



HIV and HBV Coinfections in the Highly HIV-infected Population of Rivers State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author IOO designed the study, performed the statistical analysis and wrote the protocol. Author TIC managed the analyses of the study. Authors TIC, IOO and NFP managed the literature searches and wrote the first draft of the manuscript. Author IOO and Author NFP supervised the whole study which, Author TIC used as part of her Ph.D. Thesis in the Department of Microbiology, University of Port Harcourt, Nigeria. All authors read and approved the final manuscript.

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ABSTRACT

Background: In Nigeria, hepatitis co-infection with HIV is linked with an increase in morbidity and mortality.

Objective: The goal of this study was to investigate the rate of HIV/HBV coinfection among the highly HIV-infected people in Rivers State, Nigeria.

Study Design: Cross-sectional study.

Place and Duration of Study: University of Port Harcourt Teaching Hospital (UPTH), in Rivers State, Nigeria, from February 2017 to September 2019.

Methods: A total of 226 HIV-positive people, 105 men and 121 women, were recruited for this study. ELISA was used to screen these participants for the presence of HIV and HBsAg, and this was done following the guidelines stipulated by the manufacturer. The demographic characteristics of the participants were obtained using a questionnaire designed for the study.

Results: Seven people tested positive for HIV/HBV, resulting in a 3.1 % overall prevalence. No significant association was found to exist between HIV/HBV coinfection and the characteristics of the study population.

Conclusion: A low seroprevalence was observed for HIV/HBV infection, in spite of Nigeria being endemic for HBV. Despite this low rate of HIV/HBV coinfection, routine screening for HBV markers should be carried out to reduce morbidity and mortality in this group.

Keywords: Antibodies, HIV, HBV infection, co-infections, Nigeria.

1. INTRODUCTION

Hepatitis B virus (HBV) and Human immunodeficiency virus (HIV) share similar modes of transmission which account for their co-occurrence in affected individuals. The co-infected individuals have been observed to have higher rates of mortality and morbidity when compared to their HIV negative counterparts [1]. This is due to the accelerated rate of HBV infection in such persons. HIV/HBV coinfection has also been observed to increase HBV replication and hinder the resolution of HBV infection [2]. Consequently, HIV/HBV co-infected individuals have accelerated progression of liver cirrhosis, hepatocellular carcinoma (HCC) and end-stage liver disease due to the hepatitis B virus which eventually result in death [3].

HBV infection ranks amongst the most common infections observed to occur in HIV patients and is said to affect 5–20% of the thirty-eight million people living with HIV worldwide [4,5]. Systematic review and meta-analysis by Barth *et al.* [6] revealed a 15% HIV/HBV co-infection prevalence in sub-Saharan Africa as opposed to 5–10 % prevalence in areas such as Europe, North America and Australia [7]. This is not surprising as sub-Saharan Africa alone accounts for more than 70% of the global burden of HIV infection [8].

In Nigeria, co-infection of hepatitis with HIV is linked with an increase in morbidity and mortality [9]. In the systematic review and meta-analysis of Hepatitis B/C and HIV co-infection conducted by Barth *et al.* [6], Nigeria also contributed more than two-fifth (40%) of the total population in sub-Saharan Africa. Information regarding the prevalence of this co-infection in Nigeria is therefore important for the assessment of its impact on the treatment progression, mortality of the affected populace and in the formulation of policies concerning its prevention and treatment in the country.

This study investigates the co-infection of HIV and HBV among individuals infected with HIV in Port Harcourt, Nigeria. The demographic characteristics of the patients such as age, sex

and marital status were also noted to screen for the existence of any pattern of distribution of the co-infection amongst the patients. This study conducted to investigate the current prevalence of HIV/HBV co-infections in the highly infected population of Rivers State, Nigeria, contributes to the growing information on the burden of HIV/HBV co-infection in the country.

2. MATERIALS AND METHODS

2.1 Study Area

This study was conducted among HIV positive individuals attending the Anti-Retroviral Clinic (ARV) of the University of Port Harcourt Teaching Hospital (UPTH). UPTH is a major tertiary-care teaching and research facility owned and managed by the Federal Government of Nigeria. It is located in the Alakahia community along East-West road, Obio-Akpo Local Government of Rivers State, Nigeria. Rivers State is in the south-south geopolitical zone of Nigeria and has 23 Local Government Areas. It is bordered on the south by the Atlantic Ocean, on the north by Imo, Abia, and Anambra States, on the east by Akwa-Ibom State, and on the west by Bayelsa and Delta States. According to 2006 census data, the state has a total population of about 5.19 million people with a 3.0% growth rate, making it the 6th most populous states in Nigeria. This is not surprising as it is economically significant as the centre of Nigeria's oil industry. Rivers State is home to many ethnic groups: Ikwerre, Igbo, Ijaw, Kalabari, Etche, Ogba, Ogoni and others. Rivers State with a HIV/AIDS prevalence of 3.8% ("Rivers State", n.d.), the third most prevalent in the country, is not exempt from the HIV/AIDS pandemic prevalent areas in Sub-Saharan Africa (Fig. 1).

2.2 Study Design

For this study, a cross-sectional survey design was used which sought to evaluate the dual seropositivity of HIV and HBV coinfection among HIV-infected individuals in University of Port Harcourt Teaching Hospital in Port Harcourt, Nigeria. Random sampling was used to select

consenting participants for the study from whom blood samples were collected. Descriptive statistics such as frequencies, percentages, tables and charts were used to represent data obtained.

2.3 Study Population

The study population constituted HIV seropositive individuals under clinical monitoring in the antiretroviral clinic in the University of Port Harcourt Teaching Hospital (UPTH) from February 2017 to September 2019. A total of two hundred and twenty-six (226) participants were selected and enrolled for the study (Table 1).

2.4 Inclusion and Exclusion Criteria

All consenting individuals aged 18 years and above with positive HIV diagnosis attending HIV clinic in UPTH were recruited for this study.

Patients who did not have their HIV status confirmed, who were seronegative and who did not give their consent were excluded from partaking in this study.

2.5 Sampling Technique

A sample size of 226 HIV positive individuals were chosen at random from the study population and enrolled into the study. The demographic information relevant to the study (age, gender and marital status) were retrieved from the hospital records. The information obtained were stratified as follows; the gender was classified as males (M) and females (F); the ages of the participants were grouped into six: <20 years, 20-29 years, 30-39 years, 40 – 49 years, 50 – 59 years and >59 years while the marital status of the patients was classified as married, single or widowed.

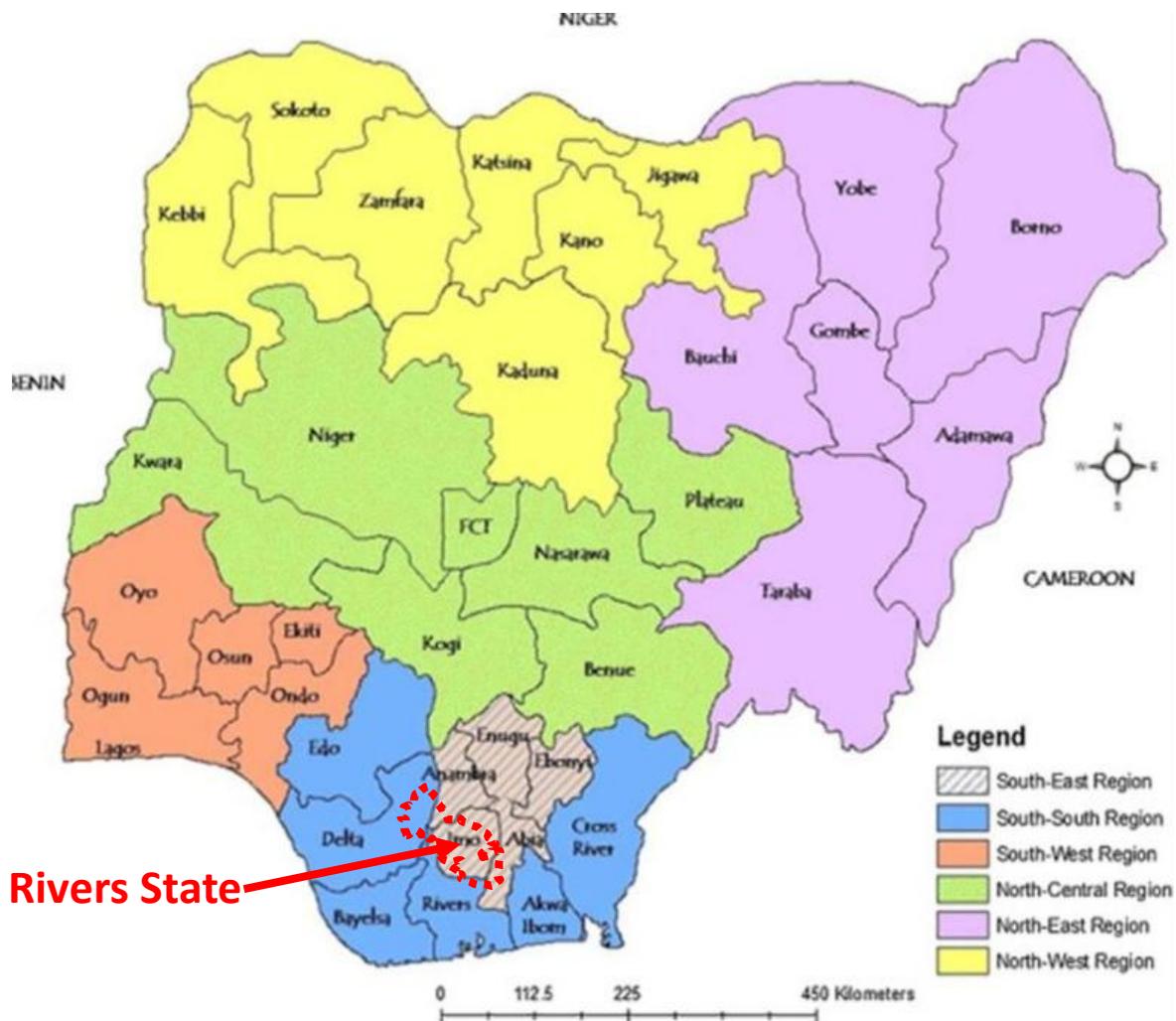


Fig. 1. Map of Nigeria showing Rivers State

2.6 Sample Collection, Preparation and Storage

Following written consents from the study participants, about 5ml of venous blood samples were aseptically collected from them and placed in sterile EDTA (ethylene diamine tetra acetic acid) tubes. The plasma was aspirated into sterile Eppendorf tubes after the blood had separated. To avoid misinterpretation of data, samples were explicitly designated with codes. Samples that were haemolyzed or clearly hyperlipemic were eliminated because they could produce erroneous results. Samples were then divided into two aliquots and stored at -20°C and -80°C .

2.7 Serological Analysis

2.7.1 HIV Ab and Ag assay

The HIV status of the participants in the study was reconfirmed by screening their plasma samples for the presence of HIV type 1, 2, and P24 HIV-1 antibodies, using commercially available Enzyme Linked Immunosorbent Assay (ELISA) manufactured by DIA.PRO Diagnostic Bioprobes Srl (Milano) – Italy.

2.7.2 HBsAg Assay

The ELISA kit produced by DIA.PRO Diagnostic Bioprobes, Milano – Italy, was used to test the samples for HBsAg. This was performed in the Virus Research Unit of the Department of Microbiology following the instructions laid down by the manufacturer.

2.8 Statistical Analysis of Data

Descriptive analysis was performed to summarize data obtained. Differences among groups were compared using Chi-square tests for categorical variables. P values <0.05 were considered statistically significant. Data analysis was done using IBM SPSS Statistics, version 22 (IBM Corp).

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Analysis of the study population

Characteristics of the study group are highlighted in Table 1. Many (53.5%, $n = 121$) of the participants of the study were females while 46.5% ($n = 105$) of the study population were males. The ratio of females to males was found to be 1.2:1. The ages of the study population ranged from 16 to 70 years with a median age of 42.5 years. A large number (30.5%, $n = 69$) of the participants were within the age group 40 – 49 years, followed by those within 30 – 39 years (26.1%, $n = 59$), 50 – 59 years (17.3%, $n = 39$) and >59 years (13.7%, $n = 31$) as seen in Table 4.1. Participants that were within younger age groups had less population; 20 – 29 years (9.7%, $n = 22$), with those that are <20 years having the least population (2.7%, $n = 6$). Many (49.1%, $n = 111$) of the study participants were found to be married. About 46.5% ($n = 105$) of them were single, while a few (4%, $n = 10$) were widowed.

Table 1. Demographic Characteristics of HIV-infected individuals

Variables	Number Tested	Percentage (%)
Age groups (Years)		
<20	6	2.7
20 – 29	22	9.7
30 – 39	59	26.1
40 – 49	69	30.5
50 - 59	39	17.3
>59	31	13.7
Sex		
Males	105	46.5
Females	121	53.5
Marital Status		
Married	111	49.1
Single	105	46.5
Widowed	10	4.4
Total	226	100

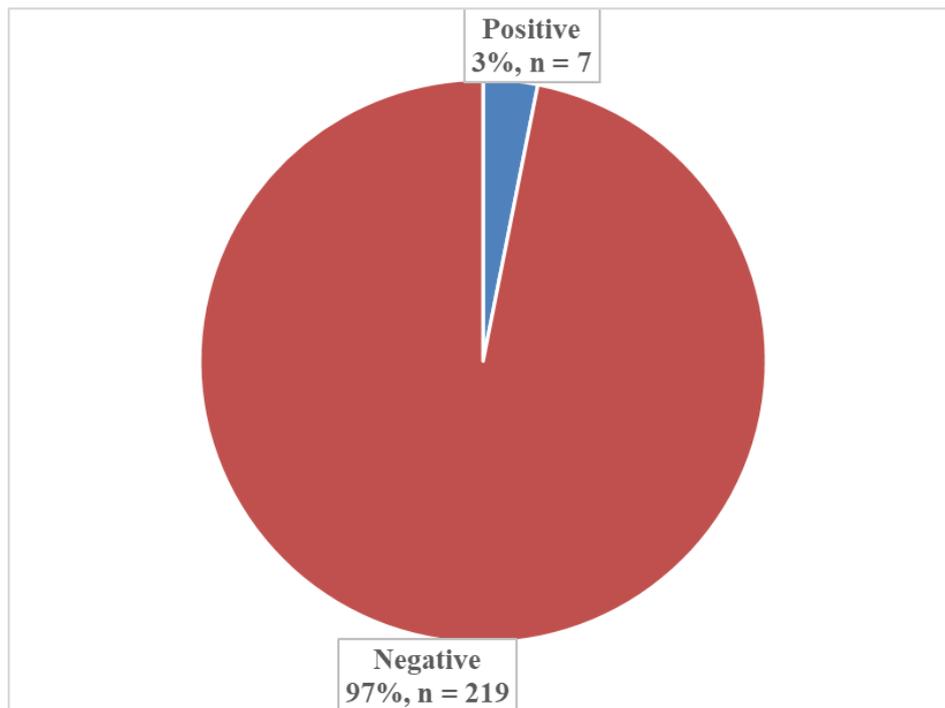


Fig. 2. Overall HIV/HBV Coinfection Rate

3.1.2 Overall seroprevalence of HBsAg in HIV-infected individuals in Port Harcourt

A total HIV seropositivity of 100% was obtained for all samples, reconfirming the HIV status of the study participants. Out of 226 samples assayed, seven were observed to be positive for HBsAg antibodies yielding an overall HBV seroprevalence rate of 3.1%.

In relation to age, seroprevalence of HBsAg was found to decrease with an increase in age; from 4.5% (n = 1) for those within 20 – 29 years, to 3.4% (n = 2) for those within 30 – 39 years, to 2.9% (n = 2) for those within 40 – 49 years, and to 0% for those within 50 – 59 years. However, this was apart from patients that were <20 years who had 0% seroprevalence and those that were >59 years who had the highest seroprevalence of 6.5%. No significant association was found to exist between HIV/HBV coinfection and the age groups of the study population ($\chi^2 = 2.78$, $p = 0.733$).

Female participants had a higher seroprevalence of 3.3% than 2.9% of male participants. No significant association was found to exist between HIV/HBV coinfection and the sex of the study population ($\chi^2 = 0.038$, $p = 0.85$). The highest seroprevalence (10%) was recorded for participants that were widowed while those that

were single and married had lower rates of 2.9% and 2.7% respectively. No significant association was found to exist between HIV/HBV coinfection and the marital status of the study population ($\chi^2 = 1.665$, $p = 0.43$).

3.2 DISCUSSION

HIV and HBV have been reported to be endemic in Nigeria over the years, as a significant burden of HIV/HBV coinfection are evident in many parts of the country. Presence of HBV in HIV patients have resulted in increased mortality rate among HIV patients undergoing HAART [10].

In establishing the presence of the coinfection of HIV/HBV, certain characteristics of the host (such as age, sex, marital status) were determined in this study to know whether an infection is successful. These characteristics were taken into consideration in this study.

The median age of the study population was found to be 42.5 years suggesting that many of the subjects were middle aged. It was observed that the proportion of the study population increased with increasing age groups, up to 40 – 49 years, after which it declined with an increase in the age group. The largest proportion (30.5%) of the study participants were within the age group, 40 – 49 years while the least was found within the youngest age group, <20 years (2.7%).

Table 2. Seroprevalence of Hepatitis B Surface Antigen (HBsAg) among HIV-positive individuals in relation to their demographic characteristics

Variables	Number Tested	HBsAg +ve	%HBsAg +ve	Chi-square test
Age groups (Years)				
<20	6	0	0	$\chi^2 = 2.78, p = 0.733$
20 – 29	22	1	4.5	
30 – 39	59	2	3.4	
40 – 49	69	2	2.9	
50 - 59	39	0	0	
>59	31	2	6.5	
Sex				
Males	105	3	2.9	$\chi^2 = 0.038, p = 0.85$
Females	121	4	3.3	
Marital Status				
Married	111	3	2.7	$\chi^2 = 1.6653, p = 0.43$
Single	105	3	2.9	
Widowed	10	1	10	
Total	226	7	3.1%	

Many (53.5%) of the participants of the study were females while 46.5% of the study population were males. This observation agrees with Okonko *et al.* [11] and Ekere *et al.* [12] who also found most HIV-infected subjects to be females. Females are at a higher risk for HIV infection in developing nations, particularly in Sub-Saharan Africa [11] as evidenced by the larger percentage of females found in this study. Also, based on the findings by the Nigeria HIV/AIDS indicator and impact survey (NAIIS), the National Agency for the control of AIDS in 2019 reported that more females (1.9%) than males (0.9%) were living with HIV/AIDS in Nigeria [13]. Many (49.1%) of the study participants were found to be married while about 46.5% of them were single and a few (4%) were widowed. This contrasts with studies by Tlou [14], Kposowa [15] and Shisana *et al.* [16] who revealed that widowed, divorced and single individuals are at higher risk of contracting HIV infection than their married counterparts.

Infections with HIV, HBV and HCV are among the most common chronic viral infections of global public health significance [17]. HIV has been reported to be associated with a higher prevalence of both Hepatitis B and C in Sub-Saharan Africa and these infections have a similar mode of transmission with HIV [10]. According to Balogun *et al.* [9] hepatitis co-infection with HIV is linked with an increase in morbidity and mortality in Nigeria. Most complications that occur in HIV patients can be traced to a co-infection with HBV [18]. The sort of treatment regimen to be followed is one of these problems, as HIV/HBV co-infected persons are

usually less receptive to HBV medications and have a higher risk of drug interactions [19,20]. The HBV infection is also accelerated, leading to liver-related morbidity and eventually death. It has been discovered that HIV/HBV co-infected patients are 17 times more likely than HBV mono-infected patients to die from liver-related problems [21].

This study revealed a 3.1% prevalence rate of HBsAg among HIV infected individuals which was the same rate observed in Brazil by [22]. According to Ott *et al.* [23], HBV endemicity can be categorized as low (<2%), low-intermediate (2%-4.9%), high-intermediate (5%-7.9%), and high ($\geq 8\%$). This suggests that Hepatitis B endemicity from this study is low-intermediate. This observation is similar to the 3.5% seropositivity to HBsAg observed by Omatola *et al.* [19] among HIV positive patients on anti-retroviral treatment programme in Anyigba, Kogi State, North-Central Nigeria [24]. However, the 3.1% seroprevalence from our study differs from the global prevalence of HIV-HBsAg co-infection reported by Platt *et al.* [25] to be 7.6% in people living with HIV, with sub-Saharan Africa bearing the greatest burden.

The HIV/HBV coinfection rate from this study is similar to some studies in Nigeria. Okonko *et al.* [11] reported 2% HBsAg prevalence among HIV Positive Fresh Undergraduate Students in Port Harcourt, Nigeria. Diwe *et al.* [26] also observed that HBsAg positive participants were 2.2% of HIV positive adult patients who presented newly at the HIV treatment unit of the tertiary hospital in Imo State, South-Eastern Nigeria, Kamenya *et al.* [27] reported 2.3% seroprevalence of hepatitis

B surface antigen among people living with HIV in Tanzania.

However, the coinfection rate observed in this study is lower than many studies reported in Nigeria. In Uyo, Innocent-Adiele *et. al.* [10] observed HBsAg positivity of 6.3% among HIV infected individuals while in Enugu, southeast Nigeria, Nnakenyi *et. al.* [28] recorded an HIV/HBV prevalence of 7.8% among HIV positive patients enrolled at the HIV outpatient clinic of the University of Nigeria Teaching Hospital. Also, HBsAg prevalence among HIV patients was observed to be 6.43% in Abuja, Nigeria's capital [29], 8.0% in Lokoja, Nigeria [30], 8.5% in Kaduna State [31] and 9.2% in Jos [32]. Elsewhere, 13.1% seroprevalence of hepatitis B virus among HIV infected patients was reported in Southern Taiwan [33], 21.7% prevalence of the hepatitis B surface antigen (HBsAg) was obtained in Sierra Leone [34] and 9.5% in Zambia [35]. The variations observed in studies on hepatitis prevalence in different geographic regions can be attributed to the characters of the population studied such as their lifestyle which can place them at the risk of contracting the viruses.

In relation to age, HBsAg was not detected in those less than 20 years. The seroprevalence however increased in the age group 20 – 29 years (4.5%) and decreased with increasing age groups (3.4% for those within 30 – 39 years, 2.9% for those within 40 – 49 years and 0% for those within 50 – 59 years) except in the oldest age group (those more than 59 years of age) where it was most prevalent with 6.5%. This finding corresponds to Katamba *et. al.* [35] who showed that one of the correlates of HIV and hepatitis B co-infections was age (between 20 and 39 years), Nnakenyi *et. al.* [28] who reported HBV coinfection prevailed most among young adults (21 to 30 years) and Omatola *et. al.* [30] who observed higher seropositivity rate in the age group, 40-49 years, followed by those 20-29 years of age. However, these studies differ from the present study that reported that those more than 59 years old had the highest prevalence of HBsAg. Furthermore, age was not found to be significantly associated with HBV coinfection at ($p > 0.05$). These age distributions have huge economic implications as they constitute the bulk of the nation's workforce, which could slow or reverse growth in the labour supply and worsen dependency ratio, as well as increase health expenditures for HIV-and liver-related illnesses reducing household incomes [35].

With respect to sex, female participants had a higher seroprevalence rates than men which agrees with Nnakenyi *et. al.* [28]. On the contrary, other studies reported that males were more likely to be coinfecting with HBV and HIV than females [26, 32]. Sex distribution is important in directing preventive strategies of antiviral prophylaxis among pregnant HIV patients such as administration of Tenofovir to prevent perinatal transmission and HBV vaccination at birth.

In comparison to the rest of the population, patients with no formal education, who were married and housewives, had greater rates of HBV infection [30] Higher seroprevalences was also obtained for those that were widowed (10%) and singles (2.9%). However, no significant difference was found to exist between the characteristics of the study participants and HBV infection. This finding agrees with the results gotten from other studies [10,11].

4. CONCLUSION

A low seroprevalence was observed for HIV/HBV infection, in spite of Nigeria being endemic for HBV. Despite the low rates of hepatitis coinfection observed in this study, education of the populace and routine screening for HBV markers in HIV positive individuals should be continually carried out to reduce hepatitis prevalence in the society and minimize morbidity and mortality in HIV/hepatitis co-infected patients.

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CONSENT

For the publication of this study, all authors assert that written informed consent was gotten from the patient (or other approved parties). A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the Research Ethics committees of University of Port Harcourt and that they have been carried out in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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