

# Hormonal profile of men investigated for infertility at the University of Maiduguri in northern Nigeria

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## ABSTRACT

**Introduction:** This study aims to determine the prevalence and pattern of endocrinological abnormalities in patients investigated for male infertility in our environment.

**Methods:** An observational, retrospective study was conducted on men investigated for infertility at the University of Maiduguri Teaching Hospital over a two-year period, from April 2004 to March 2006. Hormonal assessments were done on those with abnormalities of their sperm count.

**Results:** A total of 1,201 men, were evaluated for infertility during the study period, out of which 96 underwent hormonal assessment because of abnormalities of their sperm counts. 88 had abnormal hormonal assays, giving a prevalence of endocrine abnormality of 7.3 percent. The mean age of the patients was 35.7 years. 68 (70.8 percent) patients had primary infertility and 72 (75 percent) had azoospermia. 64 (66.7 percent) patients had elevated follicle-stimulating hormone levels, while 48 (50 percent) had decreased testosterone levels. 12 (12.5 percent) patients had elevation of serum prolactin. 40 (41.7 percent) patients had hormonal profile in keeping with hypergonadotropic hypogonadism, while the endocrinological diagnosis in four (4.2 percent) patients was hypogonadotropic hypogonadism. Patients with primary infertility were found to be more likely to have partial androgen resistance (odds-ratio 2.241, 95 percent confidence interval 0.458–10.955).

**Conclusion:** Endocrinopathy, which can be successfully treated, is not an uncommon cause of male infertility in our environment. Therefore, hormonal assessments should be performed in the evaluation of male infertility as appropriate.

**Keywords:** azoospermia, endocrinopathy, hormonal profile, hypergonadotropic hypogonadism, infertility, male infertility, seminal fluid analysis

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## INTRODUCTION

Infertility is the commonest gynaecological problem in our environment. Infertility can be defined as failure to conceive after 12 months of unprotected sexual intercourse.<sup>(1)</sup> It is classified as primary infertility if no previous pregnancies have occurred, and secondary infertility if it occurred after one or more pregnancies. Approximately 15% of couples attempting their first pregnancy meet with a failure, and another 10% face secondary infertility.<sup>(2,3)</sup> Data available over the past 20 years reveal that in approximately 30% of the cases of infertility, the pathology is found in the man alone, and in another 20%, the pathology of both the man and the woman are abnormal.<sup>(2)</sup> Therefore, the male factor is at least partly responsible for the infertility in about 50% of cases. In an earlier study from our centre evaluating infertile couples, pathology was found in the man alone in 28.6% of the cases, while both the man and the woman were having abnormalities in 30% of the cases.<sup>(4)</sup>

Male fertility depends upon an intact hypothalamo-pituitary-testicular axis to initiate and maintain quantitatively and qualitatively normal spermatogenesis, maintain normal secondary sex glands functions and sexual functions.<sup>(5)</sup> Thus, it is surprising how infrequent infertile males have a recognisable endocrinopathy, even though up to 20% of male infertility can be attributable to endocrinopathy.<sup>(3)</sup> In fact, endocrine disorders which may be associated with significant medical pathology remain an important factor to consider in the aetiology of male infertility because they are can be amenable to treatment. However, in clinical practice, endocrine evaluation is usually done only in patients with severe oligospermia or azoospermia.<sup>(3,4)</sup> The hormones initially evaluated include follicle stimulating hormone (FSH), leutinising hormone (LH), testosterone and prolactin.<sup>(3)</sup> Further studies, like the evaluation of oestradiol, sex hormone binding globulin, thyroid function test among others, can be done, depending on the clinical scenario and the results of the initial studies.<sup>(6)</sup> Based on the results of the hormonal studies, a precise endocrinological diagnosis such as hypergonadotropic hypogonadism can be made, and the patient managed accordingly. The objective of this study was to determine the prevalence and pattern of

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endocrinological abnormalities in patients investigated for male infertility in our environment.

## METHODS

This is an observational, retrospective study of men investigated for infertility at the University of Maiduguri Teaching Hospital, Nigeria over a two-year period, April 2004 to March 2006. Those with abnormalities in their sperm count underwent hormonal assessment. Relevant information including the patient's age, diagnosis, sperm count and hormonal levels were extracted from the patient's case record and the Department of Chemical Pathology records. The seminal fluid analysis was done according to the procedure described by the World Health Organisation. A minimum of two separate samples were required before the diagnosis of abnormality of the seminal fluid was made. Hormonal levels were determined using a non-competitive (sandwich) ELISA, with Microwell Strip Reader (Model EL 301, Awareness Technology Inc, Palm City, FL, USA). The hormones analysed included FSH, LH, testosterone and prolactin. Hypogonadotropic hypogonadism was diagnosed when both the gonadotropins (FSH and LH) and testosterone levels were low. The diagnosis was hypergonadotropic hypogonadism when gonadotropins were elevated and testosterone was low. Partial androgen resistance was diagnosed when LH and testosterone levels were elevated, and the diagnosis was germinal epithelial failure when only FSH was elevated. The information obtained was coded and transferred onto a proforma already designed for the study. This was then entered into an IBM-compatible PC for analysis using the Statistical Package for Social Sciences version 11.0 (SPSS Inc, Chicago, IL, USA).

## RESULTS

A total of 1,201 men were evaluated for infertility during the study period, out of which 96 had hormonal assessments done because of abnormalities in their sperm counts. Out of these 96 patients, 88 had an abnormal hormonal assay, giving an overall prevalence of endocrine abnormality of 7.3%. The age group, type of infertility, and sperm count of the patients are shown in Table I. The age of the patients ranged from 22 to 52 years, with a mean of 35.7 years. 73 (76%) of the patients were in the age group 25–40 years, 68 (70.8%) had primary infertility and 72 (75%) had azoospermia. The hormonal profile and the endocrinological diagnosis of the patients in the study population are shown in Table II. 64 (66.7%) patients had elevated FSH levels and 48 (50%) had decreased testosterone levels. 12 (12.5%) patients had elevation of serum prolactin. 40 (41.7%) patients had a hormonal profile in keeping with hypergonadotropic hypogonadism,

**Table I. Age group, type of infertility, and sperm count of subjects.**

Demographical profile	No. (%) (n = 96)
Age group (years)	
< 25	4 (4.2)
25–40	73 (76.0)
> 40	19 (19.8)
Mean (range)	35.7 (22–52)
Type of infertility	
Primary	68 (70.8)
Secondary	28 (29.2)
Sperm count (million/ml)	
0 (azoospermia)	72 (75)
< 5	24 (25)

while the endocrinological diagnosis in four (4.2%) patients was hypogonadotropic hypogonadism.

Correlation of the endocrinological diagnosis between the various age groups and the type of infertility is shown in Table III. The diagnosis was hypogonadotropic hypogonadism in 28 (29.2%) patients that were in the age group 25–40 years, and also in the same proportion of patients with primary infertility. All eight (8.3%) patients that were found to have a normal hormonal profile were in the age group 25–40 years, and all four patients that were below 25 years of age were found to have partial androgen resistance. In comparison, patients with primary infertility were found more likely to have partial androgen resistance (odds-ratio [OR] 2.241; 95% confidence interval [CI] 0.458–10.959), while those with secondary infertility were more likely to have hypogonadotropic hypogonadism (OR 8.040; 95% CI 0.799–80.943).

## DISCUSSION

The prevalence of endocrinopathy in infertile men of 7.3% found in this study was lower than that reported from Kenya,<sup>(7)</sup> an African country, but higher than that reported from Brazil,<sup>(8)</sup> a developing country like Nigeria. However, it was within the range quoted in the literature.<sup>(3,9)</sup> Male infertility is a common problem with a complex aetiology, requiring a complete andrological work-up in some cases for proper diagnosis.<sup>(10)</sup> This study showed the importance of proper endocrinological work-up in the evaluation of patients with male infertility when appropriate because these cases may have recognisable endocrinopathy that may be correctable. The ages of the patients in this study were similar to those reported from the Kenyan study. The majority (70.8%) of the patients in the study population were found to have primary infertility, which was similar to the study from the southeastern part of Nigeria,<sup>(11)</sup> and another study from a developed country.<sup>(12)</sup> However, a report from Ile-Ife in southwestern Nigeria showed a preponderance of secondary infertility.<sup>(13)</sup> This may not be unrelated to the lifestyle in that part of the country.

**Table II. Hormonal profile and endocrinological diagnosis.**

Hormone	Normal, n (%)	Elevated, n (%)	Decreased, n (%)	Mean (range)
FSH (IU/L)	28 (29.2)	64 (66.7)	4 (4.1)	20.70 (1.00–80.60)
LH (IU/L)	52 (54.2)	44 (45.8)	0	12.87 (1.00–54.00)
Testosterone (nmol/L)	42 (43.7)	6 (6.3)	48 (50)	1.50 (0.14–4.86)
Prolactin (pmol/L)	51 (53.1)	12 (12.5)	33 (34.4)	429.8 (26.6–1,687.2)
Diagnosis	No. (%)			
Hypergonadotropic hypogonadism	40 (41.7)			
Hypogonadotropic hypogonadism	4 (4.20)			
Partial androgen resistance	12 (12.5)			
Germinal epithelial failure	24 (25.0)			
Hyperprolactinaemia	8 (8.30)			
Normal	8 (8.30)			

**Table III. Endocrinological diagnosis according to age group and type of infertility and statistical correlation between endocrinological diagnosis and type of infertility.**

Endocrinological diagnosis	Age group (years)			Infertility type and OR (95% CI)	
	< 25	25–40	> 40	Primary	Secondary
Hypergonadotropic hypogonadism	0	28	12	28 0.933 (0.383–2.275)	12 1.071 (0.440–2.611)
Hypogonadotropic hypogonadism	0	0	4	1 0.124 (0.012–1.252)	3 8.040 (0.799–80.943)
Partial androgen resistance	4	8	0	10 2.241 (0.458–10.959)	2 0.446 (0.091–2.181)
Germinal epithelial failure	0	21	3	19 1.784 (0.592–5.373)	5 0.561 (0.186–1.689)
Hyperprolactinaemia	0	8	0	6 1.258 (0.238–6.647)	2 0.795 (0.150–4.199)
Normal	0	8	0	4 0.375 (0.087–1.620)	4 2.667 (0.617–11.519)

In the evaluation of male infertility, hormonal evaluation is usually done in patients with severe abnormality in their sperm count (< 5 million/ml), which was the case in our study, because endocrinopathy is rare in patients with sperm count above 5 million/ml.<sup>(3)</sup> Out of the 96 patients evaluated, the majority (75%) were found to have azoospermia, which was higher than what was found in a previous study in the same hospital,<sup>(13)</sup> a southwestern Nigerian study,<sup>(14)</sup> and another study conducted in Ghana by Yeboah et al.<sup>(15)</sup> The reason for this high percentage of azoospermics was not clear, but it may be partly because our study population consisted of only patients with azoospermia and severe oligospermia (sperm count < 5 million/ml).

The mean value of LH of 12.87 IU/L found in this study was higher than that reported from Jordan,<sup>(16)</sup> and was also higher than the normal reference value of 5–10 IU/L.<sup>(17)</sup> The mean value of FSH of 20.70 IU/L was similarly higher than the normal reference value of 5–10 IU/L. These higher values showed that infertile

males with azoospermia and severe oligospermia, which formed the study population, have higher mean values of these hormones compared to the normal population. In fact, FSH was found to be elevated in 66.7% of the study population and LH in 45.8%, although they were normal in 29.2% and 54.2% of the cases, respectively. The mean value of testosterone of 1.50 nmol/L found in this study was lower than that reported from the Jordan study, but within the normal range of 0.14–4.86 nmol/L. It was expected that the mean value of testosterone in this study would be lower than the normal values, but it was not, probably because half of the study population had normal testosterone levels (43.7%). The proportion of the patients with hyperprolactinaemia (12.5%) in this study is noteworthy, as it may signify prolactin-secreting pituitary adenoma, which is amenable to therapy. However, as prolactin elevation may be induced by some abnormalities of the thyroid gland, further evaluation of these patients should include pituitary imaging and thyroid function test.<sup>(18)</sup>

Based on the results of the hormonal assay, infertile males can be classified as having hypergonadotropic hypogonadism, hypogonadotropic hypogonadism, isolated germinal epithelial failure, partial androgen resistance, hyperprolactinaemia or normal testicular functions.<sup>(3,5,19)</sup> Hypogonadotropic hypogonadism was the feature found in 4.2% of our patients. Generally, these patients can be successfully treated with hormonal replacement. This is done by being given intramuscular human chorionic gonadotropins 2,000 IU three times every week for 6–12 months, followed by FSH or human menopausal gonadotropin (hMG) 37.5–72 IM three times weekly. Alternatively, pulsatile gonadotropin-releasing hormone (GnRH) 4 m µg can be given every three hours either subcutaneously or intravenously using an infusion pump.<sup>(20)</sup> Normally, this leads to enough spermatogenesis to produce pregnancy. Hypergonadotropic hypogonadism was found in 41.7% of the study population. This finding is significant because it suggests damage to the seminiferous tubules and the Leydig cells. Sperm retrieval and *in vitro* fertilisation using intracytoplasmic sperm injection may be successful in these patients. Partial androgen resistance was found in 12.5% of our patients. If androgen resistance is complete, the individual will develop female external genitalia,<sup>(21)</sup> but patients with partial androgen resistance develop as males although they may have abnormalities such as decreased virilisation and infertility.

Unfortunately, patients with androgen resistance are not treatable and they remain sterile. Three out of the four patients were found to have hypogonadotropic hypogonadism, and two out of the eight patients that had hyperprolactinaemia had secondary infertility. Both cases signified a probable acquired causation that warrants further evaluation. Patients with primary infertility are more likely to have partial androgen resistance (OR 2.241, 95% CI 0.458–10.959), while those with secondary infertility were likely to have hypogonadotropic hypogonadism (OR 8.040, 95% CI 0.799–80.943) and normal endocrinological findings (OR 2.667, 95% CI 0.617–11.519). This study showed that endocrinopathy is not an uncommon cause of male infertility in our environment. It also showed the relative frequencies of the various endocrine abnormalities, some of which can be successfully treated. We conclude that hormonal assessments should be performed in the evaluation of male

infertility in azoospermic and severe oligospermic patients in our environment.

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