# PATTERN OF SEMINAL FLUID PARAMETERS AND THEIR CLINICAL CORRELATES AMONGST INFERTILE MEN IN THE NIGER-DELTA REGION OF NIGERIA

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## Abstract

***Background***: Infertility is a foremost reproductive health problem globally, with sub-Saharan Africa nations most affected. The male contributions to this burden have not been properly documented in this environment

***Methods***: This was a cross-sectional study conducted in Central Hospital Benin City, involving 355 male partners of women with infertility. Specific clinical information was extracted and two semen analyses were conducted two weeks apart.

***Results***: The mean duration of infertility was 4.5 years (SD 2.17), and secondary infertility was the commonest (82.3%). Over half (59.7%) were of low socioeconomic status. Over two-thirds (66.5%) had seminal fluid abnormality; and Oligospermia was the commonest (22.8%). About two-fifth took alcohol regularly (43.9%), had previous history of urethral discharge (39.4%), or of testicular pain (42.8%). About One-fifth had a past history of mumps-orchitis (20.3%), or smoked cigarette (22.3%). Less than a tenth had varicocele (8.8%), or undescended testes (8.5%); while more than one-tenth reported use of Cimetidine (12.4%), herniorrhaphy (14.7%), scrotal surgery (15.8%), or sexual dysfunction (14.6%). There were significantly more participants with sexual dysfunction, herniorrhaphy, scrotal surgery, undescended testes; mumps orchitis; testicular pains; varicocele; history of purulent urethral discharge; tobacco smoking; alcohol consumption; and use of Cimetidine who have abnormal seminal fluid parameters. However on multivariate logistic regression analysis, history of urethral discharge, undescended testes, and Cimetidine use had negative correlation with abnormal semen parameters.

***Conclusion***: The prevalence of male factor infertility in our setting was high with significant association between male infertility and wide range of clinical and psychosocial problems.

***Key Words: Pattern, Seminal Fluid, Parameters, Clinical Correlates, Infertile Men***

## Introduction

Infertility is a foremost medical problem with profound psychological, social, cultural, and religious dimensions. When couples are unable to achieve pregnancy after a year of regular, unprotected sexual intercourse, they are regarded as been infertile[1,2]. Male fertility encompasses the production and maturation of spermatozoa, arousal, erection and, ejaculation, and fertilization. Male infertility will occur if there is impairment at any level of this cascade of events. The ultimate hallmark of male fertility is the ability to produce functionally competent spermatozoa to fertilize the ovum[3,4]. True prevalence of infertility is largely unknown as population studies are rarely available[5]. Global prevalence is 10-20% [1,2] but regional variation exists, with the developing countries worse affected[1]. A prevalence of 20-45% has been documented in Nigeria[2, 6]. An infertility belt has been described that stretches from West Africa through Central and East Africa, and encompassing many developing countries including Nigeria[2]. This belt coincides with areas with high prevalence of sexually transmitted infections. Infertility exerts social and psychological miseries on affected couples, especially in the African communities [1,7-10]. It constitutes much of the work load in the gynaecologic out- patient clinics[11]. Unlike infertility in the females, male infertility has been less extensively investigated in Africans because male factor was earlier regarded as a relatively uncommon cause of infertility. It is now recognized that abnormalities in the male contributes significantly to infertility, accounting for up to 70% of etiological factors in a study conducted in Nigeria[12]

Since male infertility centers on the production of functionally viable spermatozoa[4], diagnosis has traditionally been based on the conventional semen profile defined by the WHO[13, 14], and this incorporates the volume of the ejaculate, and the concentration, motility& morphological appearances of spermatozoa. In the 4th edition (1999) of WHO semen parameters, normal volume was accepted as >1.5 mLs; normal

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sperm concentration >20 million/mL; oligozoospermia as 5-20 million/mL and severe oligozoospermia as less than 5 million/mL. Motility was described as normal if >50% of spermatozoa were progressively motile within 60 minutes of ejaculation. Sperm morphology describes the number of normal spermatozoa with an ovoid head, stainable acrosome and a normal mid-piece and tail. Presence of >14% normal forms is regarded as normal. Although a fifth revision of normal criteria that is based on lower reference limits ($5^{th}$ percentile of normal of normal population) was released by the WHO in 2010, the earlier version is still widely in used. The WHO range of "normal values" is not evidence-based, either in terms of their diagnostic values, or their relationship to the fertile population[15].A significant proportion of men with normal criteria of semen qualities will be infertile because of defects in sperm function while a number of men with abnormal semen qualities will have normal sperm function and achieve fertility[15]. Many couples with 'unexplained' infertility can be shown to have defective sperm function when appropriate evaluations are conducted. Very few studies on the epidemiology of male infertility have used functional as opposed to descriptive diagnostic criteria[15].In addition, marked inter-ejaculate variability is a major problem in the assessment of human semen and many aspects of the profile are subjective with evidence of inconsistencies between laboratories[16]. There is evidence of secular decline in seminal fluid parameters over the past 50 years with a consequent increase in incidence of male infertility[17].This decline has been found to correlate with sexually transmitted infections, exposure to environmental toxicants, cigarette smoking, genetic factors, radiation, drugs, occupational hazards, trauma, among others. The relative contribution of these factors varies from one region to another; and their correlation with abnormal sperm parameters needed to be properly evaluated and documented in the African settings for obvious reasons. It is against this backdrop that this study was conceptualized to evaluate the pattern of seminal fluid parameters amongst male partners of women with infertility; and to determine the clinical correlates of male infertility in Benin City.

## Methods

This was a cross-sectional study conducted in the Department of Obstetrics and Gynaecology, Central Hospital Benin City. Consecutively presenting male partners of women presenting with infertility who consented to participate in the study were enrolled. Patients who found the method of sperm collection objectionable, had chronic medical conditions such as diabetes mellitus, renal or liver diseases, were on hormonal drugs, or had been previously investigated and treated for infertility were excluded from the study. The sample size of 355 was determined using the formula by D.W Taylor18 based on local infertility prevalence rate of 30%, and a10% attrition rate.A detailed history was taken and physical examination carried out on all participants. Specific clinical information that was extracted included history of herniorrhaphy, varicocele, purulent urethral discharge, undescended testis, drug use, cigarette smoking, alcohol intake, and sexual dysfunction. Thereafter, two semen analyses were conducted on each participant two weeks apart. Those with consistent results using the 1999 WHO criteria13were included in the study.

### *Specimen Collection, Delivery, and Analysis*

Semen sample were collected in the department's collection room by masturbation into a sterile wide-mouthed plastic container after a minimum of 3 to 5 days of ejaculatory sexual abstinence, and received & analysed by the laboratory personnel within 15 minutes of collection. Sperm Motility Test was conducted by placing a drop of the sperm cells suspension on a clean grease-free slide covered with a cover slip and examined. A total of 100 spermatozoa were counted and the percentage of motility recorded. To determine the Sperm Count, a 1:10 dilution of the sperm suspension was made in physiological saline and a capillary tube was used in collecting a portion and charged into Neubauer haemocytometer. The cells in the appropriate ruled areas of the counting chamber were counted and recorded. Sperm Viability Test was conducted by mixing one drop (10 - 15µl) of 0.5% eosin with one drop of semen on a slide, and examined 2 minutes later using x10 objective microscope to focus the specimen and the x40 to count the percentage of viable and non-viable spermatozoa. In assessing sperm count and morphology, a thin smear of the liquefied well mixed semen was made on a clean grease-free slide and fixed with 95% ethanol for 5-10 minutes and then allowed to air dry. The smear was washed with sodium bicarbonate formation to remove any mucus that may be present. It was then rinsed several times, and stained with dilute carbolfuchsin (1 in 20) and allowed to stain for 3 minutes followed by washing with water. Dilute (1 in 20) loeflers methylene blue was used to counterstain the smear for 2 minutes. It was then washed with water, drained and allowed to air dry. Using the x100 objective, 100 cells were counted and the percentage showing normal morphorlogy and the percentage that appears abnormal was recorded. Sample was also examined for appearance, liquefaction, viscosity, pH and cellular elements other than spermatozoa. Appropriate treatment and counseling were offered to all participants in line with the local fertility treatment practices. Approval for the study was obtained from the Ethics and Research Committee of Central Hospital Benin City.

### *Data management and analysis*

Information was extracted using a data collection sheet designed for the purpose. The data was coded and analysed using computer using Statistical Package for Social Sciences (SPSS) version 21.0. This consisted of

initial univariate and bivariates analyses, and then multivariate logistic regression analysis to identify the clinical correlates and independent risk factor of male infertility. Test of statistical significance was based on 95% confidence interval and p <0.05 using chi-square test with fisher exact correction where applicable.

## Results

A total of 355 male subjected participated in the study.

Table 1 shows the socio-demographic characteristics of the participants

**Table 1:** Socio-demographic characteristics of male partners of women with Infertility

| | N | % |
|---|---|---|
| **Age group (yrs)*** | | |
| <25 | 12 | 3.4 |
| 25 – 35 | 170 | 47.9 |
| >35 | 173 | 48.7 |
| **Duration of Infertility (yrs)#** | | |
| < 2 | 12 | 3.4 |
| ≥ 2 | 343 | 96.6 |
| **Duration of Marriage§** | | |
| Less than 2yrs | 11 | 3.1 |
| 2yrs and above | 344 | 96.9 |
| **Social Status** | | |
| Low | 212 | 59.7 |
| Middle | 95 | 26.8 |
| High | 48 | 13.5 |
| **Educational Level** | | |
| No formal education | 0 | 0 |
| Primary | 42 | 11.8 |
| Secondary | 174 | 49 |
| Tertiary | 139 | 39.2 |
| **Location of residence** | | |
| Rural | 65 | 18.3 |
| Urban | 290 | 81.7 |
| **Marital Status** | | |
| Monogamy | 326 | 91.8 |
| Polygamy | 29 | 8.2 |
| **BMI** | | |
| Underweight | 2 | 0.6 |
| Normal weight | 99 | 27.9 |
| Overweight | 201 | 56.6 |
| Obesity | 53 | 14.9 |
| **Subset of Infertility** | | |
| Primary | 63 | 17.7 |
| Secondary | 292 | 82.3 |

**=>Mean age = 34.98 (SD 4.67); Median age = 35.00; Range = 24-46.*
*# =>Mean duration = 4.50 (SD 2.17); Median duration = 4.0; Range 1-12.*
*§=> Mean duration = 4.52 (2.17); Median duration = 4.10; Range = 1-12*

The mean age of the subjects was 34.98 years (SD 4.67). Majority (96.6%) of them were 25 years and above. The mean duration of infertility was 4.5 years (SD 2.17), and this was ≥2 years in almost all (96.6%) cases. More than half (59.7%) of the subjects were of low socioeconomic status; but all of them had at least a primary school education, with upto two fifth (39.2%) attaining tertiary level of education. Most of the participants (81.7%) dwell in the urban. All the subjects were married, mostly (91.8%) in a monogamous family setting; the mean duration of marriage was 4.52 years (SD 2.17). Secondary infertility was the commonest (82.3%). Only 27.9% of the subject were of normal weight (BMI 18.5-24.9kg/m2), most others were overweight or obese [(BMI 25-29.9kg/m2) (56.6%) and (BMI > 30kg/m2) (14.9%)].

**Table 2:** Prevalence of abnormal semen parameters among male partners of women with Infertility

| Semen parameters | Frequency | Percent |
|---|---|---|
| Normal | 119 | 33.5 |
| Abnormal | 236 | 66.5 |
| Total | 355 | 100.0 |

Table 2 shows the pattern of semen fluid analysis. Of the 355 male partners, 236 (66.5%) had at least one form of seminal fluid abnormality.

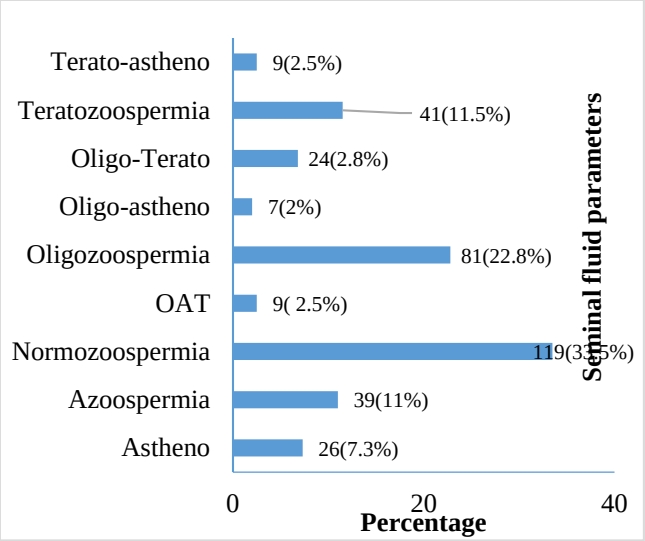


**Fig. 1:** Pattern of Semen parameters among male partners of women with Infertility

Figure 1 shows the pattern of seminal fluid analysis. Oligospermia was the commonest (22.8%), followed by azoospermia (11.0%); teratozoospermia (11.5%), and asthenozoospermia (7.3%). The mixed abnormalities were oligo-teratozoospermia (6.8%); oligo-asthenozoospermia(2.0%),oligo-asteno-teratozoospermia (OAT syndrome) (2.5%), and terato-asthenozoospermia(2.5%)

**Table 3:** Clinical characteristics of male partners of women with Infertility

| Clinical Factor | Positive | | Negative | | Total |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Sexual Dysfunction | 52 | 14.6 | 303 | 85.4 | 355 |
| Herniorraphy | 53 | 14.7 | 302 | 85.3 | 355 |
| Scrotal surgery | 56 | 15.8 | 299 | 84.2 | 355 |
| Undescended Testes | 30 | 8.5 | 325 | 91.5 | 355 |
| Mumps-orchitis | 72 | 20.3 | 283 | 79.7 | 355 |
| Pain in the testes | 152 | 42.8 | 203 | 57.2 | 355 |
| Varicocoele | 31 | 8.8 | 323 | 91.2 | 355 |
| Urethral discharge | 140 | 39.4 | 215 | 60.6 | 355 |
| Cigarette smoking | 79 | 22.3 | 276 | 77.7 | 355 |
| Alcohol use | 156 | 43.9 | 199 | 56.1 | 355 |
| Cimetidine Use | 44 | 12.4 | 311 | 87.6 | 355 |

**Table 4**: Correlates between clinical characteristics and abnormal semen parameters in male partners of women with Infertility

| Clinical Characteristics | Seminal Analysis | | | | |
|---|---|---|---|---|---|
| | Normal | Abnormal | *P*-value | OR | 95% C.I for OR |
| **Sexual Dysfunction** | | | | | |
| Yes | 6(11.5) | 46(88.5) | **0.000** | **4.56** | **1.89 - 11.02** |
| No | 113(37.3) | 190(62.7) | | | |
| **Herniorraphy** | | | **0.000** | **5.7** | **2.20 – 14.75** |
| Yes | 5(9.6) | 47(90.4) | | | |
| No | 114(37.7) | 188(62.3) | | | |
| **Scrotal surgery** | | | | | |
| Yes | 8(14.3) | 48(85.7) | **0.000** | **3.54** | **1.62 – 7.76** |
| No | 111(37.1) | 188(62.9) | | | |
| **Undescended Testes** | | | | | |
| Yes | 1(3.3) | 29(96.7) | **0.000** | **16.53** | **2.23 – 122.92** |
| No | 118(36.3) | 207(63.7) | | | |
| **Mump orchitis** | | | | | |
| Yes | 10(13.9) | 62(86.1) | **0.000** | **3.88** | **1.91 – 7.90** |
| No | 109(38.5) | 174(61.5) | | | |
| **Pain in the testes** | | | | | |
| Yes | 17(11.2) | 135(88.8) | **0.000** | **8.02** | **4.52 – 14.25** |
| No | 102(50.2) | 101(49.8) | | | |
| **Varicocele** | | | | | |
| Present | 3(9.7) | 28(90.3) | **0.003** | **5.21** | **1.55 – 17.49** |
| Absent | 116(35.8) | 208(64.2) | | | |
| **Urethral discharge** | | | | | |
| Yes | 12(8.6) | 128(91.4) | **0.000** | **10.57** | **5.52 – 20.23** |
| No | 107(49.8) | 108(50.2) | | | |
| **Cigarette Smoking** | | | | | |
| Yes | 9(11.4) | 70(88.6) | **0.000** | **5.15** | **2.47 – 10.75** |
| No | 110(39.9) | 166(60.1) | | | |
| **Alcohol Consumption** | | | | | |
| Yes | 24(15.4) | 132(84.6) | **0.000** | **5.02** | **3.00 – 8.42** |
| No | 95(47.7) | 104(52.3) | | | |
| **Cimetidine Usage** | | | | | |
| Yes | 4(9.1) | 40(90.9) | **0.000** | **5.87** | **2.05 – 16.82** |
| No | 115(37.0) | 196(63.0) | | | |

Table 3 shows the clinical characteristics of the participants. About two-fifth takes alcohol regularly (43.9%), had previous history of urethral discharge (39.4%), or of testicular pain (42.8%). About One-fifth had a past history of mumps-orchitis (20.3%), or smoked cigarette (22. 3%).Less than a tenth had varicocele (8.8%), or undescended testes (8.5%); while a little more than one-tenth reported haven taken Cimetidine (12.4%), had herniorrhaphy (14.7%), scrotal surgery (15.8%), or sexual dysfunction (14.6%).

Table 4 shows the correlation between the clinical characteristics and abnormal seminal fluid. Notably, there were statistically significantly more participants with sexual dysfunction (88.5%) (p = 0.000; OR 4.56, CI 1.89-11.02), herniorrhaphy (90.4%) (p= 0.000; OR 5.7, CI 2.20-14.75), scrotal surgery (85.7%) (p = 0.000; OR 3.54, CI 1.62-7.76), undescended testes (96.7%) (p = 0.000; OR 16.53, CI 2.23-122.92); mumps orchitis (86.1%) (p = 0.000; OR 3.88, CI 1.91-7.90); testicular pains (88.8%) (p = 0.000; OR 8.03; CI 4.52-14.25); varicocele (90.3%) (p = 0.003; OR 5.21. CI 1.55-17.49); history of purulent urethral discharge (91.4%) (p = 0.000; OR 10.57, CI 5.52-20.23); tobacco smoking (88.6%) (P= 0.000; OR 5.15, CI 2.47-10.75); alcohol consumption (84.6%) (p = 0.000; OR 5.02, CI 3.00-8,42); and taking of cimetidine (90.9%) (p = 0.000; OR 5.87, CI 2.05-16.82) who have abnormal seminal fluid parameters than participants who did not have any of these clinical pathologies. However, on multivariate logistic regression analysis of these clinical correlates of male infertility (table 5), history of urethral discharge, undescended testes, and Cimetidine use maintained negative correlation with abnormal semen parameters.

**Table 5:** Multivariate logistic regression of the clinical correlates abnormal semen parameters

| Clinical Correlates | *P*-value | OR | 95% C.I. for OR |
|---|---|---|---|
| Mump orchitis | 0.056 | 0.217 | 0.045-1.041 |
| Urethral discharge | 0.000 | 0.068 | 0.017-0.277 |
| Scrotal surgery | 0.196 | 3.008 | 0.566-15.988 |
| Undescended testes | 0.016 | 0.073 | 0.009-0.617 |
| Cimetidine use | 0.009 | 0.212 | 0.066-0.684 |
| Smoking cigarette | 0.154 | 0.489 | 0.183-1.307 |
| Alcohol | 0.093 | 0.537 | 0.260-1.109 |
| Testicular pain | 0.150 | 2.744 | 0.694-10.847 |

## Discussion

Infertility is a common reproductive health problem globally, worse in sub-Saharan Africa nations. The male contributions to the burden of infertility, and the various clinical correlate of this problem in this environment needed to be properly documented. In this study, the participants were male partners of women with infertility, and were mostly above 25 years of age. Although mostly of low socio-economic brackets, they all had at least primary school education, most of them lived in the urban areas of the state, and they were mostly overweight or obese. They had been married for a mean duration of 4 ½ years and majority had been regarded as having infertility for at least 2 years, mostly of the secondary category. This demographic profile is consistent with other local documentations. This study demonstrated at least one abnormality in semen parameters in more than two-third (66.5%) of the participants. This high prevalence of male factor infertility is similar to findings from other parts of Nigeria 19-21, 24. This calls attention to the heavy contribution of male partners to the overall burden of infertility, and the need to put this information in the public domains to tackle the misconceptions on male contributions to infertility. Various disorders of semen parameters were noted among the participants. Oligozoospermia alone (22.8%) was the most common semen disorder. This is similar to the findings in Ile-Ife[22], Abakaliki[23] and Kano[24]. Other semen abnormalities noted in the study were comparable to findings of earlier studies in Kano[24] and Benin City[25].

In this study, selected clinical risk factors of male infertility and their association with seminal fluid parameters were examined to establish correlates. Abnormal semen parameter was significantly more common in those with sexual dysfunction and indeed the subjects with sexual dysfunction had greater than four odds of having abnormal seminal fluid parameters. In this study erectile disorder was the main form of sexual dysfunction noted. Other investigators had noted similar relationship in men with sexual dysfunction resulting from spinal cord injury[26]. Having undergone herniorrhaphy was significantly associated with 6-fold chances of having abnormal semen parameters. This finding is consistent with similar studies in Orlu, Imo State[27].Herniorrhaphy may result in iatrogenic damage to the vas deferens leading to its total or partial occlusion, or the immunologic activation of anti-sperm antibodies resulting in semen abnormalities. Likewise, scrotal surgery was more than three-fold associated with abnormal semen parameters. Reports[28] indicates that scrotal and groin surgeries like hydrocelectomy and orchidopexy as well as trauma can lead to testicular injury and subsequently testicular atrophy, or disruption of the blood-testis barrier with activation of anti-sperm antibody production[28]. There was a seventeen-fold odds of abnormal semen parameters in male with undescended testes. Previous reports have indicated that undescended testes are the most common identifiable cause of primary testicular disease[28]. The pathogenetic mechanism of spermatogenic damage in maldescent of the testes remains unclear. It has been suggested that the increased temperature to which the intra-abdominal testes is exposed and the increased likelihood of testicular trauma or torsion in this position might be responsible. There was also a fourfold odds of abnormal semen parameters in male with history of mumps-ochitis. Existing data suggest that fertility is usually unaffected if orchitis occurs before puberty, but in cases of post-pubertal orchitis, the tunica albugenia forms a barrier against edema, and the subsequent rise in intra testicular pressure leads to pressure – induced testicular atrophy leading to male infertility[29]. In this study, there were eight folds odds of finding abnormal semen parameters in males with history of testicular pains. The exact mechanism of abnormal semen parameters in testicular pain remains

unclear. However, a past or ongoing infection in the testes and adjourning genital structures could be the link. Infections are known to have a direct damaging effect on the seminiferous tubules and vas deferens resulting in blockade[29-31]. Some males with huge varicocele have also reported dragging pain in the testes of the affected side[32].The potential role of varicocele in the causation of male infertility remains controversial, with findings both in support and not in support of any causal relationships[32-37]. It is usually an incidental finding during evaluation for infertility. Surveys have shown a prevalence of 5 – 20% in the general population and 10 – 40% among the infertile males. In this study, participants with varicocele have fivefold odds of having abnormal semen parameters[32-37]. This finding is similar to result of earlier workers in Benin City[38]. Purulent urethral discharge as a surrogate for sexually transmitted infections was found to have tenfold odds of being associated with abnormal semen parameters. Various organisms have been implicated as causes of sexually transmitted infections, in particular chlamydia trachomatis and Neisseria gonorrhea. The primary site of male Chlamydia infection is the penile urethra; with subsequent retrograde infection of the epididymis and testis[30]. Infection may lead to canalicular system damage, testicular atrophy and obstructive azoospermia. Infection is postulated to affect sperm motility; DNA fragmentation rate formulate of antisperm antibodies and have direct cytotoxic effect in spermatozoa[30,31].

Selected social habits were also evaluated to assess their potential contribution to male infertility. There was a statistically significant higher prevalence of abnormal semen parameters among those that smoked cigarette and took alcohol compared to males who did not indulge in these social habits. Various reports have demonstrated negative impact of cigarette smoking on human semen parameters, with direct correlation with the number of cigarette sticks smoked per day. Cigarette smoking in male affects every system involved in the reproductive process. Spermatozoa from smokers have been found to have reduced fertilizing capacity and the resultant embryos display lower implantation rates[33,34]. Although alcohol is widely used, its impact on male reproductive potential is still controversial. However, studies have shown that it has negative impacts both on semen parameters and sexual function[35]. It has been reported to affect the male reproductive system from the hypothalamus, the anterior pituitary gland to the testes[33,34]. Some common prescription drugs are known to negatively affect semen parameters. In this study, many participants reported the use of Cimetidine for the treatment of peptic ulcer disease. It was noted that male partners who used Cimetidine had six-fold odds of having abnormal semen parameters. In the multivariate logistic regression analysis, only urethra discharge, undescended testes and cimetidine-use remained statistically significant but with odds less than unity. The reason for these apparent protective odds for abnormal semen profile is not clear, but underscores the need for conduct of analytical study design to explore each of these risk factors. Scrotal surgery and testicular pain maintained positive association, these were however not statistically significant, and the confidence interval of the threefold odds recorded also crossed unity suggesting none effects.

## Conclusion

The prevalence of male factor infertility in our setting was high. There was significant association between male infertility as defined by abnormal semen parameters and wide range of clinical and psychosocial problems. A multicenter analytical study will establish the cause-effects relationship of these correlates and male infertility in Nigeria, and open up new pivots for male fertility preventive programs and policies.

## Authors' Contributions

All three authors ME, LOO and ATA were involved in conceptualization and drafting of the study protocol as well as in all stages of the conduct of the study, data management and analysis and in the writing of the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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