

Clinical Profile of Female Hyperprolactinemia at the Level of the Gynecology/Obstetrics Department of the Mali Hospital

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Abstract

Introduction: Hyperprolactinemia is an excessive supraphysiological secretion of prolactin. The aim of this work was to evaluate the clinical and therapeutic profile of patients, and to assess its impact on fertility. **Patients and method:** This is a prospective longitudinal study from January 1, 2019 to June 30, 2022 on all patients of childbearing age seen monthly in consultation. Included were any patients in whom the prolactin dosage was greater than 25 ng/ml. **Results:** We collected 43 cases of hyperprolactinemia out of a total of 5187 new consultations or 0.82%. The mean age of the patients was 28.33 years with extremes between 17 and 44 years old. The desire to become pregnant was the most frequent reason (79.06%). Primary infertility concerned 65.1% of patients. The main clinical signs were: cycle disorders 41.8%, followed by amenorrhea/galactorrhea association 46.5%; neurological signs (nervousness, headache, visual disturbances) 18.6%. The mean level of prolactinemia was between 25 and 100 ng/mml in 53.5% of cases. Brain CT was requested for cases of prolactinemia greater than 200 ng/mml and 23.25% of patients had a prolactin adenoma. Ovarian reserve was satisfactory in 60.46%. Treatment was medicated in 81.4% with cabergoline. Clinical improvement was obtained in 23.3% of patients after one month, 37.2% after 3 months. Pregnancy occurred in 39.53% of patients. All pregnancies reached term except for one case of spontaneous abortion. We noted a statistically significant relationship between the rate of prolactinemia and clinical signs ($P < 0.05$). **Conclusion:** Hyperprolactinemia is a common cause of disorders of the hypothalamic-pitui-

tary axis, thus causing female infertility. But drug treatment remains effective.

Keywords

Female Hyper Prolactinemia, Fertility Disorder, Conception and Pregnancy Outcomes, Mali Hospital

1. Introduction

Hyperprolactinemia is responsible for 20% to 25% of consultations for secondary amenorrhea, it is a frequent clinical situation. It is defined by an elevation of plasma prolactin beyond the upper limit of the assay, varying from 15 - 25 ng/ml depending on the methods used [1].

Prolactin is a hormone secreted by lactotropic cells, which represent 15% to 20% of anterior pituitary cells. Prolactin is a hormone secreted by lactotropic cells, which represent 15% to 20% of anterior pituitary cells. In addition to its role in lactation, it is involved in the differentiation of breast tissue, hydroelectrolyte exchanges and immune system responses [2]. Hyperprolactinemia can be physiological (pregnancy, breastfeeding) or pathological (medications, pituitary adenoma). Hyperprolactinemia seems to be an increasingly common pathology, although it cannot be quantified, since the signs are often neglected by patients. The prevalence of hyperprolactinemia is 0.4% in the general adult population and 9% to 17% in women with reproductive function disorders [3] [4]. Previous epidemiological studies conducted in Africa have reported the following findings: In Niger Mahamane Sani MA *et al.* [5] reported a female prevalence of 81.6% out of 38 patients suffering from hyperprolactinemia. In Mali M Mariko *et al.* [6] reported a prevalence of 54.05% out of 37 patients. A Scottish study [7] estimated the incidence of hyperprolactinemia at 0.23% in 2013 in the general population. In Mali, we do not have any previous studies on female hyperprolactinemia, which is why this study was undertaken to assess the impact of hyperprolactinemia in women of childbearing age in the gynecology department of the Mali hospital.

2. Patients and Method

Our study took place in the gynecology department of the Mali Hospital. This is a prospective longitudinal study from January 1, 2019 to June 30, 2022. We carried out an exhaustive sampling taking into account all cases meeting our criteria. All patients of childbearing age with a prolactinemia level greater than 25 ng/ml who gave their consent were included. The prolactin test was taken in the morning. The samples were taken in the morning by the hospital laboratory with a reference interval of 5 and 25 ng/ml. Bromocriptine was administered when prolactinemia was between 25 and 30 ng/ml and Cabergoline for values above 30 ng/ml. Patients were seen monthly in gynaecological consultations, sometimes in collaboration with endocrinologists. A CT scan was requested whenever prolactinemia was

above 200 ng/ml and MRI was performed depending on the case. Prolactinemia was monitored at one month, three months, nine months and then one year. Doses were regulated according to the variation in prolactinemia. Data were collected from questionnaires from gynecological records, the consultation register and by an interview administered directly to patients or by telephone call. Data entry and analysis were performed on Microsoft Word and Excel Office 2019 software. The data analysis was done on the SPSS software. For the calculation of the distribution, we used the following statistical tests: Pearson's Chi2 test and Fisher's exact test. Any P value less than 0.05 was considered significant. In terms of ethical aspects, we wanted to preserve the anonymity and confidentiality of the data collected. Our study was not intended to harm the patients included in the study, but rather to contribute to better patient management. The survey sheets were anonymous and contained only information on the sociodemographic, clinical and prognostic data of the patients. Informed consent from the patients was sought and obtained prior to the procedure.

3. Results

From January 1, 2019 to June 30, 2022, we collected 43 cases of hyperprolactinemia out of a total of 5187 new consultations, *i.e.* 0.82%. The average age of the patients was 28.33 years with extremes between 17 and 44 years old. The desire to become pregnant was the most frequent reason (79.06%). Infertility was primary in 65.1% and secondary in 32.5% of cases. Only 23.25% of patients had observed an estrogen-progestogen-based contraceptive method. The main clinical signs were: Cycle 4 disorders 1.8%, amenorrhea/galactorrhea 46.5%, pelvic headaches 4.7%. Neurological signs (nervousness, headache, visual disturbances) were observed in 18.6% of patients. These clinical signs were sometimes associated. We noted that 27.9% were asymptomatic (**Table 1**). The mean level of prolactinemia was between 25 and 100 ng/mml in 53.5% of cases and 34.9% of patients had a prolactin level greater than 200 ng/mml. Brain CT was requested for cases of prolactinemia greater than 200 ng/mml and 23.25% of patients had a prolactin adenoma. The MRI requested in the case of pituitary adenoma, as objectified by CT was not performed by any patient. The pelvic ultrasound of our patients had 20.93% of cystic dystrophies of the ovaries and a uterine myomatous in 7%. Other disturbances of hypothalamo-pituitary hormones: AMH (34.8%); FHS (2.3%); estradiol (4.7%); LH was not requested in 44.2% of patients. Treatment was medical mainly with dopaminergic agonists, including cabergoline 0.5 mg in 81.4% of patients and bromocriptine in 18.6%. (**Table 1**). Clinical improvement was achieved in 23.3% of patients at one month, 37.2% at 3 months, 20.9% at six months, 9.5% at nine months and 5% at one year (**Table 2**). We noted that 6.8% of patients had dropped out of treatment for social problems. We noted a statistically significant relationship between the rate of prolactinemia and clinical signs ($P < 0.05$). Pregnancy was contracted in 40% of our patients (**Figure 1**). The mean interval between the start of treatment and the onset of pregnancy was 3 to 4 months in

66.6% of cases; between 6 and 9 months 23.4%. All pregnancies reached term, except for one case of spontaneous abortion.

Table 1. Socio-demographic and clinical characteristics.

Socio-demographic and clinical characteristics	Workforce	Percentage
- Average age: 28.33 years (extreme 17 - 44 years)		
- Nullicity	28	65.1
- Nulliparity	32	74.4
- Infertility	Primary: 28 Secondary: 14	65.1 32.5
- Reason for consultation: (desire to become pregnant)	34	79.06
	Cycle disorders: 18	41.8
- Gynaecological clinical signs	Amenorrhea/ Galactorrhea: 20 Pelvic headache: 2	46.5 4.7
- Neurological Signs: (<i>nervousness, headaches, visual disturbances</i>)	8	18.6
- Asymptomatic:	12	27.9
- Medium prolactinemia: (<i>25 and 100 ng/mml</i>)	23	53.5
- Prolactinemia greater than <i>200 ng/mml</i>	15	34.9
- Pelvic ultrasound: (<i>ovarian cystic dystrophy</i>)	9	20.93
- Prolactin adenoma on CT	10	23.25
	- AMH: 15	34.8
- Disturbances of other hypothalomo-pituitary hormones	- FSH: 1 - Estradiol: 2	2.3 4.7
- Drug treatment	- Cabergoline - Bromocriptine	81.4 18.6
No surgical treatment		

Table 2. Evolution of prolactinemia during one year.

Evolution	Interval/Prolactinemia	Workforce	Percentage
A month old	150 - 200 ng/mml	10	23.3
At three months	50 - 100 ng/mml	15	37.2
At six months	25 - 50 ng/mml	9	20.9
At nine months	Less than 25 ng/mml	4	9.5
At one year	Normal limit	2	5
Withdrawal of treatment for a company name		3	6.8

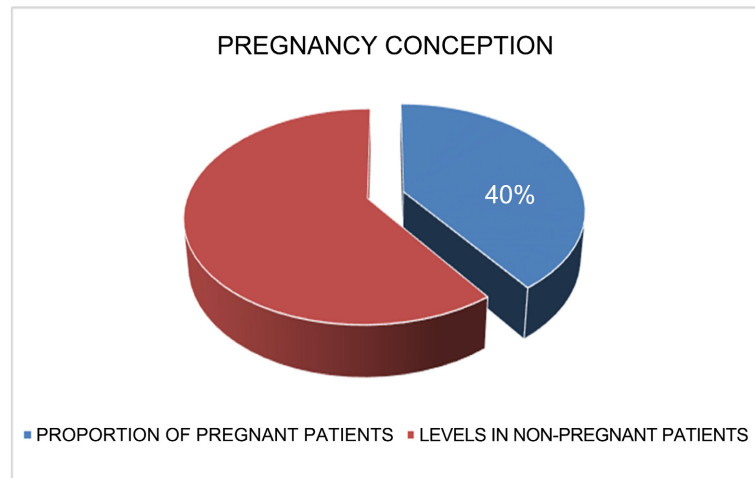


Figure 1. Pregnancy conception.

4. Discussion

4.1. Limitations

The limits of our study are of four kinds:

- The small size of our sample did not allow for a multivariate statistical analysis.
- The fact that certain examinations useful for the etiological diagnosis could not be carried out in some patients, in particular pituitary MRI, which would have made it possible to differentiate the central causes (hypothalamo-pituitary) from the other causes of hyperprolactinemia.
- Discontinuation or abandonment of treatment for social and/or financial problems after one year of treatment for every three patients.
- The fact that our protocol did not take into account hyperprolactinic drugs and other factors

4.2. Frequency

During our study, we obtained a frequency of 0.82% out of 5187 new consultations. This frequency cannot be compared to that of other authors such as Mahamane Sani MA in Niger, M Mariko in the endocrinology department of the Mali hospital and that of **Soto-Pedre E** in Scotland [5]-[7] because their sampling was on both men and women. In our study, the sampling was female and particularly on women of childbearing age. But all these authors reported a female predominance, as evidenced by the study by Mahamane Sani MA [5] 81.6%; Nguenan M [8] 83.30%, M Mariko [6] 54.05%. This female predominance is known in the literature, it had been reported by several studies including, among others; Nguenan M [6] with 83.30%. For these authors, this clear female predominance could be explained by the fact that the clinical symptomatology is richer in women than in men and that women were more active in consultations than men [5]-[8].

4.3. Socio-Demographic Data

The mean age of our patients was 28.33 years with extremes between 17 and 44

years. In the series by M Mariko *et al.*, the female predominance was 54% with the mean age of 37.32 years as reported by Essais O *et al.* [9]. The ages in our series were not juxtaposable with those of other authors, as they only focused their studies on the general population, whereas ours only focused on patients of childbearing age. This is why in the series of Mahamane Sani MA *et al.* [5], the age of the patients varied between 4 and 58 years, with an average age of 33.5 years; and the age group of 21 to 31 years was the most represented with 42.10%. The Mahamane Sani MA study [5] was similar to that of the others such as Essais O *et al.* [9] in Tunisia in 2002, Azeroual M [10] in Morocco in 2012, N'Guessan K *et al.* [11] in Côte d'Ivoire in 2003 and Nguenam M [8] and M Mariko *et al.* [6] in Mali in 2004 which found 33 years, 33 years, 33 years and 31.6 years respectively.

4.4. Clinical and Paraclinical Data

The desire to become pregnant was the most frequent reason at 79.06% in our series. This rate is higher than those reported by the series of Mahamane Sani MA *et al.* [5]; Mariko M *et al.* [6] which reported 41.93% and 50% respectively. The amenorrhea-galactorrhea combination concerned 46.5% of our patients followed by cycle disorders with 41.8%. This rate was lower than that reported by Mahamane Sani MA [5] 74.19% for the same amenorrhea-galactorrhea combination and 32.25% for cycle disorders, pelvic headaches 4.7%. M Mariko *et al.* [6] reported higher rates, 80% amenorrhea and 70% galactorrhea, a result comparable to those of Lemaire C [12]. Neurological signs in our series (nervousness, headache, visual disturbances) were found in 18.6% of patients, while M Mariko *et al.* [6] reported a higher rate of 55%. We noted that 27.9% were asymptomatic, but authors such as Mahamane Sani MA [5], Nguenam M [8], and N'Guessan K, *et al.* [11] did not report asymptomatic hyperprolactinemia.

In our series, female infertility was primary in 65.1%. Mahamane Sani MA [5], and M Mariko *et al.* [6] reported lower rates of 41.93% and 50% respectively. Authors such as Nguenam M [8], N'Guessan K [11] did not mention female infertility in their series. Mayanda Ohouana RL *et al.* [13], in Brazzaville and M. Elleuch [14] in Tunisia had only collected cases of prolactinomas in their series. Compared to hyperprolactinemic factors such as estrogen-progestogen-based contraceptives, only 23.25% of our patients had observed this method and we had not looked for drug or environmental factors, especially stress. Mahamane Sani MA *et al.* [5] reported 28.94% drug etiology and 5.26% nipple sucking, while M Mariko *et al.* [6] showed 5.40% estrogen-progestin use by patients in their series of estrogen-progestogen use. There is an established link between estrogen-progestin intake, increased prolactin secretion, and lactotropic cell hyperplasia [15].

In our study, the mean prolactinemia value was 140.95 ng/ml with extremes of 28 to 500 ng/ml. This result is lower than that of N'Guessan K [11] who reported 848.96 ng/ml and that of Mayanda O [13] who had noted an average of 321.86 ng with extremes between 64.91 and 900 ng. The mean level of prolactinemia in our study was between 25 and 100 ng/ml in 53.5% of cases and 34.9% of patients

had a prolactin level greater than 200 ng/ml. In the Mahamane Sani MA *et al.* series [5], the mean prolactinemia rate was 166.18 ng with extremes ranging from 25.43 to 3344 ng/ml. In the same Nigerien series, it was between 20 and 100 ng/ml in 73.67% of patients.

We found 23.25% of pituitary macroadenomas for prolactin values above 200 ng/ml. This result was comparable to that of M Mariko *et al.*, who reported 27.02% for prolactinemia greater than 200 ng/ml. We recall that our inclusion criteria only concerned patients of childbearing age. Authors such as M. Elleuch [14] in Tunisia and Mayanda O [13] only had cases of pituitary prolactinomas.

The reference morphological examination in the etiological diagnosis of hyperprolactinemia remains the pituitary MRI (Gold standard). It is difficult to access in our developing countries because of the high cost, which is why no patient in the series has undergone this examination.

The pelvic ultrasound of our patients had objectified 20.93% of cystic dystrophies of the ovaries and a uterine myomatous in 7%. In the series of Mahamane Sani MA *et al.* [5], it was performed in 65.78% of patients and did not objectify any particularity.

Other disturbances in the hypothalomo-pituitary hormones of our patients were as follows: AMH (34.8%); FHS (2.3%); estradiol (4.7%). We report that LH was not requested in 44.2% of patients. In the others, the assessment of other hormones in the hypothalomo-pituitary axis [5] [6] [11] [13] was not taken into account.

In our series, the treatment was mainly medical for all our patients. The same was true for the series by Mahamane Sani MA *et al.* [5] in Niger and Mayanda O [13] in Brazzaville. These results are different from those of Trials O. *et al.* [9] and Seck M [16] which reported 86.20% and 66.66% respectively. This difference could be explained by the effectiveness of medical treatments on the one hand and by the unavailability of surgical treatments in our regions.

The medical treatment of our patients was done with dopaminergic agonists, in particular cabergoline in 81.4% of patients and bromocriptine in 18.6%. Our data are slightly different from those of Mahamane Sani MA [5], M Mariko [6] who had prescribed cabergoline in 65.8% and 64.9% of cases respectively and bromocriptine in 34.2% and 27%. According to authors such as Colao A and Di Sarno A, cabergoline is the hypoprolactinemic agent that has fewer side effects and is therefore better tolerated than other dopaminergic agonists [17] [18].

Clinical improvement was obtained in 23.3% of our patients after one month; 37.2% after 3 months; 20.9% after six months; 9.5% at nine months and 5% at one year.

Mahamane Sani MA [5] stated that the course of treatment at 10 months on average was favorable in 89.47% of patients and a persistence of signs in 10.52% of patients, while Seck M [16] reported a favorable evolution at 8 months on average in 33.33% of patients and a persistence of signs in 50% of cases. We did not note cases of treatment failure, only that 6.8% of our patients abandoned treatment for social problems. We noted a statistically significant relationship between

the rate of prolactinemia and clinical signs ($P < 0.05$).

Pregnancy was contracted in 39.53% of our patients. The mean interval between the start of treatment and the onset of pregnancy was 3 to 4 months in 66.6% of cases; between 6 and 9 months 23.4%. The others, such as Mahamane Sani MA [5], M Mariko [6], N'guessan K.B [11] did not appreciate the fertility after treatment of hyperprolactinemia.

5. Conclusion

Hyperprolactinemia is a common cause of disorders of the hypothalomo-pituitary axis, thus causing female infertility. Its incidence and prevalence are poorly defined in our regions; nevertheless, it remains a pathology that exists in gynecology. The dosage and control of prolactinemia are essential for the monitoring of treatment. MRI is the morphological examination of choice, but it is still not widely available in our context, which is why CT is still useful. Efficient management necessarily involves an early diagnosis strategy for a fertility disorder. Medical treatment remains the treatment of choice and allows the conception of pregnancy in some cases.

Authors' Approval

All authors approve the submission of this article.

Consent

For this work, we have received the consent of the patients, the head of the department and the director of the Mali hospital.

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Author Contributions

- Mamadou Bakary COULIBALY: choice of subject, drafting of the protocol and writing of the final article.
- Alou Diarra, Issa Ongoïba, Soungalo DIAKITE and Bakary TRAORE: data collection and analysis.
- Alassane TRAORE, Bah TRAORE, Seydou MARIKO: supervision, definition of the methodology, critical reading of the research protocol.
- SOW Djéneba SYLLA: formatting according to the recommendations and critical reading of the manuscript.

Conflicts of Interest

There is no conflict of interest.

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