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Variation in Pituitary Hormones in Infertile Women in Douala, Cameroon. A Cross-Sectional Study

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Abstract

Background: According to the WHO, infertility is defined as the inability of a couple of reproductive age to achieve pregnancy after twelve months of regular unprotected sexual intercourse. Significant hormonal variation can be observed in infertile women. In low-income countries, conducting hormone tests on infertile women remains impractical due to the high cost involved, the aim of this study was to determine the variation in pituitary hormones in infertile women in Douala. **Methodology**: A cross-sectional analytical study was conducted from November 2022 to November 2024 in hospitals and clinics in Douala among 145 infertile women aged between 18 and 44 years. FSH, LH and prolactin levels were measured using the sandwich ELISA method with DRG Diagnostic kits. The data were entered into Excel and analyzed using SPSS 20.0 with Chi2 and logistic regression tests. **Results**: 145 women were included. The mean age was 33.14 ± 6.6 years, with the majority between 30 and 35 years of age. The mean BMI was 27.86 ± 5.37 kg/m^2, with 71.72% overweight. 61.38% had primary infertility. The average duration of infertility was 5.76 ± 4.67 years and 44% had irregular cycles. 8.28% had high FSH, 32.41% had high LH and 22.06% had abnormal prolactin levels. Age, irregular menstrual cycles, duration of infertility, and length of time in a relationship were statistically associated with variations in pituitary hormones. **Conclusion**: The FSH and LH levels are high in infertile women, while low and high prolactin levels are observed. Certain factors, including age, irregular menstrual cycles

and the length of time spent in a relationship, are statistically linked to these hormonal variations. These findings highlight the need to routinely screen for pituitary hormones in infertile women as early as possible.

Keywords

Infertile Women, Pituitary Hormones, Douala

1. Introduction

Human infertility is a complex issue that has many consequences depending on the cultural context and lifestyle of those affected. It is defined by the World Health Organization (WHO) as the inability to achieve pregnancy after 12 months of unprotected intercourse in women younger than 35 or 6 months in women 35 or older [1]-[3]. Clinically, it is defined as at least one year of unintentional failure to conceive despite unprotected sexual activity throughout the fertile period of the menstrual cycle [4]. Infertility represents a real global public health problem, partly due to the complexity of its etiology and partly due to the difficulty of preventing and diagnosing it [2]. According to a new report published by the WHO, infertility affects approximately 17.5% of the adult population, or about one in six people worldwide. Sub-Saharan Africa has the highest infertility rate in the world [5], with 42% in West Africa, 30% in East Africa and 40% in South Africa, according to a study conducted by Abebe *et al.* in 2020 [6]. In Cameroon, the prevalence of infertility among couples was 19.2% according to a study conducted in 2020 by Egbe *et al.* [7], and according to a study conducted by Nana *et al.*, female infertility accounts for 30% of all cases of infertility [8]. Pituitary hormones play a fundamental role in the reproductive process. Follicle-stimulating hormone (FSH) is necessary for the development and maturation of the gonads and for gamete production. It plays a key role in the development of astral follicles and, together with luteinizing hormone (LH), stimulates pre-ovulatory follicular growth [9]. Prolactin is the hormone responsible for lactation and has a significant impact on reproductive function [10]. Numerous dysfunctions occur during female infertility. These disorders can damage the fallopian tubes, disrupt ovulation or lead to hormonal complications [1] [11] [12]. The aim of this study was to investigate variations in pituitary hormones in patients with primary and secondary infertility.

2. Methodology

We conducted a cross-sectional analytical study in the hospitals and clinics of Douala, Cameroon over a period of two years from November 2022 to November 2024.

At each hospital, patients attending gynecological consultations were approached after their medical records—provided by the gynecologist—had been reviewed and those who agreed were included in the study.

2.1. Sample Collection

The samples analyzed were collected from women with primary or secondary infertility who consulted the gynecology departments of the aforementioned hospitals during the study period. All infertile patients aged from 18 to 44 who gave their consent were enrolled in the study. Women undergoing hormonal treatment, those taking anti-nausea medication were excluded from the study.

Blood samples were taken between the second and fourth days of the participants' menstrual cycles. We collected 5 ml of blood using a Vacutainer system in a dry tube (without anticoagulant), from the saphenous vein in the elbow crease.

2.2. Sample Preparation

The blood was allowed to clot and the serum was decanted after by centrifugation at 3000 rpm for 5 minutes for analysis of the biochemical parameter. Hemolysis sera were discarded and a fresh specimen was obtained. The serum was stored at −20˚C until the day of analysis.

2.3. Sample Analysis

The measurements of the various hormonal parameters: follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin were performed using the Enzyme link Immunosorbent Assay (ELISA) SANDWICH method with ELISA reagents from the manufacturer DRG diagnostic GmbH.

2.4. Interpretation of Results

For the hormone test parameters, normal range were taken according to the manufacturer (Table 1).

Table 1. Interpretation of hormonal parameters.

Parameters	Normal values	Abnormal value
FSH	- Follicular phase 2 - 10 mIU/mL - Ovulatory phase (Peak) 7 - 20 mIU/mL - Luteal phase 2 - 10 mIU/mL	Postmenopausal 20 - 100 mIU/mL
LH	Follicular phase and Luteal phase 0 - 20 mIU/mL	Postmenopausal 20 - 100 mIU/mL
Prolactin	Women (non-pregnant): 3 to 25 ng/mL	Low level (hypoprolactinemia): 0 - 3 ng/mL Hyperprolctinemia: ≤25 ng/mL

2.5. Statistical Analysis

The descriptive characteristics variables were expressed as mean values and stand-

ard deviation. Data were compared using the Chi-square test and Fischer's test. The odds ratio enabled us to identify the risk factors associated with infertility and hormonal abnormalities. Significance level was taken as $P < 0.05$. Statistical analysis was done using IBM SPSS version 20.0 package and MS-excel.

2.6. Definition of Operational Terms

Infertility: the inability of a couple to achieve a pregnancy after 12 months of regular, unprotected sexual intercourse.

Primary infertility: the inability of a couple to achieve a first pregnancy after 12 months or more of regular, unprotected sexual intercourse.

Secondary infertility: defined as a couple's inability to conceive another child or carry a pregnancy to term after having already had a successful first pregnancy.

- Any married woman who had been desiring pregnancy for more than one year, was having regular sexual intercourse, and had never been pregnant was considered to be suffering from primary infertility.
- Any married woman who had been trying to conceive for more than one year, was having regular sexual intercourse, and had already had a successful first pregnancy was considered to have secondary infertility.

3. Results

3.1. Socio-Demographic Characteristics (Figure 1)

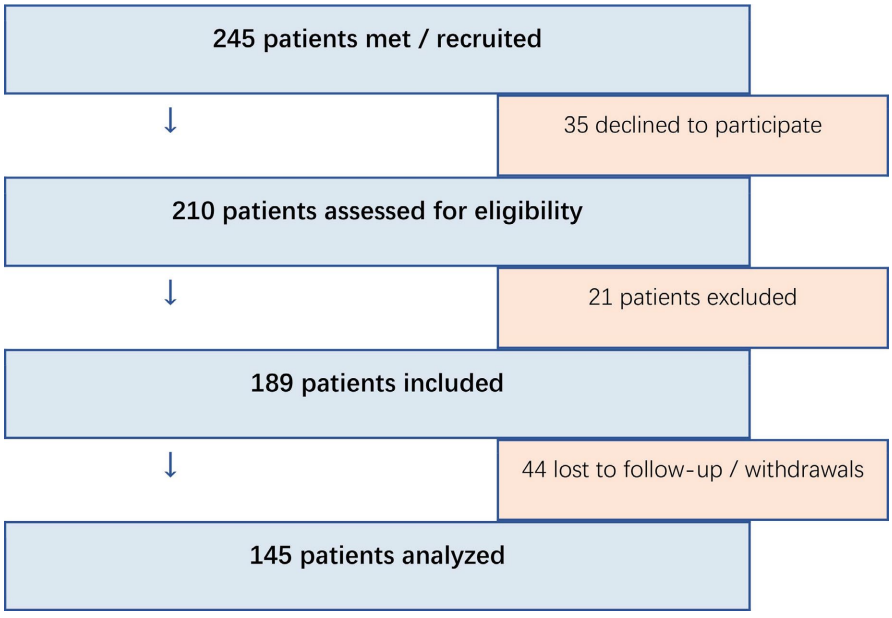


Figure 1. Flow chart.

A total of 145 infertile women were recruited for the study, with a mean age of 33.14 ± 6.66 and the most represented age group being 30 - 35 years old, with 29.7% of participants. The mean duration of being in a relationship was 7.18 ± 5.05 years, and more than 50% of the study population had been married for more

than six years. More than half of the population which is equivalent to 50.34%, was from the Grassfields region of Cameroon, as shown in Table 2.

Table 2. Sociodemographics characteristics.

Variables	Frequency (n = 145)	Percentage (%)
Age (years)		
<25	15	10.34
[25 - 30[	31	21.38
[30 - 35[	43	29.66
[35 - 40]	26	17.93
≥40	30	20.69
Region		
Grassfields	73	50.34
Sawa	27	18.62
Sudano-Sahelian	26	17.93
Forestry	19	13.10
Numbers of years of relationship (years)		
1 - 2	21	14.48
3 - 5	46	31.73
6 - 10	51	35.17
>10	27	18.62

3.2. Clinicals Characteristic

In the study population, the mean duration of infertility was 5.7 ± 4.7 years. 38.62% of women had been infertile for more than 6 years. 61.38% of them suffered from primary infertility and 38.6% from secondary infertility. The mean BMI was 27.86 ± 5.37, and more than 71.7% of participants were overweight. Myomectomy was the most common surgical procedure performed in the population, with 19.31% of participants having undergone this procedure. 84.14% of women had undergone treatment for sexually transmitted diseases and 76.55% of patients used plant-based medicine as a treatment, as shown in Table 3.

Table 3. Clinicals characteristics.

Variables	Frequency (n = 145)	Percentage (%)
Duration of infertility (years)		
1 - 3	65	44.83
4 - 5	24	16.55
6 - 10	40	27.59
>10	16	11.03

Continued

Type of infertility		
Primary	89	61.38
Secondary	56	38.62
Nature of the menstrual cycle		
Regular	80	55.17
Irregular	65	44.83
BMI (Kg/m^2)		
<25	41	28.3
25 - 30	65	44.8
>30	39	26.9
Surgical history		
Myomectomy	28	19.31
Caesarean	18	12.4
Tubuloplasty	7	4.83
Laparoscopy	7	4.83
Appendectomy	6	4.14
Cystectomy	4	2.76
Others	4	2.76
Therapeutic history		
Phytotherapy	111	76.55
Treatment of sexually transmitted infections	122	84.14
Ovarian stimulation	50	34.48
Insuflation	14	9.66
Insémination	3	2.07

3.3. Profil of Pituitary Hormons

Among the 145 patients recruited for the study, 8.28% (12 patients) had high FSH levels and 91.72% had normal FSH levels. LH was high in 32.41% of patients (47 patients). 98 patients had normal LH levels (67.59%). Low prolactin levels were observed in 11.03% of patients, while 11.04% had high prolactin levels, as reported in Table 4.

3.4. Risk Factors Associated with Abnormal Variations in Hormone Concentration

Several independent factors were used in a logistic regression model to identify variables associated with abnormal hormons levels. According to this analysis, certain factors are strongly linked to the occurrence of hormonal abnormalities.

Table 4. Profile of pituitary hormones in the study population.

Variables	Frequency (N = 145)	Percentage (%)
PRL (ng/ml)		
Low: (<3)	16	11.03
Normal: (3 - 20)	113	77.94
High: (>20)	16	11.03
FSH (mUI/ml)		
Normal: (0 - 20)	133	91.72
High: (>20)	12	8.28
LH (mUI/ml)		
Normal: (0 - 20)	98	67.59
High (>20)	47	32.41

3.4.1. Factors Associated with Abnormal FSH and LH Concentrations

The age variable was statistically associated with abnormal FSH and LH values. In fact, in patients aged ≥ 40 years, the risk of having an abnormal variation in FSH and LH concentration was very high, FSH (OR = 16; p = 0.0001), LH (OR = 2.59; p = 0.02). The menstrual cycle variable was statistically linked to FSH and LH values. Patients with an irregular menstrual cycle had a high risk of abnormal gonadotropin values, with this risk multiplied by 16 (OR = 16; p = 0.008) for FSH and by 2 (OR = 2.45; p = 0.01) for LH. Patients who had been diagnosed with infertility for ≥6 years had a high risk of abnormal gonadotropin concentrations (FSH: OR = 21.44; p = 0.003 and LH: OR = 2.45; p = 0.01) compared to patients with less than 3 years of infertility. Infertile patients who had been in a relationship for ≥6 years had a 10-fold increased risk (OR = 10.8; p = 0.02) of having abnormal FSH levels compared to patients with less than 3 years of infertility, as shown in Table 5 below.

Table 5. Factors associated with abnormal gonadotropin levels.

Variables	FSH		LH	
	OR (IC 95%)	**Valeur P**	**OR (IC 95%)**	**Valeur P**
Age (years)				
≤25	-	0.62	1.04 (0.37 - 3.09)	0.99
[25 - 30[	Ref	1	Ref	1
[30 - 35[	-	0.01	0.64 (0.30 - 1.39)	0.33
[35 - 40[	1.59 (0.43 - 5.55)	0.45	0.72 (0.28 - 1.82)	0.64
≥40	16 (4.48 - 56.82)	0.0001	2.59 (1.15 - 5.85)	0.02

Continued

Numbers of years of relationship				
1 - 2	Ref	1	Ref	1
3 - 5	0.17 (0.10 - 1.07)	0.10	0.87 (0.42 - 1.9)	0.84
6 - 10	1.95 (0.56 - 6.72)	0.34	1.22 (0.6 - 2.55)	0.58
>10	3.6 (1.14 - 11.85)	0.04	1.28 (0.52 - 3.03)	0.64
Duration of infertility (years)				
1 - 3	Ref	1	Ref	1
4 - 5	0.43 (0.03 - 2.76)	0.69	0.83 (0.32 - 2.20)	0.81
6 - 10	2.91 (0.81 - 10.17)	0.09	2.14 (1.00 - 4.52)	0.05
>10	7.92 (2.26 - 30.31)	0.004	1.73 (0.65 - 4.82)	0.35
Nature of the menstrual cycle				
Regular	0.06 (0.005 - 0.37)	0.001	Ref	1
Irregular	16.09(2.67 - 175.6)	0.001	2.43(1.19 - 4.82)	0.01
Medical history				
Insufflation	9.84(2.69 - 34.36)	0.04	1.64 (0.51 - 5.33)	0.38

3.4.2. Factors Associated with Abnormal Prolactin Levels

Table 6 shows the adjusted odds ratios for the parameters that are statistically associated with abnormal variations in gonadotropin levels in infertile women. The variable duration of relationship was statistically linked to abnormal prolactin levels. Patients who had been in a relationship for three years or less were at greater risk (OR = 3.29; p = 0.01) of developing abnormal prolactin level compared to patients with more than 3 years of relationship. In addition, patients who had sex more than 4 times a week were twice as likely (OR = 2.48) to develop abnormal prolactin levels, although this result is not significant (p = 0.05), as reported in Table 7.

Table 6. OR adjusted of factor associated to abnormal gonadotropins level.

Variables	FSH		LH	
	OR (ajusté)	P-value	OR (ajusté)	P-value
Age ≥ 40 years	15.99 (3.99 - 64.06)	0.001	2.59 (1.13 - 5.91)	0.02
Duration of infertility ≥ 6 years	21.44 (2.91 - 170.89)	0.003	2.45 (1.20 - 5.01)	0.01
Irregular menstrual cycle	16.06 (2.01 - 127.87)	0.008	2.44 (1.2 - 4.94)	0.01
Duration of couple relationship: ≥6 years	10.86 (1.36 - 86.2)	0.02	1.22 (0.6 - 2.55)	0.58
Insuflation	9.84 (2.59 - 37.30)	0.0008	1.64 (0.51 - 5.33)	0.38

Table 7. Factors associated with prolactin levels variation.

Variables	PRL	
	OR (IC 95%)	**Valeur P**
Weekly frequency of sexual intercourse		
1	Ref	1
2 - 3	0.47 (0.21 - 1.07)	0.10
4 - 5	2.48 (1.10 - 5.73)	0.05
Numbers of years of relationship (years)		
1 - 2	**3.29 (1.29 - 8.86)**	**0.02**
3 - 5	Ref	1
6 - 10	0.54 (0.23 - 1.34)	0.21
>10	1.01 (0.37 - 2.82)	>0.99

4. Discussions

We recruited 145 infertile women from health facilities in the city of Douala.

The mean age in our study population was 33.1 ± 6.7 years, and the most represented age group was 30 - 35 years. This result is similar to that of a study conducted by Egbe *et al.* in Cameroon, in which the most represented population was 30 - 39 years old with an mean age of 30.1 ± 5.7 [7], and to that of Prasad *et al.* in India [13], which had 30 - 40 years as the most represented age group. Another study conducted in Cameroon by Kemfang *et al.* reveals that the mean age of the participants' first pregnancy was 27.93 years [14]. This decline in age may be due to several factors, such as the increase in the level of education among women in our environment, the widespread participation of women in the workforce with the pursuit of careers and the search for professional stability before starting a family.

In the study population, 50.35% of women were from the grassfields region. This result is similar to that of Esther *et al.* in 2024 [15] in a study conducted in the city of Yaoundé, where 39.5% of the infertile women in their study were from the grassfields region. This result could be explained by the importance of motherhood in these cultures.

The mean duration of infertility found in our patients was 5.7 ± 4.7 years, with a minimum of one year and a maximum of 20 years. This result is similar to that of Ramezanzadeh *et al.* in Iran [16]. The duration of infertility between 1 - 3 years was the most common, at 44.83%. This result could be explained by the increase in consultations by couples seeking to conceive. Furthermore, some studies reveal that the duration of infertility between 2 - 3 years was associated with higher rates of depression and corresponded to the period of increased consultations by the couple [8].

The prevalence of primary infertility was 61.38% in the study population. 85.52% of the study population had used plant-based medicine as their first line

of treatment for infertility. This result could be explained by the fact that infertility is conceived as much as a spiritual problem than as a medical issue which lead to the importance of cultural practices in managing infertility issues.

The study showed a statistically significant correlation between abnormal FSH (OR = 16; p = 0.0001) and LH (OR = 2.59; p = 0.02) values and patients aged 40 and over. In fact, patients aged 40 and over were 16 times more likely to have abnormal FSH concentrations and twice as likely to have abnormal LH values. This result is correlate with that of Al-Fahham *et al.* [12], who found a correlation between FSH variation and the age of the patients in his study. In her study, Voundi Voundi *et al.* found that age is a determining factor in infertility and the disorders it can cause [15]. The irregular nature of the menstrual cycle was statistically linked to abnormal FSH gonadotropin values (OR = 16.06; p = 0.008) and LH (OR = 2.42; p = 0.01). The risk of a patient with an irregular menstrual cycle having abnormal FSH levels was multiplied by 16 for FSH and by 2 for LH. Voundi Voundi *et al.* found that irregular menstrual cycles are a factor in changing hormone levels in infertile patients [15]. These results are the same as those found in the study conducted by Odiba *et al.* in Nigeria [17]. This could be explained by the fact that with age, there is a gradual loss of follicles and oocytes and a deterioration in gamete quality [18]. In addition, irregular menstrual cycles are often the result of a lack of ovulation, which can be caused by an imbalance in FSH and LH production, hindering normal follicle development and the onset of ovulation. In women, the hypothalamic-pituitary axis is controlled by positive or negative feedback depending on the stage of the cycle, so an irregular menstrual cycle hinders this regulation [19], which could lead to early menopause in women of childbearing age who have menstrual cycle disorders.

Prolactin levels were abnormal in 22.07% of cases, a result similar to that found by Al-Fahham *et al.* in 2016, who found abnormal prolactin levels in 18.18% of their study population [12]. A statistically significant correlation was found between abnormal prolactin levels and a relationship duration of ≤ 3 years. In fact, patients who had been in a relationship for less than 3 years were 3 times more likely (OR = 3.29; p = 0.01) to have abnormal prolactin levels. This result could be explained by the fact that abnormal prolactin level is the most common hormonal abnormality found in infertile women. In their study, Moussa D *et al.* found that 86% of women had abnormal prolactin levels [20]. Furthermore, the 1 - 3-year period corresponds to the period when couples wishing to have children increase their visits to the gynaecologist, thus enabling early diagnosis of hormonal variations.

5. Conclusion

There are several abnormalities in pituitary hormones during female infertility, one of the most significant determinants being age. According to WHO guidelines, age is the most important factor in predicting ovarian reserve. It is therefore essential to diagnose infertility as early as possible in order to address hormonal abnormalities.

Ethical Considerations

In accordance with the declaration of Helsinki, a consent form was signed by every participant. Ethical clearance has been granted by the Institutional Ethics Committee for research on human health of the University of Douala (N˚3989 CEI-UDo/08/2023/T).

Author Contributions

FKF, NMJP, CTN, and AD designed this study. FKF collected field data and performed laboratory analyses. FKF drafted the first version of the manuscript and analyzed and interpreted the data. NMJP also contributed to the interpretation of the data. AFTK, NMJP, CTN, HE, and AD reviewed the manuscript. AD supervised all stages of the work. All authors read and approved the final manuscript.

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Conflicts of Interest

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

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List of Abbreviations

BMI:	Body Mass Index
ELISA:	Enzyme Link Immunosorbent Assay
FSH:	Follicle-Stimulating Hormone
LH:	Luteinizing Hormone
SPSS:	Statistical package for the social science
WHO:	World Health Organization