

Viral infections among couples for assisted reproduction in a fertility clinic in Nigeria

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Abstract

Context: The risk of laboratory cross-contamination may limit the availability of assisted conception for couples infected with chronic viruses. However, assisted conception is the standard of care for people living with human immunodeficiency virus (HIV) to minimize risk of transmission or reinfection.

Aims: To assess the burden of viral infection among couples that present for assisted reproductive technology (ART) with a view to evaluating implications for their care.

Settings and Design: A cross-sectional descriptive study carried out among 138 couples at a private fertility clinic in Nigeria.

Materials and Methods: Screening for HIV, hepatitis B virus (HBV) and hepatitis C virus were carried out among these clients. The males' seminal parameters were analyzed according to World Health Organization (WHO) criteria.

Statistical analysis Used: Statistical Package for Social Sciences was employed. Analysis was by Chi-square test; statistical significance was set at 0.05.

Results: Viral infections were found in 10/138 women (7.2%) and 15/138 (10.9%) men. The most prevalent infection was HBV. Twenty-one couples were sero-discordant. Two couples had concordant HIV and HBV infections, respectively. There was no significant association between sperm quality and chronic hepatitis infection.

Conclusion: Nearly a fifth of the couples had at least one partner infected with a chronic virus – a proportion significant enough to demand attention. Apart from separate laboratory and storage facilities, basic principles to minimize transmission are recommended: HBV vaccination in sero-discordant partners of HBV carriers (and immunoprophylaxis for the baby) and antiretroviral therapy for HIV-positive partners to reduce the viral load before fertility treatment is commenced.

Key words: Assisted reproduction, hepatitis B virus, hepatitis C virus, human immunodeficiency virus

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Introduction

Assisted reproductive technology (ART) has been available in Nigeria for the past couple of decades. For those whom it is affordable for, it has done much to assuage the scourge of infertility in the study area. The absence of a local regulatory agency or a national protocol leaves most practitioners having to borrow protocols and practices from other countries who have established guidelines. One of the thorny issues is the management of patients that have viral

infections, especially human immunodeficiency virus (HIV), Hepatitis B virus (HBV), and Hepatitis C virus (HCV). The misgivings are those of cross-contamination in the laboratory, vertical transmission to the resultant offspring and possible deleterious effect of pregnancy on the progress of the disease (which may lead to the offspring being orphaned early in life). HIV,^[1] HBV,^[2] and potentially,

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HCV^[3] infection have been described to have occurred during donor insemination. Laboratory cross-contamination of HCV between *in vitro* fertilization (IVF) patients has also been demonstrated.^[4] Some workers also demonstrated a decreased ovarian response during IVF/intracytoplasmic sperm injection (ICSI) cycles of HCV-seropositive patient.^[5] Carriers of chronic viral infections have therefore been viewed as a risk, which for many years has led to screening for these viruses and selection of candidates for gamete donation. However, with improved level of care through availability of highly active antiretroviral therapy (HAART), those infected with HIV are now able to seek procreation. Many countries' guidelines have evolved over the past decade and now it is generally recommended that samples from viral carriers be processed in a separate laboratory or designated space within the main laboratory, utilizing dedicated equipment, to minimize the risk of cross contamination, and that there are separate storage facilities, a different one for each infection.^[6,7] The Ethics Committee of the American Society for Reproductive Medicine^[8] has stated that fertility services cannot be withheld ethically from individuals with chronic viral infections, including HIV, if a center has the resources to provide care. Those centers that do not have the resources or facilities to provide care should facilitate referral to a center with protocols in place to manage such patients.^[5]

Assisted reproduction in Nigeria has largely been limited to relatively small, private, nonacademic centers. The practice had mostly been to desist from offering care to patients infected with these chronic viruses, because of the fear of cross-contamination, as separate storage facilities are not available. The magnitude of the problem has grown, however, as people living with HIV in Nigeria have begun to benefit from antiretroviral therapy, and are now able to pursue their desire for procreation. Standard of care for these individuals involve assisted reproductive techniques, to minimize risk of transmission or reinfection within the couple. This study aims to assess the burden of viral infections among couples that present for ART with a view to evaluating implications for their care.

Materials and Methods

This was a cross-sectional, descriptive study of 138 consenting couples who presented consecutively to a private fertility clinic in Nigeria for infertility evaluation and treatment over a 5-month period. They were all apparently healthy patients; none of them were on chronic medication. They were counseled and their consent was taken for investigations and management and for the use of their data for clinical audit and evaluation. Patients at this facility are informed that there will be no withdrawal of services or loss of benefits to them if they decline to have their data used for research purposes. Opt-out method of HIV screening was used.

As part of their routine evaluation, rapid screening for HIV was done in parallel with SD Bioline HIV 1/2 3.0 (Standard Diagnostics Inc., Kyonggi-do, Korea) and Determine HIV-1/2TM (Abbott Diagnostics, North Chicago, IL, USA). Hepatitis B surface antigen (HB_sAg) and Hepatitis C virus antigen were screened for with Diaspot DS-HB301 and DS-HC302 strips (Sam-Tech Diagnostics, Nairobi, Kenya), respectively. Samples with reactive results were sent out for confirmation with western blot for HIV and polymerase chain reaction for HCV, respectively. Samples that were positive for HB_sAg were tested for Hepatitis B envelope antigen (HB_eAg) and antibody (anti-HB_e).

The results for the men were compared with their seminal fluid analyses; which were performed according to standard World Health Organization (WHO) criteria.^[9]

Results

A total of 276 individuals (i.e., 138 men and women, respectively) were recruited into the study. Two women (1.4%) tested positive for HIV, and one (0.7%) for HCV [Table 1]. The most prevalent viral infection was HBV; with 11 men (8%) and 7 women (5.1%) testing positive. In all, 10 women (7.2%) and 15 (10.9%) men had a chronic viral infection. Infection with either HBV or HCV was reported as chronic hepatitis. Sero-discordance between the couples is also shown. One couple was sero-discordant for two infections; the husband tested positive for HBV infection, while the wife tested positive for HIV. Both partners of another couple tested positive for HIV (this male partner was the only male among the study subjects that was infected with HIV), while another couple had HBV infection. Table 2 shows the association between chronic hepatitis infection and sperm quality. Fourteen men had chronic hepatitis. There were no significant associations

Table 1: Chronic viral infection among study population

Infection	Men (N=138) No (%)	Women (N=138) No (%)	Sero-discordance no of couples (%)
HIV			
Positive	1 (0.7)	2 (1.4)	1 (0.7)
Negative	137 (99.3)	136 (98.6)	
HBV			
Positive	11 (8.0)	7 (5.1)	16 (11.6)
Negative	127 (92.0)	131 (94.9)	
HCV			
Positive	3 (2.2)	1 (0.7)	4 (2.9)
Negative	135 (17.8)	137 (99.3)	
Chronic hepatitis			
Positive	14 (10.1)	8 (5.8)	
Negative	124 (89.1)	130 (94.2)	

HIV=Human immunodeficiency virus, HBV=Hepatitis B virus, HCV=Hepatitis C virus

Table 2: Chronic hepatitis infection (HBV and HCV) and sperm quality

Sperm quality measure	Chronic hepatitis		χ^2	P value
	Positive (n=14) No (%)	Negative (n=124) No (%)		
Sperm count				
Azoospermia	2 (14.3)	10 (8.1)	0.743	0.863
Severe oligozoospermia	1 (7.1)	13 (10.5)		
Oligozoospermia	4 (28.6)	34 (27.4)		
Normozoospermia	7 (50.0)	67 (54.0)		
Mean progressive motility				
Azoospermia	2 (14.3)	10 (8.1)	1.51	0.680
Immotile	-	3 (2.4)		
Poor motility	-	9 (7.3)		
Fair motility	5 (35.7)	51 (41.1)		
Good motility	7 (50.0)	51 (41.1)		
Percent motility				
Azoospermia	2 (14.3)	10 (8.1)	1.40	0.706
Immotile and <30%	1 (7.1)	22 (17.7)		
>30% and <60%	6 (42.9)	63 (50.8)		
>60%	5 (35.7)	29 (23.4)		
White cell count/hpf				
0-2	11 (78.6)	76 (61.3)	1.612	0.204
>2	3 (21.4)	48 (38.7)		

HBV=Hepatitis B virus, HCV=Hepatitis C virus, HIV=Human immunodeficiency virus

with sperm count or motility or the presence of white blood cells in semen with chronic hepatitis.

Discussion

Nearly a fifth of the couples presenting to this clinic had at least one partner infected with a virus. This proportion is significant enough to demand attention. Hepatitis B was the most prevalent of the viral infections that were detected; this is what usually exists in the general population.^[10]

In this study, sperm parameters were not influenced by chronic viral infection, similar to findings by Garrido *et al.*^[11] One must keep in mind, however, that these subjects presented on account of infertility, and were being compared with other infertile couples. Other authors have assessed sperm parameters in voluntarily infertile couples (i.e., those consistently using barrier contraception to limit the risk of transmission of the virus), who now present for assisted reproduction as a safe option for procreation. Significantly higher rates of abnormal seminal parameters were found in these studies, when they were compared with fertile men who do not have these viral infections.^[12,13] This emphasizes further, the need for assisted reproduction in these couples and why they should not be denied care.

Apart from separate laboratory and storage facilities, basic principles in minimizing horizontal and vertical transmission would need to be followed: Antiretroviral therapy for HIV-positive partners to reduce the viral load to an almost undetectable level at which transmission is less likely; HBV vaccination in sero-discordant partners of HBV carriers (and immunoprophylaxis for the baby); and use of peginterferon-alpha and ribavirin in chronic HCV carriers to reduce the viral load before fertility treatment is commenced.^[6] Patients with HBV and HCV require a referral to a hepatologist for treatment and follow-up in view of the long-term risk of cirrhosis and liver failure. The cost of all this medication in the study environment is often prohibitive; but it is hoped that patients who can afford privately funded assisted conception may be able to afford the treatment for these viral infections. The most feasible therapy that could be ensured would be for HIV, as there are many dedicated governmental and nongovernmental facilities that provide HIV care, including HAART, at little or no cost to people living with HIV/AIDS. Clients attending the PEPFAR (the US President's Emergency Plan for AIDS Relief) clinic at our tertiary hospital, who desire to procreate, are optimized with administration of HAART (if eligible) and management of opportunistic infections, while their viral load is monitored. Artificial insemination is offered to sero-discordant couples with HIV-positive female partners. However, the management of concordant couples or discordant ones with an infected male is more challenging, as referral for further assisted reproduction is limited by lack of centers with facilities for managing clients with viral infections. Most patients end up having unprotected timed intercourse, which expectedly has its risks.^[14]

Consecutive recruitment, as was done, limits the study as it may be biased. Moreover, this was a cross-sectional study, and is therefore limited in being able to evaluate whether there were any differences in the fertility treatment outcome between couples infected with chronic viruses and those who were not infected. This may have further implications for management.

However, the findings do suggest that apparently healthy individuals may have medical disorders that may predispose them to serious health consequences in the future. One may conclude that providers of assisted conception would need to counsel and refer patients in whom routine screening reveals chronic illnesses and viral infections. Further research may be useful to identify the implications of these infections on infertility and its management.

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