

Seroprevalence and clinical correlates of human immunodeficiency virus infection among women with infertility in northwestern Nigeria

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ABSTRACT

Background: Infertility is a major cause of social and psychological problems among couples, especially in our environment where child bearing is regarded as one of the major reasons for marriage. Studies have shown that fertility among human immunodeficiency virus (HIV)-infected women may actually be reduced posing social and psychological disturbance among a group of people that are already burdened with disease.

Objective: The aim of the study was to determine the prevalence and clinical correlates of HIV infection among women with infertility attending a gynecology clinic in northwestern Nigeria.

Materials and Methods: It was a cross-sectional descriptive study comprising of women attending the gynecology clinic due to infertility that satisfied the inclusion criteria. The sample size was 250. Ethical clearance was obtained from the health research and ethics committee of the study setting. Clients were recruited consecutively as they presented to the infertility clinic from May 2015 to January 2016 and tested for HIV infection. HIV testing was done in the Department of Medical Microbiology after collecting 5 ml of blood from the clients using sterile syringes. Investigations to determine the cause of infertility were also conducted. Obtained data were analyzed using Statistical Package for Social Science version 20.0.

Results: A total of 250 clients were recruited for the study. The age range of respondents was- 17 – 47 years with a mean age of 30.3 years. Hausa was the predominant ethnic group in all respondents (61%). Most of the respondents had secondary education (39%). Only 4% had postgraduate education. Out of the 250 respondents, 21 (8.4%) were found to be positive for HIV infection. Chi-square test showed an association between tuboperitoneal infertility and HIV infection.

Conclusion: The prevalence of HIV infection in women with infertility attending our clinic was high and an association was seen between HIV infection and tuboperitoneal infertility.

Key words: Clinical correlates; human immunodeficiency virus infection; infertility.

Introduction

Human immunodeficiency virus (HIV) infection is a pandemic that has altered the morbidity and mortality patterns of many medical conditions. It is also a major cause of social and psychological problem among infected individuals, their families and the community at large. Currently, there are about 36.7

million people living with HIV infection worldwide.^[1] Majority of the people living with HIV infection are in sub-Saharan Africa.^[1]

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Infertility affects 3.5%–16.7% of couples worldwide.^[2] Infertility also leads to social and psychological problems especially in environments where child bearing determines the position of a woman in the family and society at large. However, infertility is often neglected as a health problem of public importance as it is perceived to be the couples' problem.^[3]

HIV infection has been associated with both male and female factor infertility. Interplay of several biological and social factors has been identified as possible linkage between HIV infection and infertility.^[4] Age, marital status, coital frequency, use of contraception, and presence of other sexually transmitted infections can all affect fertility in HIV infected individuals. It has also been argued that women with fertility problems are at increased risk of marital instability and, therefore, HIV infection; consequently, preexisting subfertility among HIV infected women may contribute to the observed association.^[5]

Even though social and behavioral factors have been implicated in the decreased fertility seen in HIV-infected women in the sense that they may not desire more children due to the fear of dying and leaving them with no care and support,^[6] Oladapo *et al.*^[7] reported that infertile HIV positive women were still desirous of having more children. In a study on fertility desires and intentions of HIV positive patients at a suburban specialist center, only 4.3% of women who desired children before finding out their HIV status did not intend to have any afterward.^[7] Fabiani *et al.*^[8] also argued that social factors play a minor role in infertility among HIV-positive women.

Studies have revealed a wide variability in the prevalence of HIV infection among infertile couples ranging from 0.3% as reported by Balasch *et al.*^[9] in an infertility clinic in Barcelona to 18% as seen in Tanzania.^[10] Prevalence rate of up to 20% was reported in a study from South Africa.^[11] Favot *et al.*^[10] in a study on HIV and sexual behavior among women with infertility in Tanzania reported that prevalence of HIV infection was higher among clients with infertility (18.2%) as compared to fertile women (6.6%). In Gabon, Western equatorial Africa, the seroprevalence of HIV 1 infection among clients with both primary and secondary infertility was reported to be 9.3% by Schrijvers *et al.*,^[12] while prevalence of primary and secondary infertility among non-HIV-infected clients was reported as 0.7% and 2.1% respectively in the same setting.

Despite the observed differences in the prevalence rate of HIV infection among fertile and infertile women, the surveys

conducted to estimate the prevalence of infertility in many countries are conducted on antenatal attendees thus women with infertility are not part of the surveys. The prevalence of HIV infection among women attending antenatal clinic is generally considered to be the prevalence of infection among adult women population and the general population at large.^[13] This may not reflect the true prevalence in the community because infertile women are excluded from such estimates countries.^[14] Thus, there is need to know the prevalence of HIV infection among couples with infertility. This will determine whether the burden of HIV infection among clients with infertility is enough for a policy of routine screening or at least group counseling and opt out method to be adopted in infertility clinic in our center as practiced in our antenatal clinic.

Different factors may lead to infertility among HIV-infected couples ranging from lower fertility rates, increased tubal disease, anovulation to abnormal semen parameters.^[15-19]

The aim of this study was to determine the prevalence of HIV infection and clinical correlates among clients with infertility.

Materials and Methods

A total of 250 out of 278 women who presented for evaluation for infertility at the gynecology clinic between 1st May 2015 and 31st January 2016 were recruited to participate in the study. The sample size was determined by the Fisher's formula for calculating sample size in cross-sectional studies. Prevalence of 18.2% obtained from study by Favot *et al.*^[10] was used to calculate the sample size. The level of precision was set at 5% (0.05). Ethical clearance was obtained from the Health Research and Ethics Committee.

Clients were counseled for HIV test using the 'opt out' technique. A written informed consent was obtained. Blood sample (5 ml) was obtained into a vacutainer specimen bottle using aseptic technique. Patients that were known to be HIV positive were not tested again. After collection, the sample was centrifuged at 5000 revolutions per minute for 5 min to separate blood cells from serum. The serum was then used to detect the presence of HIV antibodies using Alere Determine HIV-1/2 test kit by Abbot.^[20] The HIV (1 + 2) Ag&Ab ELISA test kit by Chemux Bioscience Inc.^[21] was used to confirm positive results. The HIV test was done in the Department of Medical Microbiology Ahmadu Bello University Teaching Hospital Shika. Partner counselling and testing was also done for HIV-positive women.

Investigations to determine the cause of infertility included a pelvic scan, hormonal profile, seminal fluid analysis, and

hysterosalpingogram. A questionnaire was used to obtain information on sociodemographic data, reproductive profile, infertility profile, and HIV profile.

The data obtained were analyzed with Statistical Package for Social Science version 20.0. Chi-square test was done to determine association between HIV infection and type of infertility. The confidence interval was set at 95% with *P* value of 0.05. Thus, statistical significance is $P < 0.05$.

Results

A total of 250 clients were recruited for the study. The age range of respondents was 17–47 years with a mean age of 30.3 (SD 6.3) years. Hausa was the predominant ethnic group in all respondents (61%). Most of the respondents had tertiary education (39%). Only 4% had postgraduate education.

Out of the 250 respondents, 21 (8.4%) were found to have HIV 1 and/or II antibodies. A total of 14 HIV-positive clients were already aware of their HIV status, while seven clients were newly diagnosed. Most HIV-positive clients (42.9%) were within the 35–39 year age range. None was below 20 years of age. Hausa is the predominant ethnic group in HIV-positive clients (52.3%). Most of the HIV-positive clients had secondary education (28.6%). Only 9.5% of the HIV-positive clients had postgraduate education.

History of at least one-term pregnancy and one live birth was reported in 52.4% and 42.9% of HIV-positive women, respectively.

History of multiple sex partners was 85.7% HIV-positive clients and 76.2% had never used condom in the past. They also had history of reproductive tract infection (71.4%). History of blood transfusion was present in 33.3% of the HIV-positive clients and 4.8% of their partners, respectively.

Secondary infertility was the commonest (81%) type of infertility seen in HIV-positive clients. Tuboperitoneal factor infertility was seen in 71.4% of HIV-positive clients. Polycystic ovarian syndrome (PCOS) was seen in 14.2% of the clients. Uterine factor and male factor infertility were each seen 9.5% of the clients. Only 4.8% of the clients were reported to have hyperprolactinemia as a cause of infertility. Some of HIV-positive clients (9.5%) had more than one documented cause of infertility. Tuboperitoneal factor was the only cause of infertility that was significantly associated with HIV infection (95% confidence interval, $P = 0.048$).

Serodiscordance was seen in 42.9% of HIV-positive women. Majority of the HIV-positive clients (90.5%) were diagnosed

within the last 10 years. Most of the HIV-positive clients were diagnosed with HIV after they have been diagnosed with infertility. Most of the clients (52.4%) were at stage II HIV disease and 66.7% of the clients are on highly active antiretroviral therapy (HAART).

Discussion

The sociodemographic characteristics of HIV positive clients with infertility are similar to HIV-negative clients with infertility in this study [Table 1]. Generally, the age-specific fertility rates of HIV-positive women are said to be reduced as compared to uninfected women except for those in the 15–19-year age range where fertility is said to be higher based on reports from many countries.^[22] This may account for the fact that even though infertility cuts across all reproductive age groups among clients that are HIV negative, none of the HIV-positive clients was within the 15–19-year age bracket. The distribution of clients based on their tribes is similar in both HIV-positive and HIV-negative clients and this reflects what is obtained in Zaria generally. More than 80% of the HIV-positive clients had some form of western education. Islamic education, which is sometimes taught in Arabic, was the only form of education attained by 19% of the clients. This may be accounted for by the fact that even though Zaria is a predominantly Muslim community, it has a long history of Western colonization and considered as a center of learning. There was no significant statistical association between age, tribe, and level of education with HIV status.

The prevalence of HIV infection among clients with infertility was found to be 8.4%. This is lower than the values reported from Gabon (9.3%), Tanzania (18.2%), and South Africa (20%). In Gabon and South Africa, the national prevalence of HIV infection is higher than the national prevalence in our setting. Despite the fact that the prevalence of HIV infection among women infertility in our study (8.4%) appears to be lower than that observed in Gabon (9.3%) and South Africa (20%), the burden may still be significant when compared to our national prevalence of HIV infection.

The prevalence of HIV infection among women with infertility in our clinic is double the national prevalence of 4.1% and also higher than the prevalence of 5.1% in our state.^[23] This is similar to findings in other African countries where the prevalence of HIV infection among clients with infertility was found to be generally higher than the prevalence of HIV infection in the general population. In Tanzania, prevalence of 18.2% was reported among clients with infertility as compared to 6.6% among fertile women.^[10] In Gabon, the national prevalence of HIV infection is 3.8%,^[11] while prevalence of HIV infection among clients with infertility is 9.3%.^[12] In

Table 1: Sociodemographic profile of participants

Profile	HIV positive		HIV negative		P
	Frequency	Percentage	Frequency	Percentage	
Age					
15-19	0	0	20	8.7	0.108
20-24	1	4.8	26	11.4	
25-29	4	19	92	40.2	
30-34	5	23.8	38	16.6	
35-39	9	42.9	31	13.5	
40-44	2	9.5	16	7	
45-49	0	0	6	2.6	
Total	21	100	229	100	
Tribe					
Hausa	11	52.3	143	62.4	0.891
Yoruba	2	9.5	18	7.8	
Igbo	0	0	6	2.6	
Kataf	5	23.8	21	9.2	
Others	3	14.2	41	17.9	
Total	21	99.9	229	99.9	
Highest level of education					
Primary	5	23.8	22	9.6	0.069
Secondary	6	28.6	78	34.1	
Tertiary	4	19.0	94	41.0	
Post graduate	2	9.5	8	3.5	
Islamic education	4	19.0	27	11.7	
Total	21	99.9	229	99.9	

*Statistically significant $P < 0.005$

South Africa the national prevalence of HIV infection is 19.1%,^[1] while the prevalence of HIV infection among clients with infertility is 20%. In all these countries, the prevalence of HIV infection is derived from the antenatal attendees. This means that women with infertility were not included in the estimates. Couples with infertility constitute about 3.5%–16.7%^[2] of the general population. The fact that the prevalence of HIV infection among these group of women differ significantly raises concern with regards to the ability of antenatal deduction of the prevalence of HIV infection to accurately estimate the true prevalence of the infection in the general population.

Conflicting literature has been published by different authors in different countries with this regard. Although some authors reported that antenatal surveillance of HIV infection closely relates to the estimates observed in the general population,^[2] some reported that it underestimates the population based estimates^[24] and others reported that it overestimates the true population estimates.^[25] Thus, there is need for population-based studies in each country to actually estimate the prevalence of HIV infection in the general population which will help in policy making and also assessing the measures put in place to combat this pandemic.

The reproductive profile of HIV positive clients may suggest pregnancy-related complications and possible perinatal and infant mortality. The number of term pregnancies among the HIV positive clients was higher than the number of live births. They also had a higher number of live births than number of surviving children. It has been documented in the literature that complications of pregnancy are said to be commoner among HIV-positive women leading to overall lower births rates among them.^[26-28] Also, HIV-exposed infants have a high perinatal and infant mortality rates.^[29,30]

Many of the HIV-positive clients (85%) had a history of multiple sexual partners and 76.2% had never used condoms. This is in keeping with the fact that having multiple sexual partners is a strong predictor of risk of HIV infection.^[31] Other risk factors include use of blood transfusion which was positive in 33.3% of HIV-positive clients and 4.8% of their partners.

Secondary infertility is the commonest type of infertility seen in 81% of HIV-positive clients. This pattern is seen globally.^[3] Tuboperitoneal factor was the commonest cause of infertility seen in 81% of HIV-positive clients and the association between tuboperitoneal infertility and HIV infection was statistically significant (95% confidence interval, $P = 0.048$) [Table 2]. This is in keeping with what has been reported by researchers in sub-Saharan Africa.^[16,17,32] Tuboperitoneal infertility which is the commonest type of infertility seen in the so called infertility belt of Africa has been associated with HIV infection by other authors. Adegoke *et al.*^[16] reported that tuboperitoneal abnormalities were more common among infertile women infected with HIV as compared to those without HIV infection. Adesiyun *et al.*^[17] in a study on hysterosalpingographic tubal abnormalities and HIV infection among black women with tubal infertility in sub-Saharan Africa reported higher incidence of tubal disease among women infected with HIV compared with their counterparts. The association between HIV infection and tuboperitoneal infertility may not differ from the association between reproductive tract infection and infertility. It may also coexist with other sexually transmitted infections like chlamydia and gonorrhoea which are known causes of tuboperitoneal infertility. Moreover, presence of other sexually transmitted genital tract infections is known to facilitate HIV transmission.

PCOS was seen in 14.2% of the clients, while 4.8% of the clients were reported to have hyperprolactinemia as a cause of infertility. Endocrine factor has also been implicated as a cause of infertility among HIV-positive women. This is supported by the fact that anovulation and amenorrhoea are associated with HIV infection.^[18] Antiretroviral drugs have also been associated with lipodystrophy characterized by fat redistribution, insulin resistance, dyslipidemia, and increased

Table 2: Association between HIV status and Infertility

Infertility profile	HIV Positive		Negative		P
	Frequency	Percentage	Frequency	Percentage	
Duration of infertility	14	66.7	126	55	0.169
<5 years	7	33.3	103	45	
≥5 years	21	100	229	100	
Cause of infertility					
Tuboperitoneal	15	71.4	112	49.0	0.048*
Uterine	2	9.5	22	9.6	0.990
PCOS	3	14.2	79	34.5	0.059
Hyperprolactinemia	1	4.8	13	5.7	0.861
Male factor	2	9.5	23	10.0	0.939
Endometriosis	0	0	1	0.4	0.762
Multiple factors	2	9.5	2	9.2	-

*Statistically significant = $P < 0.005$

luteinizing hormone follicle-stimulating hormone ratio, thus producing a picture similar to PCOS.^[33] Premature ovarian failure has also been associated with HIV infection leading to infertility with elevated follicle-stimulating hormone mimicking a menopausal state. Clark *et al.*^[34] reported the incidence of anovulation and early menopause of 8% among a clinical trial group. However, larger studies did not agree with this theory.^[18,35] This study did not demonstrate any statistically significant association between HIV infection and anovulatory infertility (P value; PCOS = 0.059 and hyperprolactinemia = 0.861) [Table 2].

Male factor infertility was documented in 9.5% of the clients. Male factor infertility is also a recognized cause of infertility among HIV-infected couples as HIV infection has been associated with decrease semen volume, sperm motility, and concentration and abnormal morphology.^[19] The damage to sperm cells has been attributed to HAART rather than the disease process itself.^[36] However, some authors argue that HAART does not affect semen parameters.^[37] Semen parameters are said to correlate with CD4 count. Nicopoulos *et al.* reported that use of HAART is associated with decrease total sperm count, progressive motility, and postpreparation count while significantly increasing the proportion of abnormal sperm forms following experience from a decade of sperm washing.^[38] Androgen insufficiency, hypogonadism, low testosterone (gonadal and extragonadal), diminished libido, and impotence are all documented causes of male infertility.^[39] Tindall *et al.*^[40] reported prevalence of impotence to be as high as 60% among males with advanced disease. Other drugs used commonly in HIV-positive patients like glucocorticoids and ketoconazole may produce side effects that may impair fertility. These drugs cause suppression of the hypothalamopituitarygonadal axis leading to low testosterone.^[41] This study did not demonstrate any significant association between male factor infertility and HIV infection ($= 0.762$) [Table 2].

Some of HIV-positive clients (9.5%) had more than one documented cause of infertility. This may be due to interplay of many factors.

Serodiscordance was seen in 42.9% of HIV-positive couples. This is of significance in view of possibility of horizontal transmission of the virus and also fertility treatment options. Fertility treatment options include timed unprotected intercourse, intrauterine insemination of sperm, in-vitro fertilization, and adoption. In the same context, there may be need to screen male partners of all clients with infertility irrespective of the HIV serostatus of the female partner. This is important in view of choosing a fertility treatment option that will eliminate or minimize risk of horizontal as well as vertical transmission of HIV infection.

Most of the HIV-positive women (52.4%) were in stage II of the disease and none progressed to acquired immunodeficiency syndrome (AIDS). Duration of the disease among clients that were already known to be HIV positive was less than 10 years in 90.5% of clients. This means that they were within the latency period. Even though 9.5% of the clients were more than 10 years postdiagnosis of HIV infection, use of antiretroviral therapy prevents progression to AIDS after 10 years of disease as seen in the natural history of the disease without intervention. Most of the HIV positive clients (66.7%) were already on antiretroviral therapy. This may explain the reason why none of the clients were in the advanced stage of the disease.

Conclusion

The prevalence of HIV infection among women with infertility is much higher than the national prevalence deduced from antenatal attendees. Thus, the deduction from antenatal women may not be representative of the actual prevalence in the general population.

The sociodemographic characteristics and causes of infertility were similar among both the HIV-positive and-negative clients. Tuboperitoneal infertility was the commonest cause of infertility in our clients and was significantly associated with HIV infection. The major drawback of this study is the fact that only characteristics of few patients have been presented; thus, it may not reflect the overall association between HIV infection and infertility.

Recommendations

There is need to screen all infertile couples for HIV infection. Studying the prevalence of infertility among HIV-positive clients may provide more information about the association between HIV infection and infertility. There is also need to study the prevalence of HIV in the general population in order to make appropriate policies that will help in combating the pandemic because deduction from antenatal attendees may not actually be accurate in estimating the burden of the disease in the general population.

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Conflicts of interest

There are no conflicts of interest.

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