

# Hyperprolactinemia in Hospitals in Lomé: Diagnostic and Therapeutic Aspects

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## Abstract

**Introduction.** Hyperprolactinemia represents a supraphysiological secretion of prolactin. In clinical practice, it is the most frequently encountered anterior pituitary disorder. However, its real prevalence is little known in Africa. The purpose of this study is to list all cases of hyperprolactinemia over the past four years and to make an inventory of the various etiologies found and their management. **Methodology.** This is a cross-sectional descriptive study on the files of patients who came for consultation in the internal medicine and endocrinology department with hyperprolactinemia retrospectively collected from January 2017 to December 2020. Included were patients followed or whose the diagnosis of hyperprolactinemia was established in endocrinological consultation during the study period. **Results.** This study recorded 26 cases of hyperprolactinemia. The female sex represented 73.08% (sex ratio M/F 0.37) and the average age was 33.92 years. The 40 - 50 age group was the most represented with 30.77%. In women, galactorrhea accounted for 73.07%, amenorrhea 57.69% of clinical pictures and infertility 23.08%. In men, infertility accounted for 7.69% of presentations, gynecomastia 11.54% and erectile dysfunction 15.38%. The duration of evolution of the signs was 4 months in 23.08% of the patients. The mean prolactinemia was 702.58 ng/ml. CT was performed in 80.85% of patients. The main etiologies were pituitary adenomas (77%). All our patients were treated with dopaminergic agonists. Cabergoline was prescribed in 77% of patients. The evolution was favorable in 96.25% of patients. **Conclusion.** Hyperprolactinemia is a pathology that exists in our regions. The main etiology remains pituitary adenomas and treatment with cabergoline.

## Keywords

Hyperprolactinemia, Hospital Environment, CHU SO, Togo

## 1. Introduction

Hyperprolactinaemia is defined as a rise in plasma prolactin concentration above the upper limit of the assay, which varies according to the method used, most often between 15 and 25 ng/ml [1]. Clinically, it is the most frequently encountered anterior pituitary disorder. It is responsible for 20% - 25% of consultations for secondary amenorrhoea [1]. The prevalence of hyperprolactinaemia is 0.4 in the general adult population and 9 to 17 in women with reproductive disorders [2] [3]. In a Scottish study published in 2017, over 20 years of patient follow-up between 1993 and 2013, the number of prolactin tests increased, as did the prevalence of hyperprolactinaemia, rising from 0.02 to 0.23 in 2013 [4]. In sub-Saharan Africa in general, its incidence and prevalence are poorly defined. It remains an infrequent pathology; the various studies in the literature such as that of N'guessan in Côte d'Ivoire in 2003 [5], Seck in Senegal in 2003 [6], Mariko in 2017 in Mali [7], Azhar in Morocco in 2017 [8], Ma in Niger in 2018, and Etoga in Cameroon in 2020 [9], the actual frequency was not calculated and discussed. In 2020, Sedzro [10], in a study of pituitary adenomas, found that 66.67% of the 12 cases of pituitary adenomas identified were prolactinomas. Given the absence of studies on hyperprolactinaemia in Togo, we felt it necessary to initiate this study, the general aim of which was to determine the epidemiological, clinical, diagnostic and therapeutic aspects of hyperprolactinaemia in hospitals in Togo.

## 2. Patient and Method

This was a descriptive cross-sectional study of the records of patients with hyperprolactinaemia collected retrospectively from 1<sup>st</sup> January 2017 to 31 December 2020, *i.e.* a study period of 04 years in the Internal Medicine and Endocrinology Department of the Sylvanus Olympio University Hospital, Lomé.

We used the records of patients attending endocrinology consultations during the study period in the Department of Internal Medicine and Endocrinology. All patients of any age and sex diagnosed as having hyperprolactinaemia on the basis of an elevation of prolactin above the upper limit of the normal value were included in the study. Incomplete records of patients with hyperprolactinaemia were not included. We also excluded the files of patients with galactorrhoea, with normal prolactinoma, as well as those of pregnant women and the study of all patients with galactorrhoea or amenorrhoea - breastfeeding women.

The various data studied were:

- socio-demographic data: age, sex, profession, ethnic group, place of residence.

- clinical data: Medical or surgical history, history of head trauma, history of medication use (H2 antihistamines, neuroleptics, tricyclic antidepressants, serotonin reuptake inhibitors, antiemetics, antihypertensives, opiates), presence of clinical symptoms such as amenorrhoea, galactorrhoea, amenorrhoea-galactorrhoea, hirsutism, sexual impotence, couple infertility; the presence of tumour syndrome (headaches, reduced visual acuity, visual field amputation) and signs of antero-

pituitary insufficiency (asthenia, pallor, ideomotor slowness, muscular disorders, hair loss, orthostatic hypotension, bilateral hemianopia, bradycardia, chills, constipation).

- paraclinical data: hormone assays for prolactin (PRL), luteinising hormone (LH), follicle-stimulating hormone (FSH), oestrogen (estradiol), thyroid-stimulating hormone (TSHus) in the first instance and then in the case of macroprolactinoma to explore the other pituitary axes are: determination of 8 o'clock cortisol, 8 o'clock or 9 o'clock ACTH, tri-iodothyronine (T3L), thyroxine (T4L), ultra-sensitive thyroid-stimulating hormone (TSHus), growth hormone (GH) and insulin growth factor (IGF1); pituitary computed tomography or magnetic resonance imaging to look for a microadenoma or macroadenoma.

- therapeutic data: medical treatment received, surgical treatment. The data were collected on a pre-established individual survey from the files of patients seen for consultation in the internal medicine and endocrinology department. Data were analysed using Epi info software. Quantitative variables were presented as means  $\pm$  standard deviation. Qualitative variables were presented as numbers and percentages.

### 3. Results

#### 3.1. Description of the Sample

During the study period, 26 patients were included in our study out of a total of 1021 registered, representing a hospital frequency of 2.5%. The mean age was  $33.92 \pm 11.01$  years, with extremes of 16 and 56 years. The 40 - 50 age group was the most represented, with a proportion of 30.77%. Women predominated, with a M/F sex ratio of 0.37. The socio-professional category of patients was dominated by craftsmen (19.23%), followed by shopkeepers (15.38%).

#### 3.2. Clinical Data

Hyperprolactinaemia was discovered incidentally in 38.46% of cases (10 patients) and in the remaining 16 patients when a clinical sign was detected. These 16 patients had been referred from gynaecology, neurosurgery, ophthalmology and urology departments. The main reason for consultation was the finding of amenorrhoea in 19 patients (73.07%), followed by secondary amenorrhoea in 15 patients (57.69%). In our series, the disease had been evolving for 4 months in 6 patients (23.08%).

The amenorrhoea-galactorrhoea syndrome was the most frequent clinical sign in 19 patients (73.07%), followed by secondary amenorrhoea in 15 patients (57.69%), as shown in **Table 1**.

The tumour syndrome was dominated by headache and reduced visual acuity, which was present in 57.69% of cases (**Table 2**).

#### 3.3. Paraclinical Data

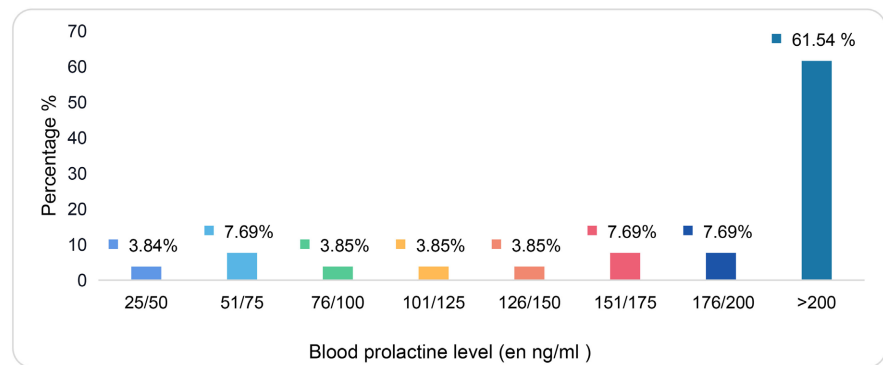
The median prolactin level was 702.58 ng/ml, with extremes of 33.6 and 27454.64. In 61.5% of cases, the prolactin level was greater than 200 ng/ml (**Figure 1**).

**Table 1.** Distribution of patients according to the presence of endocrine syndrome.

	Workforce	Percentage
Amenorrhoea galactorrhoea	19	73.07
Infertility in couples	8	30.76
Hyperandrogenism	2	7.69
Secondary amenorrhoea	15	57.69
Gynecomastia	3	11.53
Libido disorder	4	15.38

**Table 2.** Distribution of patients according to the presence of tumour syndrome.

	Number	Percentage
Headaches	15	57.69
Reduced visual acuity	15	57.69
Amputation of the visual field	1	3.8

**Figure 1.** Blood prolactin level.

Prolactin levels varied according to sex. The levels found in men ranged from 342.12 to 27454.4 ng/ml and in women from 33.6 to 853.65 ng/ml. All men had prolactin levels above 200 ng/ml. Oestradiol was measured in 2 patients and came back low. Testosterone levels were low in 2 patients. LH levels were measured in 4 patients. The mean level was  $1.52 \pm 1.38$  with extremes of 0 and 2.9. TSHus was measured in 4 patients. The mean level was  $2.17 \pm 0.96$  with extremes of 1.09 and 3.38. Free T4 was measured in 4 patients. The mean level was  $13.79 \pm 0.8$  with extremes of 12.74 and 14.53. Free T3 was measured in 4 patients. The mean level was  $3.46 \pm 0.92$  with extremes of 2.41 and 4.44. Finally, the 8-hour cortisol level measured in 7 patients came back low in all patients, with a level of less than 50  $\mu\text{g/l}$ .

On imaging, 21 patients (80.76%) in our series underwent MRI, 7 patients (26.92%) underwent CT and MRI and 1 patient (3.85%) underwent CT alone. Of the 21 scans performed, 19 patients had pituitary adenomas. Macroadenomas were more common in men than in women. This difference was not statistically

significant ( $p > 0.05$ ). Blood prolactin levels were statistically significantly higher in macroadenomas than in microadenomas.

### 3.4. Main Aetiologies

The most common cause of hyperprolactinaemia was pituitary adenoma in 73.07% of cases in 19 patients (**Table 3**).

### 3.5. Therapeutic and Developmental Data

Of the 26 patients, 25 received medical treatment and 1 patient was lost to follow-up. Medical treatment consisted of Cabergoline and Bromocriptine. Cabergoline was used most frequently in 20 patients (77%).

In terms of outcome, of the 25 patients put on medical treatment, there was a reduction in prolactinaemia. Similarly, 14 of the 25 patients were cured. Of the 26 patients, one was lost to follow-up and none died. In addition, there were no relapses.

## 4. Discussion

### 4.1. Main Results

During the study period, 1021 patients consulted the endocrinology unit of the CHU-SO, 26 of whom were suffering from hyperprolactinaemia (2.5% hospital frequency). The patients were predominantly female, with a sex ratio M/F of 0.37. The mean age was 33.92 years, with extremes of 16 and 56 years. The combination of amenorrhoea and galactorrhoea accounted for 78.95% of cases of hyperprolactinaemia in women and erectile dysfunction in men. Prolactin adenomas were the most frequent aetiology of hyperprolactinaemia (73.07%). All patients received medical treatment, mainly Cabergoline.

### 4.2. Discussion of the Method

The retrospective nature of data collection meant that some information was missing from the files. In addition, the high cost of paraclinical examinations in a difficult socio-economic context was the main limitation of our study. Some of the hormonal tests were carried out in France through a representative of the CERBA laboratory in Togo, which hampered the rapid acquisition of results and their cost.

**Table 3.** Causes of hyperprolactinaemia.

	Number	Percentage
Pituitary adenoma	19	73.07
No etiology	5	19.23
Rupture of the pituitary stalk due to head trauma	1	3.85
Medicines	1	3.85
<b>Total</b>	<b>26</b>	<b>100</b>

However, these limitations only slightly affect the quality of the results presented in our study. To our knowledge, this study of hyperprolactinaemia is the first of its kind in Togo, and this is one of its strengths.

### 4.3. Discussion of the Results

Our study showed a clear predominance of hyperprolactinaemia in women (73.08%) compared with (26.92%). The mean age was around 33.92 years, with extremes of 16 and 56 years, and the 40 and 50 age groups were the most represented. The distribution according to sex is not in agreement with Azhar *et al.* [8] in the United Arab Emirates in 2019, Ma *et al.* in Niger [11] in 2018 had found 38 patients and the age of the population varied from 4 to 58 years with an average of  $33.5 \pm 10.36$  years, the age range between 21 and 30 years, the female sex was predominant with a proportion of 81.60% against 18.40% for the male sex.

This clear predominance in women may be explained by the fact that clinical symptoms are more common in women than in men. Similarly, the existence of sexual problems in men rarely leads to consultation and consideration of the possibility of hyperprolactinaemia. Moreover, hyperprolactinemic factors (estrogen-based contraception) are more common in women than in men [12].

In women, the combination of amenorrhoea and galactorrhoea accounted for 73.07% of cases. This result is similar to those of Ma [11], Seck [6] and N'guenan [13] who found 74.19%, 80% and 80% respectively. These results confirm the data in the literature which show that amenorrhoea-galactorrhoea was the most common reason. However, this result is higher than those of Nouedoui *et al.* [14] and N'guessan *et al.* [5], who found 52% and 15.60% respectively.

In men, disorders of sexual function were most common in 15.38%. Gynecomastia was found in 11.54% of patients. This result is lower than that reported by Nouedoui *et al.* [14] in Cameroon who found 75% and those of Mariko *et al.* [7] in Mali in 2017 and N'guessan *et al.* [5] who reported respectively 29.4% and 21.4% of cases.

These results could be explained by the fact that in our region, men rarely consult a doctor for sexual problems. This gynecomastia was bilateral, painful to pressure and without galactorrhoea. This result is also lower than those of Ma [11], Abram *et al.* [15] and N'guessan *et al.* [5] who reported 14.28%, 23% and 20% of cases respectively.

These data support those in the literature, which state that gynaecomastia with or without galactorrhoea is much rarer in men.

Headaches were present in 57.39% of patients; this result is higher than that of Mariko *et al.* [7] in Mali, who reported 47.1%, linked to the macroadenomas diagnosed in the studies.

Regarding, paraclinical data, the median prolactin level was 702.58 with an interquartile range of [151.84 to 1293.72] and extremes of 33.6 and 27454.64.

This level was significantly higher than that of Ma *et al.* [11] which was 166.18

ng/ml and approached that of N'guessan *et al.* [5] which was 848.96 ng/ml. In the majority of cases, the blood prolactin level was above 200 ng/ml as Vilar *et al.* in 2018 in Brazil [16]. This could be explained by our small sample size.

In our study, Prolactin levels varied according to sex. The levels found in men were statistically significantly higher than those found in women. N'guessan *et al.* [5] found higher rates than men.

In our investigations, hyperprolactinaemia was largely due to prolactin adenomas (73.07%). Microadenomas were present in 70% of cases. These results are very similar to those of N'guessan *et al.* [5], Azhar *et al.* [8], Vilar *et al.* [16] and Soto Pedre *et al.* [17]. In our study, blood prolactin levels were statistically significantly higher in macroprolactinomas than in macroprolactinomas. Vilar *et al.* reported the same findings in their study [18].

The highest prolactinemia levels (above 200 ng/ml) were mainly found in men, with a maximum level of 27454.64 ng/ml. Unlike N'guessan *et al.* [5] and Azhar [8], the maximum level was found in women. The highest prolactin levels and the tumour syndrome were mainly observed in macroadenomas.

According to treatment, all patients received medical treatment except one who was lost to follow-up. This result is comparable to that of N'guenan [13] who also reported that 100% of their patients benefited from medical treatment. These results differ from those of Essais *et al.* [19] and Seck [6] who reported 86.20% and 66.66% of cases respectively. No patient underwent surgery. This could be explained by the efficacy and good tolerance of the medical treatment. There was no indication of surgery in any of the patients in our study.

The 3 drugs used were cabergoline, bromocriptine and desmopressin. Cabergoline was used at a dose of 0.5 g/take, bromocriptine at a dose of 2.5 g/take and desmopressin at a dose of 60 g/take. Cabergoline monotherapy was used in most patients. Medical treatment was continued. This result is comparable to that of Mariko *et al.* [7] in Mali in 2017, who found 64.9%, and Ma *et al.* [11] in Niger in 2018, who found 65.8%. This could be explained by its efficacy and good tolerability, which had been studied by Wang *et al.* [20] in a comparative study between the two dopamine receptor agonists, cabergoline and bromocriptine. The two drugs share many features and adverse effects, such as headache, nausea and vomiting, among others, although the frequency and severity of adverse effects appear to be less with cabergoline than with bromocriptine. Earlier concerns about valvular heart disease [21] [22] with the use of these agents have been largely refuted by more recent reports [23] [24].

A large body of moderate-quality evidence supports the use of dopamine agonists to normalise prolactin levels and resolve symptoms associated with mass effect and elevated prolactin levels. The main therapeutic effect of dopamine agonists was to reduce prolactin levels and improve symptoms [25] [26].

The efficacy of surgery and radiotherapy in certain patients was also supported. Radiotherapy and surgery appeared to be effective in patients with resistance or intolerance to dopamine agonists. However, surgery as primary therapy has also been described in a recent consecutive series of 212 patients with pro-



lactinomas [27]. This study reported a short-term remission rate, particularly in patients with microadenomas and cystic tumours.

In evolution, the results of medical treatment were good. Of the 25 patients who received medical treatment, prolactinemia decreased, contrary to N'guessan *et al.* [6] in 38.4% of cases the level remained high; it decreased in 15.4% of cases and normalised in 30.8% of cases. One patient was lost to follow-up.

## 5. Conclusion

We conducted a study that enabled us to describe the epidemiological, clinical, diagnostic and therapeutic aspects of hyperprolactinaemia in the internal medicine and endocrinology department of the CHU-SO in Lomé. Hyperprolactinemia has become more common as access to care has improved. While endocrine signs predominated in women, those related to sexual disorders were more common in men. Pituitary adenoma was the main aetiology. Treatment was both medical and surgical. Early detection of hyperprolactinemia will enable appropriate management.

## Conflicts of Interest

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

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