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Research Article

Semen quality of male partners of infertile couples living with HIV infection

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ABSTRACT

Background: Infertility among HIV positive couples are increasingly been reported in various gynaecology clinic. Unfortunately research into aetiology of infertility is out tune with this emerging trend. This study was conducted to determine the semen quality among infertile HIV positive couples.

Methods: A retrospective analysis of information obtained during routine care of infertile HIV positive couple at a large HIV treatment in Lagos Nigeria.

Results: Over thirty percent (31.7%) of the male partners of HIV positive couple in study had abnormal semen quality. Secondary infertility was the commonest (79.2%). The quality of semen of the HIV negative men in the study was significantly better compared to that of HIV positive men ($p < 0.001$). Of the five semen parameters compared, HIV positive participants with more severe diseases had significantly lower mean sperm volume ($p = 0.003$), sperm concentration ($p = 0.0002$) and total sperm concentration ($p < 0.001$) compared to of HIV positive participants with less severe diseases . Approximately 22% of the semen of the men in this study was infected, with Staph aureus, E coli and Klebsiella being the most common microbial isolates.

Conclusions: Male factor contributes about one third of infertility in this study and severity of HIV diseases impacts on semen quality. Further studies are needed to evaluate if antiretroviral therapy will reverse the effect of HIV infection on semen quality.

Keywords: Men, Infertility, Semen, Spermatozoa, HIV, Couple

INTRODUCTION

HIV/AIDS epidemic has emerged as one of the major challenges for the world, going from a relatively small problem in the 1980s to one of the leading causes of mortality in the 1990s.¹ Most of the persons infected reside in sub-Saharan Africa, with women accounting for over 50% of cases. In addition, majority of those infected are within the reproductive age group.² As a result of the very high morbidity and mortality associated with HIV infection then, fertility issues were relegated to the background as the major thrust was to reduce mortality and transmission of Infections.³

In the last decade, the grin picture has changed as the development and introduction of highly active antiretroviral therapy (HAART) has transformed the prognosis for HIV-infected individuals. The resultant increased longevity and quality of life has caused an increasing number of reproductive-age heterosexual HIV positive couples desiring to have children.⁴

Infertility among HIV positive couples are increasingly been reported, but unfortunately there are limited references, standard values and rates for the interpretation of results and comparison.⁵

Nigerian falls within both the infertility belt and HIV high burden setting of sub-Saharan and thus expected to

also have high infertility burden among HIV positive persons.⁶ From extensive literature search, there paucity of information on infertility among HIV positive couple. This study was therefore conducted to determine the pattern of anomalies in the semen of male partners in HIV positive couples, aimed at establishing the contribution of male factors to infertility among HIV positive couples in our environment.

METHODS

Study design and setting

This is a retrospective review of data obtained in the management of HIV positive couples referred for the management of infertility at the gynaecology clinic over a 10 year period (January 2004-December 2013).

The study setting was the Gynaecologic clinic, Clinical sciences Division, Nigerian Institute of Medical Research, Lagos. The division also host a large HIV treatment centre that started operations in 2002 from where the HIV positive couples are referred to the clinic. The centre currently provides comprehensive, HIV care, treatment and support for over 23,000 HIV positive patients. Sixty five percent of the patients come from Lagos and the rest from the other 5 states of south west Nigeria, as well as from north-central, south-south and south-eastern Nigeria. A little over 0.03% comes from the neighbouring West African countries. Patients are

Study population

Participants in this study were infertile couples referred to the gynaecology clinic from the HIV treatment clinic, specialist clinics, clinical diagnostic laboratory, NIMR and other private and public laboratory and clinics outside the Institute.

Investigation of male Infertility at the gynaecology clinic

The diagnosis of male fertility is dependent on the findings of seminal fluid analysis, hormonal investigation and microbiological assessment. Further investigations are based on the outcome of the basic test. Simultaneous we assessed the female partner, even if abnormalities are found in the male since both partner could have problem.

Semen samples are collected and processed according to WHO standard Semen sample collections is performed following abstinence from ejaculation for 3-5 days and transported to the laboratory within less than 1 hour of production while maintaining sample at body temperature.⁷ Samples were collected using masturbation only into sterile screw capped plastic universal containers. Using WHO standard semen analysis was carried out at the clinical diagnostic laboratory by determining semen liquefaction, volume, appearance, pH, sperm concentration, motility, morphology, viability, and

the presence of WBC or RBC. Each semen sample is cultured in appropriate culture media at 37°C for 24-48 hours to detect any associated bacterial pathogens.⁷ Positive samples are sub-cultured to determine the sensitivity pattern to antimicrobial agents. If values are normal according to WHO criteria, one test

Suffices, however If the results are abnormal, semen analysis is repeated.

Hormonal screening are limited to determining follicle stimulating hormone (FSH), luteinising hormone (LH), and testosterone levels in case of abnormal semen parameters. Further hormonal test are dependent on the outcome of these initial tests.

Data management

Relevant information was collected from the case records and laboratory results of the patients using a Proforma designed for the study. Information obtained includes sociodemographic characteristics, medical, reproductive and HIV treatment history and the results of infertility investigations. The cause of infertility in the partner was also obtained. The obtained information is transferred into an electronic database designed by trained data entry clerks. The entered data was further reviewed against the proforma to avoid transcription error. SPSS for windows version 20.0 statistical package was used to analyse the data. Results are reported as frequencies and mean, with level of significant set at less than 0.05 ($P < 0.05$).

RESULTS

A total of 419 infertile HIV positive couple were investigated during the study period, of which majority have serodiscordant HIV status with male negative (221; 52.7%) and HIV serocordance with both partners positive in the remaining 198(47.3%) cases. The infertility was of secondary type in the majority of couples (332; 79.2%). The remaining where cases of primary infertility (87; 20.7%).

Sociodemographic and HIV related characteristics of patients

The sociodemographic characteristics of the male partners of the HIV positive couple is shown in table 1. Their ages ranged from 27 to 67 with a mean of 42.4 (SD: 10.5) years. Over two-third of the patients (68.2%) were 40 years and above. Majority of the patients were gainfully employed (341; 81.4%), married (395; 94.3%) and had at least a secondary education (334; 79.7%). There were no statistically significant difference between the sociodemographic of the HIV positive and negative male partners ($P > 0.05$).

The HIV related characteristics of 198 HIV positive patients in the study are presented in Table 2. The CD4 cell count ranged from 106 to 613 cells/mm³ with a mean

of 421.7 ± 169.1 . The majority 144 (72.7%) of the HIV positive men had CD4 cells counts below 500 cells/mm³ and were already on antiretroviral therapy (122; 61.6%). While 80 (40.4%) had HIV viral load of less than 1000 copies, 122 (61.6%) women were on highly active antiretroviral therapy (HAART) at the time of first contact at the gynaecology clinic.

Table 1: Sociodemographic characteristics of the male partner of the HIV positive couples presenting with infertility.

Characteristics	Number of male partners of the infertile couples			P value
	ALL n=419 (%)	HIV positive n = 198 (%)	HIV negative n = 221 (%)	
Age (years)				
< 30	19(4.5)	6(3.0)	11(5.0)	
30 – 39	114(27.2)	57(28.8)	57(25.7)	
40-49	205(48.9)	89(44.9)	106(48.0)	
≥ 50	81(19.3)	46(23.2)	47(21.3)	
Range	27 – 67	29 – 67	27 – 59	
Mean(SD)	42.4(10.5)	43.9(9.1)	43.2(7.9)	0.25
Marital status				
Married	395(94.3)	186(93.9)	209(94.6)	0.23
Single	-	-	-	
Co-habiting	24(5.7)	12(6.1)	12(5.4)	0.78
Work status				
Working	341(81.4)	159(80.3)	181(81.9)	0.68
Not working	78(18.6)	39(19.7)	40((18.1)	0.78
Educational status				
< Secondary	85(20.3)	39(19.7)	46(20.8)	
≥ Secondary	334(79.7)	159(80.3)	175(79.2)	

Semen parameters of patients

The seminal fluid volume ranged from 0.5mls to 7.5mls with a mean of 3.8 ± 2.3 mls. The mean seminal fluid volume of 3.9 ± 2.5 mls among the HIV negative male partners group was higher than a mean of 2.9±mls among the HIV positive male partner group ($P < 0.001$). The semen concentration ranged $0-152.5 \times 10^6$, with a mean of $83.1 \pm 11.4 \times 10^6$. The mean sperm concentration of $97.3 \pm 9.5 \times 10^6$ among the HIV negative male partners group was significantly higher ($p < 0.001$) than $76.3 \pm 12.1 \times 10^6$ among the HIV positive male partners. The mean total sperm count of the male patients ranged from 0 to 744.8×10^6 with a mean of 315.4×10^6 . The mean total sperm count of $379.5 \pm 49.1 \times 10^6$ among the male HIV negative group was also significantly higher than the mean of $201.3 \pm 62.1 \times 10^6$ among the male HIV positive group ($p = 0.0002$).

The pattern of semen density of the male partners of infertile HIV positive couple is shown in table 3. Of the 419 male patients in the study, majority had normospermia (286; 68.3%) and the remaining 157 men had oligozoospermia (126; 30.1%) or azoospermia

(17;1.7%). The proportion of individuals with abnormal sperm density was significantly higher in the HIV positive men (38.4%) compared to 25.8% in the HIV negative men ($P < 0.039$).

Table 2: HIV related history and laboratory characteristics of the 198 HIV positive male in the study.

Characteristics	Number of patients (%)
CD4 cell count	
< 500	144(72.7)
≥ 500	54(27.3)
Range	106 – 613
Mean(SD)	421.7(169.1)
Viral load	
< 1,000	80(40.4)
1,000-100,000	64(32.3)
≥ 100,000	54(27.3)
HIV treatment status	
On treatment	122(61.6)
Not on treatment	76(38.4)

Table 3: The pattern of semen density of the male partners of infertile HIV positive couples in the study.

Sperm density	All n = 419 (%)	HIV positives n = 198 (%)	HIV negatives n = 221 (%)	Remarks
Normospermia	286 (68.3)	122 (61.6)	164 (74.2)	OR: 1.5
Oligozoospermia	126 (30.1)	70 (35.4)	56 (25.3)	95% CI: 1.0-2.3
Azoospermia	17 (1.7)	6 (3.0)	11 (0.5)	P = 0.039

The other common semen abnormalities observed among the patients were morphological abnormalities of teratozoospermia (97;23.2%) and asthenozoospermia (56;13.4%). A larger percentage of men in the HIV positive groups (34.3%;68) have morphological abnormalities compared to 19.7% (44) in their HIV negative counterparts ($p = 0.001$; OR:2.2;95% CI:1.4-3.4). Multiple abnormalities of oligoteratozoospermia (19;4.5%), asthenoteratozoospermia (16;3.8%), oligoasthenozoospermia (13;3.1%), and oligoasthenoteratozoospermia (6;1.4%) were also common. The proportion of men who have these semen abnormalities were statistically significantly higher in the male HIV positive group (25.8%; 51) compared to the 16.3%;36) HIV negative group ($p = 0.022$; OR:1.7; 95% CI:1.1-2.8).

Sperm quality and severity of HIV diseases among HIV positive patients

The relationship between the semen quality and severity of HIV disease among the male HIV positive partners is shown in table 4. The CD4 cell count levels were used as

marker for severity of HIV disease. Semen parameters were compared between patients with CD4 counts level below and above 350cells/mm³. Of the five semen parameters (table 4) compared, HIV positive participants with more severe diseases (CD4 < 350cells/mm³) had significantly lower mean sperm volume (p=0.003), sperm concentration (p=0.0002) and total sperm concentration (p<0.001) compared with HIV positive participants with less severe diseases (CD4 >350cells/mm³). No statistical significant difference were observed in mean % normal morphology (p=0.34) and mobility (p=0.75).

Table 4: Relationship between CD4 cell count and semen parameters.

Semen Parameters	CD4 < 350 cells/mm ³	CD4 ≥ 350 cells/mm ³	P value
Mean volume (ml)	2.6±1.3	3.1±1.5	0.003
Sperm concentration (10 ⁶)	69.3±10.7	84.7±6.7	0.0002
Total sperm count (10 ⁶ /ml)	136.5±31.7	237.1±47.9	<0.001
Mean % normal Morphology	64.9±15.3	71.3±10.7	0.34
Mean % mobility	61.3±17.9	64.7±12.4	0.75

Table 5: Bacterial Isolates from semen of male partners of HIV positive couple.

Organisms	Number (%)
<i>Staph aureus</i>	45(33.1)
<i>E. coli</i>	27(19.9)
<i>Klebsiela</i>	23(16.9)
<i>Candida albica</i>	17(12.5)
<i>Proteus</i>	12(8.8)
<i>Step feacali</i>	9(6.6)
<i>Pseudomonas</i>	4(2.9)

Microbial isolates from semen of patients

Table 5 shows the microbial isolated from 123 (29.3%) of the 419 semen samples. Although more organisms were isolated from the semen of the HIV positive samples (64; 32.3%) compared to 26.7% (59) isolated from HIV negative samples, the difference was not statistically significant (P=0.21). More microorganisms were isolated in the normospermic samples than in the oligozoospermia samples (31.1% vs. 27.0%), but the difference was not statistically significant (P =0.40). A total of 139 organisms were isolated from 123 infected specimens. In 16 (13.0%) semen samples more than one organism was isolated. *Staphylococcus aureus* (33.1%), *E. coli* (19.9%) and *Klebsiela* (16.9%) were the most common organism isolated from the semen samples.

DISCUSSION

Over thirty percent of the male partners of HIV positive couple seeking infertility care in our centre over the study period had abnormal semen quality (31.7%). The quality of the semen of the HIV negative men were significantly better compared to HIV positive men. Among HIV positive men, those with severe disease tend to have lower quality semen. Approximately 22% of the semen of the men in this study was infected, with *Staph aureus*, *E coli* and *Klebsiela* being the most common microbial isolates.

The finding of over one third of the male partners of infertile couple having abnormal semen quality is similar to findings by other researchers in Ile Ife and Ibadan South Western Nigeria.^{8,9} It is however lower than rate reported by Ugwuja et al in Abakiliki in South Eastern Nigeria.¹⁰ Available but limited evidence shows that HIV positive women tend to have lower semen quality compared with HIV negative men.¹¹ Looking at this gross comparison of prevalence of abnormal semen quality, it seems as if the assertion was not true. However comparing specific semen parameters, our study did detect significantly lower quality of semen in HIV positive men compared to HIV negative men. The later finding is similar to the findings of previous studies that addressed the effect of HIV infection on semen quality.¹¹⁻¹³ In these studies several semen parameters were altered in the HIV positive population. The most obvious findings were the reduction in sperm morphology and mobility. Other observed abnormalities were in the volume, sperm concentration and total sperm count. It is important to also note that other studies have reported varying anomalies which vary from study to study.^{12,13} The obvious difference may therefore be attributable other factors other HIV, which may include methodologic variations, population studied, sample size and severity of HIV diseases.^{11,14,15}

In this study, we also investigated the effect of the severity of HIV diseases measured by CD4 cell count and semen characteristics. HIV positive patients with CD4 cell count less than 350 cells/mm³ have worse semen parameters of volumes, sperm concentration and total sperm count compared to those with CD4 count above 350 cells/mm³. However no differences were noted in sperm morphology and mobility. The reported relationship between low CD4 count and some semen parameters is similar to findings by Politch et al and Dulioust et al.^{11,16} As currently there is no clear link between HIV infection and germ cell from available research findings, the effect observed may be due to specific behaviour of HIV positive individuals or concomitant occult infection.¹¹

The findings in this study of approximately 32% of semen specimen being infected with microbial organisms is similar to findings in three previous studies.^{8,17,18} Infection of the male genital tract is an important cause of

impairment of sperm function. It is also important to note that the isolated bacterial organisms may not be the cause of the low sperm quality but concomitant findings as result of compromised immunity due to HIV infection. The higher but microbial isolates from semen of HIV positive men compared to HIV negative men support this line of thought.

CONCLUSION

Male factor contributes about one third of infertility in this study and severity of HIV diseases impacts on semen quality. Further studies are needed to evaluate if antiretroviral therapy will reverse the effect of HIV infection on semen quality.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of Nigerian Institute of Medical Research Lagos who gave the ethical approval for the study and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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