

Prolactin Levels Among Infertile Women in Maiduguri, Nigeria

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Abstract

Objective: The objectives of this study were to determine the manner of clinical presentation of women with unexplained infertility in Maiduguri, North-Eastern Nigeria and their plasma levels of prolactin.

Materials and Methods: The records of 104 females undergoing infertility investigation at the University of Maiduguri Teaching Hospital and for whom no organic cause had been found were scrutinised to extract the details of their modes of clinical presentation. All had plasma prolactin level assays.

Results: The patients were aged between 20 and 40 years (mean: 28.3 years). Thirty-three (31.7%) of them had primary infertility while 71 (68.3%) had secondary infertility. Of the 104 patients, 33 (31.7%) had abnormal plasma prolactin levels. The women with secondary infertility were more likely to have abnormal prolactin levels: 22 (21.1%) compared to only 11(10.6%) among patients with primary infertility. About one-third of the patients presented with amenorrhoea (2% with primary and 34.6% with secondary amenorrhoea). Among patients presenting with amenorrhoea only 13 (12.5%) had elevated prolactin levels. Twenty four (23.1%) of the patients had galactorrhoea, of whom only 10 (9.6%) had hyperprolactinaemia. Patients with secondary infertility were more likely to have galactorrhea (17.3%) compared to patients with primary infertility (5.8%). The association of hirsutism, amenorrhoea and hyperprolactinaemia was not a common finding in our patients.

Conclusion: The use of dopaminergic-agonist therapy in women with unexplained infertility requires careful consideration, ensuring that the plasma prolactin levels and the clinical mode of presentation are factored into the decision to prescribe the drugs.

Key Words: Infertility, Anovulation, Prolactin, Amenorrhoea [Trop J Obstet Gynaecol, 2003, 20: 97-100]

Introduction

Infertility is common worldwide, occurring in about one in ten couples. The prevalence of infertility is particularly high in sub-Saharan Africa, ranging from 20 to 46% in some parts of West Africa^{1,2}. In our centre, infertility is the reason for nearly 40% of all gynaecological consultations³.

Fertility depends on complex psycho-physiological, anatomical, endocrinological and immunological factors. The male needs normal sperms produced and deposited in the reproductive tract of the female. The female needs a functionally intact hypothalamico-pituitary-ovarian axis to regulate and provide normal follicular development, ovulation and priming of the endometrium for implantation of the zygote, which has to pass through a normal fallopian tube following fertilisation. Failure of any of these complex processes leads to infertility.

Prolactin is one of the hormones of the anterior pituitary. The normal plasma level ranges from 64 to 450 mIU/litre. Elevated levels can interfere with the normal function of the hypothalamico-pituitary-ovarian axis resulting in anovulatory infertility. Hyperprolactinaemia does this by inhibiting the effects of gonadotropins, possibly by an action at the level of the ovary⁴. Previous studies by Giwa-Osagie

*et al*⁵ and Kuku⁶, had shown a high prevalence of hyperprolactinaemia in infertile Nigerian women, findings that were in agreement with reports on infertile women from other populations^{7,8,9}.

Hyperprolactinaemia is of diverse aetiology and is known to produce a variety of disorders of ovarian function, including amenorrhoea, oligomenorrhoea, short luteal phase, and anovulation with normal menstruation^{7,8,9,10}, all of which are frequently seen in infertile women. Hyperprolactinaemia might be the result of a prolactinoma, drugs or psychological stress. Irrespective of the cause, administration of dopaminergic-agonists such as bromocriptine and carbergoline readily suppresses prolactin secretion, and brings about a reduction in the plasma level of the hormone. This may be followed by ovulation and the occurrence of pregnancy.

The objective of this study was to determine the mode of clinical presentation and the plasma levels of prolactin in women with infertility in whom no organic factors could be identified as being responsible for infertility (unexplained infertility).

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Materials and Methods

The records of all patients registered for outpatient gynaecological consultations at the Medical Records department of the University of Maiduguri Teaching Hospital were examined and those complaining of infertility were identified and their case notes were retrieved for detailed study. The patients with identifiable organic factors responsible for their infertility were separated from those without any identifiable pathology that could account for infertility (unexplained infertility). The latter group had their case notes examined in detail. Data retrieved include age, parity, secondary sexual characteristics, menstrual pattern, the presence or absence of hirsutism or galactorrhoea and the plasma prolactin levels. A total of 104 patients who met the criteria had their case notes recovered for analysis.

The method of prolactin assay used in our laboratory is briefly described below:

Sample: Freshly drawn non-haemolysed, non-lipaemic serum is the preferred sample. Serum samples not assayed immediately are stored, frozen, in small aliquots.

Procedure: Prolactin level is determined using a non-competitive (sandwich) ELISA ¹¹, with a micro-well strip-reader EL 301 (BIO-TEK Instruments, Inc., Highland Park, Winooski, VT 05404-0998, USA). The colour intensity produced at the end of the series of reactions is directly proportional to the amount of prolactin present.

Results

The age range of the patients was 20 to 40 years, with a mean of 28.3 years (s.d.: 4.94). A total of 71 (68.3%) had a normal prolactin concentration while 33 (31.7%) had abnormal prolactin levels. The prolactin levels in the patients ranged from 7.2 mIU per litre to 2290.9 mIU per litre. The mean prolactin level was 340.7 mIU/L (s.d.: 328.2 mIU/L).

Of the 104 patients, 33 (31.7%) had primary, while 71 (68.3%) had secondary infertility. Eleven (33%) of the 33 patients with primary infertility had abnormal prolactin levels with 10 having hyperprolactinaemia. Of the 71 patients with secondary infertility 22 (31%) had abnormal prolactin concentrations, with 15 patients having levels beyond the upper limit of normal and 7 having subnormal concentrations of the hormone as shown in Table 1. Thus, the women who had secondary infertility were just as likely to have abnormal prolactin levels as the women with primary infertility.

Amenorrhoea was present in 38 (36.5%) of the 104 patients. There were only two patients with primary amenorrhoea, one of whom had an elevated level of

prolactin, compared to the women who had secondary amenorrhoea amongst whom 12 (33.3%) had abnormal prolactin concentrations, with 27.8% having raised prolactin levels. These are all shown in Table 1.

Table 1
Relationship of Prolactin Levels to the Clinical Characteristics of the Infertile Women

Variable	Plasma Prolactin Levels (mIU/L)			Total N (%)
	< 64.4 n (%)	64.4 – 450 n (%)	> 450 n (%)	
Type of Infertility				
Primary	1 (1.0)	22 (21.1)	10 (9.6)	33 (31.7)
Secondary	7 (6.7)	49 (47.1)	15 (14.4)	71 (68.3)
Menstrual Disturbance				
Normal Menstruation				
Primary Amenorrhoea	0 (0.0)	1 (1.0)	1 (1.0)	2 (1.9)
Secondary Amenorrhoea	2 (1.9)	24 (23.1)	10 (9.6)	36 (34.6)
Hirsutism With Menstrual Problems				
Normal Menses, No Hirsutism				
& Hirsutism	0 (0.0)	2 (1.9)	0 (0.0)	2 (1.9)
Amenorrhoeic, No Hirsutism	1 (1.0)	22 (21.2)	9 (8.6)	32 (30.8)
Amenorrhoeic & Hirsutism	1 (1.0)	3 (2.9)	2 (1.9)	6 (5.8)
Galactorrhoea				
Absent	7 (6.7)	58 (55.8)	15 (14.4)	80 (76.9)
Present	1 (1.0)	13 (12.5)	10 (9.6)	24 (23.1)
Total	8 (7.7)	71 (68.3)	25 (24.0)	104 (100.0)

Table 1 also shows that only 24 (23.1%) of the patients presented with galactorrhoea. Only 10 (41.7%) of them had hyperprolactinaemia. Thus, it is evident that galactorrhoea may be present even when plasma prolactin levels are within the normal range. A higher proportion of the patients with secondary infertility 18 (17.3%) had galactorrhoea compared to 6 (5.8%) with primary infertility.

Table 1 also shows that the combined presence of hirsutism, amenorrhoea and abnormal prolactin levels is not commonly found in our patients.

Discussion

The finding of 33 (31.7%) of our patients with prolactin concentrations outside the normal range was in agreement with findings reported from other parts of Nigeria^{6, 12}. Generally, prolactin levels in females show a moderate increase at puberty and stay at this level during the reproductive years. Hormonal studies of each menstrual cycle reveal a mid-cycle, oestrogen-related, modest prolactin peak. This may or may not have any significant effect on fertility. There is also a nocturnal surge in prolactin levels in most women. This surge in prolactin levels at night, which is also oestrogen-dependent has a bearing on fertility¹³. Prolactin levels decline at menopause along with the decrease in oestrogen level. The prolactin estimation in these women was done at various points of the cycle and the impact of this on the assays was not assessed.

Hyperprolactinaemia is seen in 21% of the women with secondary infertility in this study, compared to 31.6% reported in a group of 615 women from Egypt¹³. Hyperprolactinaemia is often associated with menstrual disturbances, particularly secondary amenorrhoea¹⁴. Menstrual disturbances were seen in 36.5% of our patients, an incidence much higher than the 15.6% earlier reported from Jos in North-central Nigeria¹².

The other common clinical feature in women with hyperprolactinaemia is galactorrhoea^{15, 16}. It is seen in about one-third of women with hyperprolactinaemia¹⁷. About one-fifth of our patients presented with galactorrhoea and it seemed to be a bit more

common in patients with secondary infertility. It has been stressed that the absence of galactorrhoea does not exclude hyperprolactinaemia, which is often strongly associated with anovulatory infertility. This assertion is supported by the findings from this study where nearly 20% of those without galactorrhoea had hyperprolactinaemia.

The mechanisms by which hyperprolactinaemia leads up to menstrual abnormalities, galactorrhoea, anovulation and infertility have been described by various authors^{4, 16, 20}. It is also pertinent to note that interpretation of prolactin results in infertile women is not as straightforward as it is with other hormones. What appears normal for one woman may not be for another. This has been attributed to the interpersonal variation that can occur in the secretion pattern of prolactin among patients and also the occurrence of different molecular forms, which have been found to exert characteristic physiological effects.

In conclusion, it is important that we keep it at the back of our mind that prolactin assay should be part of our routine infertility work up and its interpretation should be done in conjunction with other modes of presentation, notably galactorrhoea and amenorrhoea, in the individual patient. Treatment with dopaminergic agonists ensures prompt return of prolactin levels to normal, return of menstruation and pregnancy rates as high as 90% have been reported^{17, 21, 22, 23}.

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