Hormonal abnormalities in azoospermic men in Kano, Northern Nigeria

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Background & objectives: We undertook this study to observe the pattern of hormonal abnormalities and testicular pathology in azoospermic male Africans in Kano, Northern Nigeria.

Methods: Eighty consecutive azoospermic infertile males attending fertility clinic in Aminu Kano Teaching Hospital, Kano, were selected for the study. Their semen were analyzed three times at eight weeks interval, after which serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone and prolactin were assayed in serum samples, and histological examination of testicular biopsies done.

Results: Of the 80 subjects studied, 32 (40%) had abnormal hormonal levels, 48 (60%) had normal hormonal values and 36 (45%) had testicular pathology.

Interpretation & conclusion: Endocrinopathies are common in azoospermia. Their contribution to male factor infertility cannot be overemphasized. The main reason for the endocrinopathies is not known but environmental factors, endocrine disruptors and genetic polymorphism have been suggested to be contributory.

Key words Azoospermia - follicle stimulating hormone - luteinizing hormone - prolactin - testosterone

Infertility is an important medical and social problem in the world. In about 60 per cent of all couples experiencing infertility, male factor is responsible in about 40 per cent of the couples. It is now generally accepted that the treatment of male factor infertility is equally as important as the treatment of the female factor. Studies from Nigeria have shown that azoospermia was present in 6.55 per cent of males attending a general infertility clinic and 35 per cent in those attending male infertility
The causes of azoospermia such as failure of spermatogenesis and obstruction of the ductal system particularly the vas deferens have been investigated. It was reported that obstruction of the vas deferens was not a major cause of azoospermia in Nigeria. Infection of the seminal fluid has been implicated as the major cause of azoospermia in infertile males in eastern Nigeria. Since infections are known to damage the vas deferens and seminiferous tubules, the study of circulating levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone are required. Post bacterial infections and idiopathic testicular pathology are documented as common causes of azoospermia.

The present study was undertaken to examine the circulating levels of FSH, LH, prolactin (PRL) and testosterone as contributory factors to azoospermia in azoospermic male Africans attending the fertility clinic a hospital in northern Nigeria. The role of testicular pathology in the study group was also evaluated.

Material & Methods

A total of 80 consecutive infertile azoospermic males attending the fertility clinic of Aminu Kano Teaching Hospital Kano, Nigeria during 2002 to 2004, were included in this study. The age of these men ranged from 25 - 46 yr with a mean of 38.4 ± 3.2 yr. Twenty normospermic males aged 28 - 48 yr with a mean age of 39.5 ± 2.6 yr were included as control subjects. Ethical clearance was obtained from the Aminu Kano Teaching Hospital Ethics Committee and the medical records of the subjects were retrieved from the medical records department.

Information regarding the past medical history, social history, physical examination of the testes, results of semen analysis and histological evaluation of testicular biopsy were extracted from medical records of individual patients. These subjects had no history of diabetes or hypertension and of previous surgical operation. Only 10 patients (12.5%) admitted to consumption of alcohol occasionally while 50 (62.5%) admitted smoking cigarettes. Their azoospermic condition was confirmed when a repeat semen analysis showed no sperm cells while the mean sperm density of control subjects was 46.8 cells/ml.

Blood samples were obtained for estimation of testosterone, prolactin (PRL), follicle stimulating hormone (FSH) and luteinizing hormone (LH). Sera were obtained after centrifugation at 1000 g for 10 min. The serum samples were kept at -20°C until they were analyzed. FSH, LH, PRL and testosterone levels were quantitated by ROCHE ELECSYS 1010 using electrochemiluminescence immunoassay technique.

Student’s t test was used to compare the mean values and level of significance was set as $P<0.05$.

Results

Of the 80 males, 32 (40%) had abnormal hormonal levels (Table), ten had elevated FSH and LH, diminished testosterone and normal prolactin levels, 12 had diminished FSH, LH, and prolactin and normal testosterone while four had elevated prolactin levels and normal levels of FSH, LH and testosterone. Two had isolated elevation of FSH and three had isolated elevation of LH level. Forty eight (60%) of these azoospermic subjects had normal levels of prolactin, FSH, LH and testosterone. Only one who had no ejaculate despite repeated achievement of orgasm had diminished level of
FSH, while prolactin, LH and testosterone were normal. Statistically significant differences were observed ($P<0.001$) when compared with the control subjects.

On testicular biopsies of these azoospermic males, 17 (21.3%) had partial or complete spermatogenic arrest, eight (10%) had testicular atrophy, seven (8.75%) had moderate to severe hypospermatogenesis while two (2.5%) had epididymal ducts devoid of spermatozoa. One person each had testicular dysgenesis, and germinal cell aplasia. Forty four (55%) had no significant testicular pathology.

Of the 10 subjects with primary hypogonadism, eight had testicular atrophy, one each had germinal cell aplasia and testicular dysgenesis. Ten of the 12 subjects with secondary hypogonadism had spermatogenic arrest and two had epididymal ducts devoid of spermatozoa, while four subjects with hyperprolactinaemia had hypospermatogenesis. However, seven males with normal hormonal levels had spermatogenic arrest while three had hypospermatogenesis. Two subjects with increased and one with decreased FSH and three with increased LH had normal testicular morphology.

**Discussion**

Our findings showed that hormonal abnormalities, underlying testicular pathology were common in this group of infertile azoospermic males.

Evaluation of the infertile men requires a complete medical history, physical examination and laboratory investigations with the aim to identify and treat correctable causes. The purpose should be to counsel patients and spare the spouse of invasive procedures and potential complications.

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**Table** Hormonal levels of azoospermic infertile males and control subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (yr)</th>
<th>Prolactin (ref range 86-390 mIU/ml)</th>
<th>FSH ref (range 4.6-12.4 mIU/ml)</th>
<th>LH (ref range 4.0-8.6 mIU/ml)</th>
<th>Testosterone (ref range 2.8-8.0 ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary hypogonadism (n=10)</td>
<td>37.4 ± 2.8</td>
<td>293.97 ± 32.6</td>
<td>40.7 ± 4.90**</td>
<td>11.94 ± 1.02**</td>
<td>1.99 ± 0.43**</td>
</tr>
<tr>
<td>Secondary hypogonadism (hypogonadotropic hypogonadism) (n=12)</td>
<td>37.3 ± 3.2</td>
<td>203.1 ± 22.3</td>
<td>1.84 ± 0.28**</td>
<td>2.36 ± 0.2**</td>
<td>3.01 ± 1.02**</td>
</tr>
<tr>
<td>Hyperprolactinaemia (n=4)</td>
<td>43.8 ± 3.8</td>
<td>726.0 ± 54.8**</td>
<td>12.3 ± 1.84</td>
<td>6.23 ± 0.26</td>
<td>5.85 ± 0.50</td>
</tr>
<tr>
<td>Isolated increase in FSH levels (n=2)</td>
<td>36.5 ± 2.1</td>
<td>301.2 ± 73.0</td>
<td>22.6 ± 1.51**</td>
<td>5.52 ± 0.97</td>
<td>2.53 ± 0.32**</td>
</tr>
<tr>
<td>Isolated increase in LH Levels (n=3)</td>
<td>41.0 ± 3.2</td>
<td>313.5 ± 29.4</td>
<td>7.11 ± 2.07</td>
<td>11.31 ± 0.92</td>
<td>7.67 ± 0.60</td>
</tr>
<tr>
<td>Azoospermia with normal hormones (n=48)</td>
<td>37.4 ± 5.2</td>
<td>212.3 ± 12.7</td>
<td>7.13 ± 042</td>
<td>6.64 ± 0.27</td>
<td>5.68 ± 0.30</td>
</tr>
<tr>
<td>Normospermic males (46.8 x 10^6 cell/ml) (n=20)</td>
<td>38.2 ± 2.4</td>
<td>216.67 ± 16.1</td>
<td>7.89 ± 0.60</td>
<td>6.42 ± 0.33</td>
<td>5.58 ± 0.30</td>
</tr>
<tr>
<td>No ejaculation (n=1)</td>
<td>30</td>
<td>386.7</td>
<td>1.43</td>
<td>5.05</td>
<td>4.09</td>
</tr>
</tbody>
</table>

**$**P<0.001
associated with such procedures. Oligospermia and azoospermia are common causes of male infertility in sub-Saharan Africa. Our results showed that 40 per cent azoospermic males had abnormal hormonal levels, the pattern of abnormalities however varied, ten had primary hypogonadism. This is an indication of testicular failure in which there is loss of negative feedback by testicular products. There is defect in the testes despite increased levels of FSH and LH, the testes cannot produce adequate quality sperm cells. Marked elevation of FSH in the azoospermic patients strongly suggest testicular failure and a poor prognosis. This result is partly consistent with previous studies elsewhere. Fifteen per cent of our subjects had secondary hypogonadism. Hypogonadotropic hypogonadism is a result of decreased gonadotropin stimulation of potentially normal testes. Hyperprolactinaemia observed in four subjects partly confirms the earlier reports that it is common in infertile Nigerian men. These hormonal abnormalities can be corrected if the patients report to the hospital early. It is usually recommended that clinical evaluations of the male partner be done after a year of unprotected intercourse has passed without conception.

The isolated increase in FSH level may indicate disturbance of seminiferous tubules function probably due to deficient secretion of inhibin and sex steroids. However, clinical experience suggests that in some men an elevated FSH level may represent a hormone of reduced biologic activity or an imbalance in the gonadal-pituitary feedback mechanism and not irreversible germinal epithelial damage. Similarly isolated elevation of LH level may suggest the presence of a cross-reacting substance such as hCG. One patient, who had no ejaculate despite achieving orgasm, had diminished FSH level with the other parameters within normal limits. The medical history of this patient revealed that his testes were pulled during a football match a couple of years earlier.

Histological examination of testicular biopsies revealed that the azoospermic condition was not due to primary testicular defects in half of the subjects. Spermatogenic arrest, testicular atrophy and hypospermatogenesis were the most common testicular abnormalities observed in this study. The main causes of these conditions are not known, but the rapid pace of increasing incidence of azoospermia and other conditions responsible for male factor infertility point to environmental factors. Chromosomal abnormalities have also been reported to be as one of the genetic factors contributing to male infertility. Endocrine disrupting chemicals and genetic polymorphisms have been hypothesized to influence male reproductive health.

The effects of environmental factors such as pesticide and heavy metal contamination require further investigation. Clinicians also need to bear in mind the possibility of intrinsic abnormalities of the testes as factors responsible for male infertility. In such situations prompt identification and correction of treatable conditions is vital in restoring fertility. Counseling is essential in selected patients such as testicular dysgenesis, where fertility cannot be improved, and alternative approaches such as artificial donor insemination, surrogacy and adoption should be considered. Hormonal therapy should be administered where appropriate to correct endocrine abnormalities.

In conclusion, male infertility is becoming an increasingly prominent contributory factor in the evaluation of infertile couples. Practitioners particularly reproductive endocrinologists and
fertility specialists require to recognize the varied spectrum of abnormalities in the male subjects. A comprehensive detailed laboratory work-up incorporating hormonal assessment, semen analysis and in selected patients histological evaluation of testicular biopsy material will substantially facilitate appropriate patient management.

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