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Evaluation of hormonal and physical factors responsible for male infertility in Sagamu South Western Nigeria

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ABSTRACT

Gonadotropins (FSH, LH) and testosterone abnormalities are usually associated with abnormal spermatogenesis. Plasma luteinizing hormone (LH), follicle stimulating hormone (FSH) and testosterone levels were estimated in sixty eight infertile men (age group 20-56 years) of at least 2 years duration of infertility, being a stepping toe into investigating the causes of infertility in the couples and before embarking on more expensive investigating procedures in the female partners. Thirty normal males (age group 27- 46 years) of the same socioeconomic status were selected as control group. Clinical examination was carried out on all the subjects and information about age and history of infertility in the family was obtained. Results showed that 14 (20.6%) of the infertile men were azoospermic, 50 (73.5%) were oligozoospermic and 4 (5.9%) were normospermic. Using the physical factors, 32 physical challenges were observed comprising of 5 (15.6 %) hyhpoplasic testes, 1 (3.1%) testicular atrophy and 26 (81.3 %) varicocele. There was a statistically significant ($p < 0.05$) increase in the mean FSH and LH levels in all the infertile males studied when compared with the controls ($n=30$). However, there was no significant difference in the mean levels of testosterone between the infertile and fertile men.

Key Words: Male infertility, Follicle stimulating hormones, Luteinizing hormones, testosterone, varicocele

INTRODUCTION

The psychosocial consequences of infertility and the different etiological factors had been established mainly in female especially in Sub Saharan Africa with fewer efforts on male infertility due to African norms. However, male factor had been shown to account for 20-50% of the cases of infertility in different parts of Nigeria [12] and this had brought about the need to investigate male partners in infertile couples unlike what it used to be in the past when the blames of infertility was mostly passed on female and so investigated.

The hypothalamo-pituitary-testicular axis is of great importance in male fertility. The release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland is elicited by gonadotropin releasing hormone (GnRh) secreted by the hypothalamus [10]. FSH binds with receptors in the sertoli cells and stimulates conversion of spermatids to spermatozoa (spermatogenesis) [17]. LH stimulates the production of testosterone by the Leydig cells, and in turn acts on the sertoli and peritubular cells of the seminiferous tubules to stimulate spermatogenesis [19]. Testosterone is essential for growth and division of germinal cells in forming spermatozoa.

The secretion of gonadotrophins by the hypothalamus is controlled by testosterone, estradiol and inhibin [22], thus failure of the pituitary gland to secrete FSH and LH will result into male infertility.

One of the major determinants of male fertility is the semen quality. Variations in semen quality is a reflection of biological factors such as testicular size, sperm production by the testes, accessory organ secretions, recent febrile illness and period of sexual abstinence, which should be recorded and taken into account in interpreting the results of investigations [5]. Sperm concentration is not a direct measure of testicular sperm output, as it is influenced by the functioning state of other accessory reproductive organs; but the total number of sperm ejaculated (sperm concentration multiplied by semen volume) is a measure [11].

Though sperm concentrations in semen may be the same in young and old men, total sperm numbers may differ, as both the volume of seminal fluid and total sperm output decreases with age, at least in some populations [18]. However, this may be improved by abstinence during which spermatozoa accumulated in the epididymis may overflow into the urethra and are flushed out in urine [6, 8]. Sperm vitality and chromatin are unaffected by increased length of abstinence [8, 21] unless epididymal function is disturbed [7].

During ejaculation the first semen fractions voided are sperm-rich, whereas later fractions are dominated by seminal vesicular fluid [4]. Hence, losing this sperm-rich first portion of the ejaculate should be avoided in semen analysis as this has more influence on the results of semen analysis than does losing the last portion. Also, the size of the testis influences the total number of spermatozoa per ejaculate [1, 2, 23, 14]. Testicular size is a reflection of spermatogenic activity levels, which also affects sperm morphology [15].

This study aims at estimating the FSH, LH, and testosterone levels in infertile males and determines any association of these with the result of semen analysis.

MATERIALS AND METHODS

The study was a prospective cross sectional one carried out at an outpatient infertility clinic of a private hospital with a standard laboratory facility between February and July, 2011. A total of sixty eight infertile men and thirty age-matched controls with proven fertility were selected for the study. Informed consent was obtained from the subjects after the procedures had been explained to them. FSH, LH and testosterone levels were evaluated in all the infertile men and controls. The hormonal assays were done by radioimmuno assay (RIA) using the kits supplied by Immunometrics (UK) Limited. Clinical examination of all the subjects was carried out to detect any abnormality in the genitalia and scrotum after the history taken for dermatographic and other characteristics.

10ml fresh blood sample was aseptically collected from ante cubital vein of each subject, transferred into a clean plain labeled tube, allowed to clot, and then centrifuged at 6000 rpm for 5 minutes at room temperature. The clear serum was separated and kept at 20 °C till assayed. FSH, LH and Testosterone assessment was done using the method of Fahie-Wilson [13].

Semen was collected from the infertile subjects by masturbation, after haven abstained from sexual intercourse for a minimum of two days and a maximum of seven days, in a private room near the laboratory in order to limit the exposure of the semen to fluctuations in temperature and also to control the time between collection and analysis. The collection was done into a clean, dry, wide-mouthed container made of glass that is non-toxic for spermatozoa. The specimen container was kept in an incubator at 30 °C temperature. The estimation of sperm counting was done using the Neubauer haemocytometer chamber. Sperm analysis was carried out according to the World Health Organization guidelines [25].

Based on the sperm count, the subjects were classified as normospermia (> 20 million sperm/ml), oligospermia (<20 million sperm/ml) and azoospermia (no spermatozoa). In proven fertile controls, the sperm count ranged from 20 –120 million sperm/ml.

The results obtained were analysed using descriptive statistics and student t-test with SPSS version 17.

RESULTS

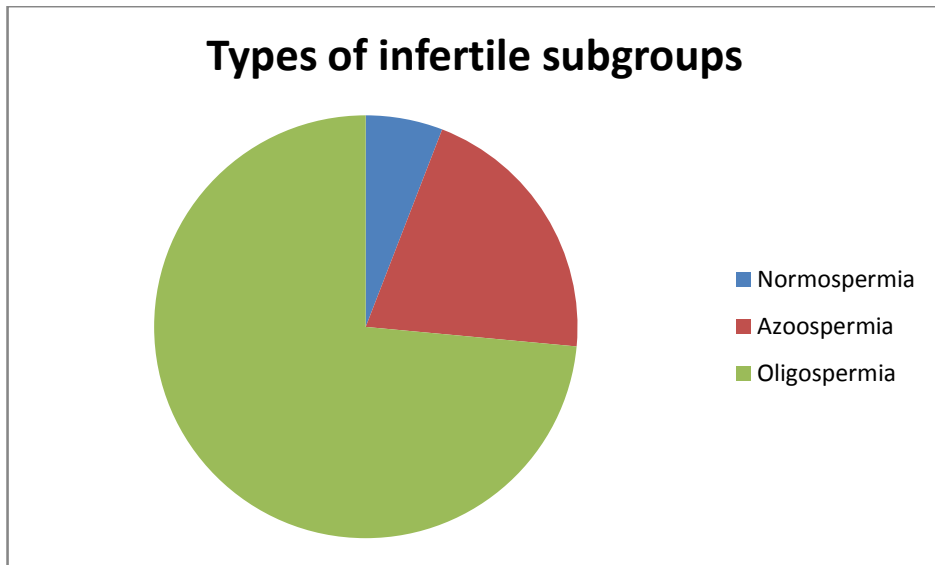


Figure 1 shows the results on the types of infertile subgroups. In all, 4 (5.9 %) of the subjects were normospermic, 14 (20.6%) azoospermic and 50 (73.5%) were oligospermic.

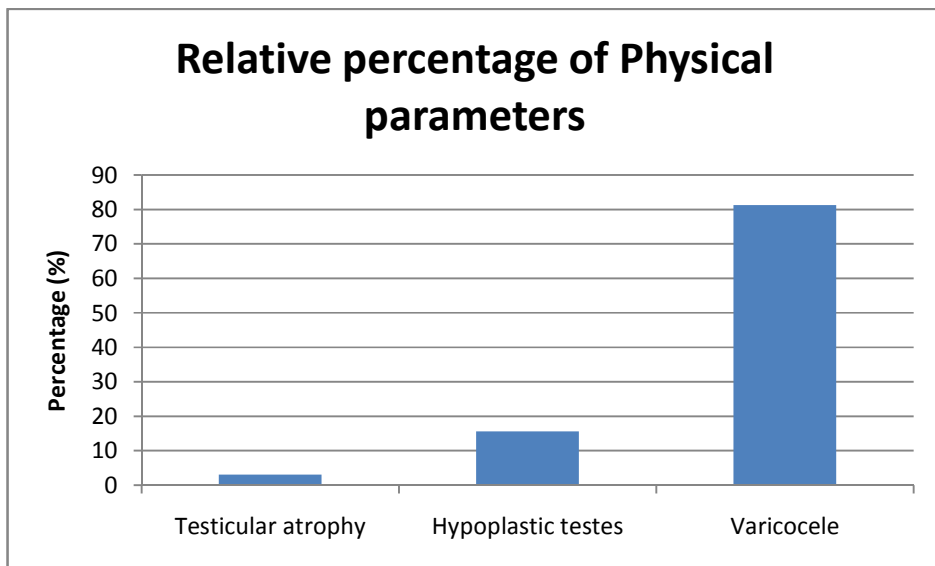


Figure 2 shows the results on the physical parameters and their relative percentages. 3.1% of the subjects were having testicular atrophy, 15.6% had hypoplastic testes and 81.3% had varicocele.

Table 1:

Parameters	Control group n=30	Infertile group n=68	t-value	p-value
FSH (iu/L)	6.83 ± 0.20	19.53 ± 0.60	12.58	0.00
LH (iu/L)	6.80 ± 0.21	17.07 ± 0.96	9.80	0.00
Testosterone (nmol/L)	24.33 ± 0.84	22.50 ± 0.64	0.95	0.35
Sperm count (x 10 ⁶)	24.87 ± 0.49	8.67 ± 0.93	17.48	0.00

Table 2 shows the mean serum FSH, LH, and testosterone levels and sperm count in control and infertile groups. There was a statistically significant ($p < 0.05$) increase in the levels of LH and FSH and a significantly decrease in sperm count in the infertile men. There were no significant changes in the testosterone levels amongst the two groups.

DISCUSSION

Generally, the production of spermatozoa requires the presence of FSH, LH and testosterone. While FSH acts directly on the sertoli cells to stimulate spermatogenesis, LH acts indirectly by first stimulating the production of testosterone in Leydig cells, which will in turn act on the Sertoli and peritubular cells of the seminiferous tubules to stimulate spermatogenesis. Thus, changes in these hormones usually reflect in the quality of spermatozoa produced. From this study significantly high plasma levels of FSH and LH were observed in infertile males. This is in agreement with the work of Weinbauer and Nieschlag [22]. The difference in the mean serum testosterone levels between fertile and infertile men was not statistically significant. Similar observation was made by Subhan et al [20].

The observed increase in the FSH and LH levels are to stimulate the sertoli and leydig cells for proportionate synthesis and secretion of testosterone thereby enhancing spermatogenesis. At certain yet to be determined plasma threshold of FSH and LH the high gonadotrophin level exercise a negative feedback effect on the hypothalamo-pituitary-testicular axis and thus the plasma testosterone become low or normal.

Based on sperm count, 5.9% of the subjects were normospermic, 20.6% of the subjects were azoospermic and this confirm the earlier work of Jarvi et al who gave the prevalence to be 20% [16] while 73.5% of the studied subjects were oligospermic.

Based on physical parameters, 32 physical factors were observed comprising of 5 (15.6 %) hypoplastic testes, 1 (3.1%) testicular atrophy and 26 (81.3 %) varicocele. However, it was discovered from this study that varicocele account for 38.2% of male infertility corroborating the earlier determined prevalence of about 6% to 47%, depending on geographical regions [24]. In varicocele, high temperature from the dilated veins damage the produced spermatozoa and hence responsible for low or total absence of spermatozoas in infertile men with varicocele. Also associated with varicocele are increased intratesticular pressure, hypoxia from disturbance of blood flow, reflux of toxic metabolites from the adrenal glands and hormonal profile abnormalities [26]. The observed azoospermia and oligospermia may be associated with the higher concentration of FSH in infertile men. This had been considered to be a reliable indicator of germinal epithelial damage and increasing severity of seminiferous epithelial destruction by Bergmann, et al [3] and de Kretser respectively [9]. Although there was no significant decrease in the testosterone levels in infertile males when compared with the fertile controls, the increase in the levels of gonadotropins might have disrupted the spermatogenic process leading to the decline in the sperm count and infertility.

In addition, there was no family history of infertility in all the cases studied and hence the infertility observed might be attributed to primary or secondary hormonal factors. The overall results clearly indicate significant increase in gonadotropins (FSH and LH) in all the infertile subgroups (azoospermia, oligospermia and varicocele) and a significant decrease in sperm count in male infertility.

CONCLUSION

It could rightly be concluded from this study that high plasma levels of gonadotrophins, low sperm count and low or normal levels of testosterone are pathognomonic of male infertility. The high level of gonadotrophins is an indication of testicular problems as the cause of infertility in the studied subjects and need further investigation which may involve testicular biopsy. In the case of the normospermic infertile men, the cause of infertility in them might be due to some other factors other than hormonal abnormalities.

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