, Senegal

1. Introduction

Basedow's disease was named after the German physician Karl Adolph von Basedow who published research on this disease in 1840. Since Japan draws from the German medical tradition, the disease is referred to as Basedow's disease in Japan. In the United States and some other European countries, the disorder is known as "Graves' disease," named after the Irish doctor Robert James Graves. Basedow's disease is a typical disorder that causes hyperthyroidism, a condition in which thyroid hormones are overproduced. Since thyroid hormones are an important factor in stimulating metabolism, overproduction can lead to burdens on organs throughout the body. Hyperthyroidism is among the most common endocrine disorders. It is a pathology that affects 1% to 2% of the adult female population, but does not spare children, men and the elderly [1]. Hyperthyroidism is characterized by hypermetabolism and an increase in serum concentrations of free thyroid hormones that leads to a state of thyroid hormone intoxication (or thyrotoxicosis) [1] [2]. Thyrotoxicosis is also a syndrome related to excess thyroid hormones but includes all causes leading to excess circulating hormones, including those related to glandular destruction (thyroiditis) or exogenous intake [3]. Thyrotoxicosis includes several of the following symptoms, the intensity of which varies greatly from one subject to another: tremor of the extremities, palpitations, tachycardia, hyperthermia, weight loss, diarrhea, nervousness and anxiety, mood disorders, insomnia, increased thirst [3]. Hyperthyroidism has multiple causes [4]. In order of frequency, we find Graves' disease, linked to the stimulation of the thyroid gland by autoantibodies directed against the TSH receptor. Unlike most autoantibodies which are inhibitory, this autoantibody is stimulating, thus causing the synthesis and continuous secretion in excess of T4 and T3 [2] [4]. Graves' disease accounts for 80% of hyperthyroidism in Iceland [1] and 73.3% of hyperthyroidism in France [5]. In Africa, the prevalence of the disease is 82% in Cameroon [6], 72% in Guinea Conakry [7], and 77.44% in Abidjan (Ivory Coast) [8]. In Senegal, during a retrospective study conducted from January 1, 2010 to December 31, 2013 in the Internal Medicine department of the Aristide Le Dantec University Hospital by N Diagne, 834 patients consulted and 150 patients, or 18%, had hyperthyroidism. Graves' disease in Senegal, since 2015, studies on the prevalence of Graves' disease are rare [9].

2. Objectives

2.1. General Objective

Our objective was to describe the epidemiological, clinical, therapeutic and evolutionary aspects of comorbidities associated with Graves' disease at the Abass hospital center. Over a 12-month period (from January 2020 to December 2020).

2.2. Specific Objectives

- Describe the epidemiological characteristics of the study population.

- Describe the clinical aspects of Graves' disease.
- Describe the different comorbidities.
- Describe the therapeutic management and progression of Graves' disease and its comorbidities.

3. Materials and Methods

3.1. Study Framework

This was a cross-sectional and descriptive study conducted from January 2020 to December 2020. It focused on patients followed for Graves' disease at Abass Ndao hospital of Dakar. Epidemiological, clinical, therapeutic and evolutionary data were evaluated. Three hundred and three eighteen (318) cases were collected. The study was carried out at the Abass Ndao Hospital Center of Dakar. In its design, the hospital of Abass Ndao was built in 1935 by Alfred Goux to serve as a rest home for elderly prisoners. This earned it the name "Repos Mandel". The Medical Clinic II of the Abass Ndao Hospital of Dakar (Senegal) brings, the Internal Medicine department, the outpatient consultation and monitoring unit for internal medicine and endocrine pathologies. In addition to care activities, the Medical Clinic II provides theoretical and practical teaching to students of the Faculty of Medicine, Pharmacy and Dentistry of Dakar. Research activities mainly focus on diabetes mellitus, endocrino-metabolic pathologies and those of Internal Medicine.

3.2. Type and Period of the Study

This was a descriptive retrospective study of patient records followed for adult Graves' disease associated with comorbidities over a 12-month period (from January 2020 to December 2020).

3.3. Study Population

The study population was made up of patients followed for Graves' disease.

3.3.1. Inclusion Criteria

Included in our work were all patients followed for Graves' disease during the study period associated with one or more comorbidities.

3.3.2. Non-Inclusion Criteria

Patients with:

- Hyperthyroidism due to a cause other than Graves' disease.
- And incomplete files.

3.4. Parameters Studied

3.4.1. Socio-Demographic Data

The socio-demographic data collected are: age, gender, address.

3.4.2. Background

The patients' personal and/or family history such as: HTA, diabetes, menopause,

thyroid pathologies, autoimmune pathologies (lupus, rheumatoid arthritis, Biermer's disease, adrenal insufficiency, etc.), asthma, sickle cell disease, A state of pregnancy was also sought in the patients.

3.4.3. Clinical Data

- Reason for consultation: goiter, exophthalmos, asthenia, insomnia, nervousness, palpitation, exertional dyspnea, dysphagia, weight loss, thermophobia, tremor of the extremities, dysphonia, headaches, motor diarrhea, hot flashes.

3.4.4. Paraclinical Data

- Blood count: anemia was defined as a hemoglobin level below 12 g/dl in men and 11 g/dl in women.

- Fasting blood sugar: the normal level was 0.8 to 1.10 g/l.

- HbA1c: normal rate <5.7%.

- Lipid profile: hypercholesterolemia was determined by a total cholesterol level greater than 2 g/L or an HDL cholesterol < 0.4 g/L or an LDL cholesterol > 1 g/L and hypertriglyceridemia was defined by a triglyceride level > 1.5 g/L.

- Thyroid Hormone Assessment: Euthyroidism or normal free thyroxine (free T4) is between 10 and 25 picomol/l; free T3 was normally between 1.6 and 3.8 pg /ml and TSH (Thyroid Stimulating Normal hormone level is between 0.2 and 4 µIU/ml.

- The depth of hypothyroidism was classified as follows:

- Mild: when the TSH level is between 5 and 10 µIU/l.
- Moderate: when the TSH level was higher than 10 µIU/l and lower than 50 µIU/l.
- Severe: when TSH is greater than or equal to 50 µIU/l.

- TSH receptor antagonists (TRAK) were positive if the value was greater than 34 IU/ml.

3.5. Comorbidities

Cardiovascular comorbidities:

High blood pressure (HBP) is defined as systolic pressure greater than or equal to 14 mmHg and/or diastolic blood pressure greater than 9 mmHg or a patient known to be hypertensive. Patients being monitored for heart disease and those with signs of heart failure on ECG.

- Endocrine comorbidities

  Type 2 diabetes, Polycytic ovarian syndrome, Obesity.

- Autoimmune comorbidities

  Biermer's disease, adrenal insufficiency, type 1 diabetes, lupus, dermatomyositis, rheumatoid arthritis.

- Other comorbidities

  Anemia and dyslipidemia not related to hypothyroidism, hepatitis B, etc.

3.6. Data Entry and Analysis

Data were entered into Microsoft office Excel software and analyzed by SPSS and

WPS office software.

4. Results

We collected 318 records of patients with Graves' disease. The prevalence of comorbidities associated with Graves' disease was 70 cases (22.01%). Epidemiologically, the average age of patients was 38.45 years with extremes ranging from 15 to 71 years (Figure 1).

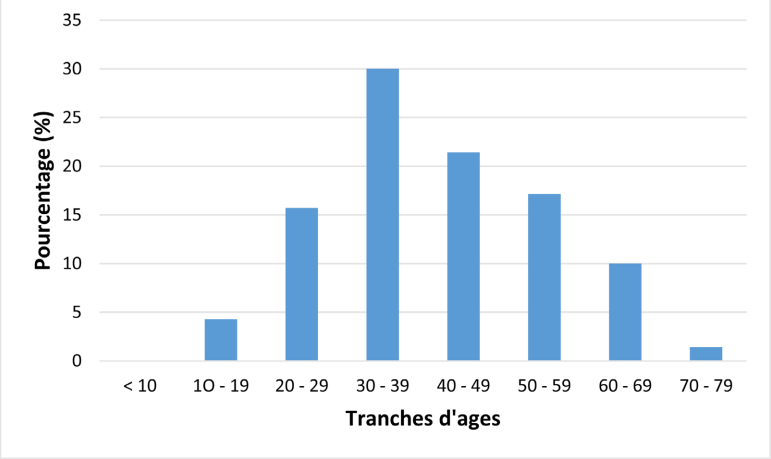

Figure 1. Distribution by age.

Figure 2 shows that Women represented 91.42% of cases (sex ratio = 0.09).

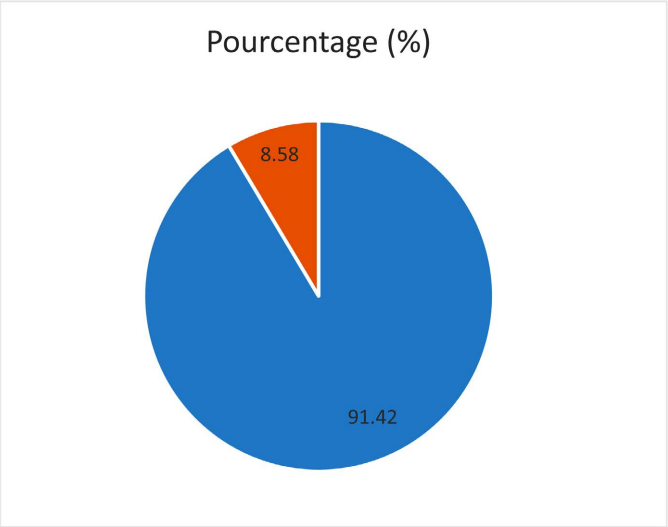

Figure 2. Distribution by sex.

A notion of familial goiter was reported in 4 patients (4.65%). An evolving pregnancy was associated with Graves' disease in 10 women (11.62%). We noted a diagnostic delay in our study. 24.29% of patients were diagnosed after one year. Only 11.42% of patients waited less than a month before consulting. 30% of

patients had goiter, 11.42% had orbitopathy, 52.85% had palpitation, 41.42% had weight loss, 12.85% suffered from asthenia, 34.28% had insomnia, 20% complained of nervousness, 14.28% had thermophobia, 22.85% had tremors of the extremities. 1.42% suffered from motor diarrhea, clinically palpitation was the most common cause found in 37 patients (52.85%) followed by weight loss in 56 patients (41.42%). Mean blood pressure was 129.85 mmHg for systolic and 77.71 mmHg for diastolic. The mean pulse was 95.92 beats per minute. Tachycardia was noted in 29 patients (41.42%). 11 patients had cardiothyreosis or 15.71% and 1 patient had a psychiatric complication. On the paraclinical level, anemia was noted in 60 patients or 38.7%. It was normochromic normocytic in 16 cases and macrocytic in 2 cases. 4 patients had achieved glycated hemoglobin or 6.66%. The mean glycated hemoglobin was 8.47%. Three patients had poorly balanced hemoglobins, i.e. 75%. 61 patients had positive anti -TSH receptor antibody (TRAK) values, i.e. 87.14%. Table 1 shows distribution of anti-TPO antibodies. Cardiovascular comorbidities were dominated by hypertension with 30%. Type 1 diabetes was the most represented endocrine comorbidity noted in 8.57% of patients. Concerning auto immune comorbidities: type 1 diabetes was associated with Graves' disease in 6 cases (8.57%). Biermer's disease was found in 2 cases. PEAI was noted in 8 subjects or 11.42%.

Table 1. Comorbidities endocrines distribution.

Comorbidities endocrine	number (n=)	Number (%)
Type 1 Diabetic	6	8.57
Type 2 Diabetic	5	7.14
Gestational Diabetic	2	2.85
Obesity	3	4.28

On the etiological level, female gender was the main etiological factor found in 91.42 of patients followed by stress noted in 7 patients (10%). In multivariate analysis, only the intensity of thyrotoxicosis (OR = 1.98 [1.52 - 2.60]), the high attack doses in ATS (OR = 2.10 [1.32 - 3.34]), the absence of maintenance treatment before 6 months (OR=0.67 0.49 - 0.90]) and the long consultation period (OR = 0.73 [0.55 - 0.95]) were statistically associated with the risk of treatment failure. Durable remission was obtained in 25.54% (346) of cases and recurrence in 117 patients (8.63%). In multivariate analysis, the lower intensity of thyrotoxicosis (OR = 0.66 [0.49 - 0.89]) and the low doses of ATS attacks (OR = 0.52 [0.32 - 0.85]), early maintenance treatment before 6 months (OR =1.51 [1.08 - 2.13]) were statistically associated with durable remission. On the therapeutic level, 43 patients were on thyrozol, 41 patients were on propranolol or and 14 patients were on carbimazole. A good balance of thyroid function was noted in 24 cases (34.28%) after 18 months of treatment.

5. Discussion

5.1. Epidemiological Data

5.1.1. Age

The mean age of patients with Graves' disease in the literature is 34.6 years [9]. In our study the mean age was 38.45 years. Our results are comparable with the study of Insaf Hadj Ali *et al*., where the mean age was 38.17 years [10]. The most affected age group in our series was between 30 - 39 years with 30%. For A. Toft *et al*., the peak frequency of Graves' disease is between 30 and 40 years [11].

5.1.2. Gender

Graves' disease is more common in women. In our study 91.42% were women with a sex ratio = 0.09. A work done by M. Mbodj *et al*. showed a lower percentage of which 79% of patients with Graves' disease were women [12].

5.1.3. Background

- **Familial goiter**

A notion of familial goiter was objectified in 4.65% of cases. The study of Ndour Oumar shows a higher percentage of which 25% of people diagnosed with Graves' disease had a positive family history of goiter [13].

- Pregnancy

In our study 8.14% of patients had a history of abortion. Our results can be correlated with those of the study of H. Marhari *et al*., including 16.66 % of abortion cases for 12 cases of Graves' disease associated with pregnancy [14].

5.1.4. Clinical Data

1) Consultation period

We noted a diagnostic delay in our study. 24.29% of patients were diagnosed after one year. Only 11.42% of patients waited less than a month before consulting. This situation can be explained either by the non-specificity of the signs of hyperthyroidism favoring diagnostic wandering; or by the low socio-economic level of the population who have difficulty accessing quality care. For Khatraty cheikh saad bouh, the consultation time varies between 10 days and 10 years with an average of 2 and a half years [15].

2) According to clinical manifestations

In our study 30% of patients had goiter, 11.42% had orbitopathy, 52.85% had palpitation, 41.42% had weight loss, 12.85% suffered from asthenia, 34.28% had insomnia, 20% complained of nervousness, 14.28% had thermophobia, 22.85% had tremors of the extremities, 1.42% suffered from motor diarrhea. Our results are similar to those of Nafissatou Diagne and al including 32.4% of patients had goiter, 38% had orbitopathy, 46.3% had palpitation, 39.8% had weight loss, 17.6% suffered from asthenia, 20.4% had insomnia, 24.1% complained of nervousness, 19.4% had thermophobia, 33.3% had tremors of the extremities, 5.5% suffered from motor diarrhea [15].

5.1.5. Paraclinical Data

➢ **Anti-TSH receptor antibody assays**

In our study, anti-RTSH antibodies were performed in 06 patients and were positive in 100% of them. Our results are similar to those of Nafissatou Diagne *et al*., in whom 28 patients had benefited from the dosage of anti-RTSH antibodies and were positive in 100% of them [9]. A study carried out in Morocco [16], found anti-RTSH antibodies at a positive rate in 87.5% of cases.

5.1.6. Distribution According to Complications

Cardiothyreosis is a common cardiovascular complication of Graves' disease. In our study, 15.71% of patients had cardiothyreosis. Our results can be correlated with those of Nafissatou Diagne *et al*., who objectified cardiothyreosis in 11.1% of cases [9]. According to Allanic *et al*., cardiothyreosis accounts for 65.7% of cases [17].

5.1.7. Distribution According to Comorbidities

- HTA

HTA appears insidiously and silently, all the earlier subject is exposed to certain risk factors: aging, which promotes the loss of elasticity of the arteries, constitutes the first non-modifiable risk factor. But other risk factors are determined by habits or a lifestyle that can be modified: being overweight, being sedentary, high salt consumption, smoking or alcohol [18]. In our study, high blood pressure is the most common cardiovascular comorbidity with 30% of subjects.

- Type 1 diabetic

In our study 8.57% had type 1 diabetics. For N. Rekik *et al*., out of a total of 60 subjects with T1D 28.33% had Graves' disease [19]. For M. Bennour *et al*. Graves' disease was found in 3.89% of patients with type 1 diabetes [20].

- Type 2 diabetic

In our study 7.14% had type 2 diabetic.

- Biermer's disease

In our study 2.85% suffered from Biermer's disease. For MT Oh *et al*., out of a total of 28 subjects with Biermer's disease 21% had Graves' disease [21]. For M. Mtir *et al*. Graves' disease was found in 5.97% of patients with diabetes and Biermer's disease [22].

5.1.8. According to the Etiological Factors

- The female sex

In our study, the predominant etiological factor was female gender with 91.42%. Several studies have shown the clear female predominance observed in Graves' disease with prevalence's of 19 per 1000 women [23].

- Stress

The origin of autoimmune diseases is multifactorial. Stress is probably one of the etiological components. It is indeed often found during questioning of patients with an autoimmune disease or during relapses of the latter as a triggering element. The biological consequences of stress are increasingly better understood. During stress, glucocorticoids and catecholamines released by the hypothalamic-

pituitary axis will modify the balance of the Th1/Th2 and Th17/ Treg cytokine balances and be at the origin of an inhibition of cellular immunity, a decrease in immune tolerance and a stimulation of humoral immunity. These modifications expose individuals to autoimmune diseases among other things [24]. In our study, 10% of patients suffered from stress.

5.1.9. According to the Treatment

Treatment is always medical at first, then it can be supplemented by surgical or isotopic treatment depending on the indication, the age of the patient and the evolution of the thyroid disease. In our study 61.42% of patients were on thyrozol. 58.57% of patients were on propranolol or 58.57%. 20% of patients were on carbigene.

5.1.10. According to the Evolution

In the literature, the recurrence rate after medical treatment with Synthetic Antithyroid drugs reaches 50%. In order to have an optimal effect of Synthetic Anti Thyroid (ATS) the duration of treatment must be between 12 and 24 months [25]. In our study, the evolution was favorable in 22.41% of patients and was marked by a normalization of thyroid hormones after medical treatment well followed for a period of 6 months. At 18 months the evolution was favorable in 34.28% of patients. A prospective study published by Allanic [26], comparing the respective effects of a 6-month and 18-month treatment, shows that 58.3% of patients treated for 6 months relapse. This figure decreases to 38.2% in patients treated for 18 months.

5.1.11. Limitation of the Study

The limitations encountered were mainly:

- This was a retrospective study;
- Some files were incomplete compared to the explorations;
- Long-term monitoring difficulties.

6. Recommendations

Towards the populations:

An information, education and communication campaign reinforced and adapted to the populations with the aim of:

- Provide tools for prevention of Graves' disease and its comorbidities.
- Raise awareness of the value of early consultation in the event of persistence of certain signs such as asthenia
- Raise awareness of the importance of monitoring and good therapeutic compliance.

To the medical staff:

- Promote ongoing training of the medical team on new international recommendations.
- Adopt early and appropriate management of Graves' disease and its comorbidities.

- Facilitate good therapeutic education and psychological support.

- Introduce into the health check-up, particularly in pregnant women, the search for and correct monitoring of thyroid disorders.

- Systematically look for cardiovascular, endocrine and autoimmune comorbidities in patients monitored for Graves' disease

- Promote early and energetic management.

To health authorities:

- Improve the technical platform in health structures.

- Promote specialized management of Graves' disease at all levels.

- Pilot epidemiological studies for a better understanding of Graves' disease and its comorbidities.

7. Conclusion

To the people reinforced and adapted information, education and communication campaign was necessary for the prevention of Graves' disease and its comorbidities. For medical staff, it will be necessary to promote the continuing training of the medical team on the new international recommendations. To the health authorities, it will be necessary to improve the technical platform in health structures and promote specialized management of Graves' disease at all levels and pilot epidemiological studies for a better understanding of Graves' disease and its comorbidities.

Conflicts of Interest

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

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