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SEROLOGICAL EVIDENCE OF HBV, HCV AND HEV INFECTION AMONG ART-NAÏVE HIV-1 INFECTED INDIVIDUALS IN A TERTIARY HEALTH FACILITY IN PORT HARCOURT, NIGERIA FROM 2016– 2017

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ABSTRACT

Aim: Coinfection of HBV with HIV is associated with significant morbidity and mortality globally. Despite increasing reports of HIV/HBV co-morbidities in Nigeria, little or no data exists on this subject among ART-naïve HIV-1 infected individuals in Port Harcourt, Rivers State, Nigeria. This, therefore, is the major driving force to evaluatethe serological evidence of HBV, HCV and HEV among ART-naïve HIV-1 infected individuals in Port Harcourt, Nigeria.

Methods: A sampling of 106 HIV-1 infected were randomly done. Sera samples were gotten from 106 consented ART-naïve HIV-1 individuals and were screened for HBsAg, anti-HCV antibody and HEV-IgG and IgM antobodies. PartecCyFlow® Counter was used to perform CD4 cell count while Abbott Real-Time HIV assay US Protocol was used to analyze the plasma viral load of the blood samples.

Results: From the study, 6.6% of HIV patients tested positive to HBsAg, none for HCV and none for HEV. Concerning their age, the highest serological evidence of HBV was seen in patients within the age of 36-45 years (10.3%). The females (7.8%) had a higher serological prevalence of HBV than males (7.1%). A higher rate of HBV occurred among widows/widowers (12.5%). With respect to their CD4 counts, those with ≥500 cell/µl had higher rate of HBV (12.1%). A higher rate of HBV occurred among HIV-1 patients with viral loads (VL) less than 40 copies/mL (57.1%).

Conclusion: The serological evidence generated may reflect the true burden of disease in the study area since only hospital-based cases were considered. Higher prevalence of HBV infection in patients with married status and those within the age range 36 to 45 years indicates that the means of transmission is through unprotected sex and therefore propel the need for health public enlightenment shedding lighter on their sexual lives. Lack of HCV and HEV reported here may be as result of Routine screening for HBV in the HIV-infected populations especiallyin developing countries is recommended.

Keywords: HBV, HCV, HEV, HIV, Serological Evidence, Nigeria

I. INTRODUCTION

Human immunodeficiency virus (HIV) has been one of the most important viral infections that have befallen man. The HBV, HCV and HIV are debilitating viruses that have similar epidemiological characteristics such as risk populations and routes of transmission. Consequently, individuals positive for HIV are more likely to be co-infected with either hepatitis B or hepatitis C viruses, or both.

For HIV and HCV co-infection (HIV/HCV), the rate of seroprevalence ranges from eight to thirty per cent among HIV-infected individuals.[1-5] For HIV and HBV co-infection (HIV/HBV), the seroprevalence rates ranging from 6.3% to 39.0% have been reported.[2,3,5-7] In Nigeria, a country with high prevalence of HBV and HIV, HBV co-infection have been reported in 10% to 70% of HIV-infected individuals.[7-12]For HEV, Hepatitis E virus (HEV)

infection is an importantpublic health problem.[13] It is a major publichealth concern in low-income countries, yetincidence and prevalence estimates are oftenlacking.[14]

These co-infections can have devastating consequences on the individual. Coinfection with HBV and/or HCV can affect the way HIV infection progresses, is managed and its eventual outcome.[5,15] The presence of hepatitis with HIV can accelerate the progression of HCV and HBV infections. It can increase the risk of antiretroviral drugs damaging the liver and the likelihood of an AIDS-defining illness commencing, compared with infection with HIV-1 alone.[16,19-20] Furthermore, HBV co-infection with HIV is linked with an increased morbidity and mortality.[17-18]Co-infection with HBV increases the risk for hepatotoxicity of HAART and likelihood of an AIDS-defining illness commencing, compared with infection with HIV-1 alone.[16,19-20] Another important issue is the interaction between HIV and HBV or HCV.[2,19] HCV and HBV infections also intensify the toxicity to antiretroviral medications.[2,19]

The occurrenceof HIV and HBV has attracted a lot of attention in recent times because their impact goes beyond the infected person to affect even national economies. Despite having different biological properties, they share common routes of transmission and risk factors, and only differ in how efficient certain types of exposures transmit them.[21] Sexual and vertical transmission is, however, the main routes of HIV and HBV transmission in human beings thereby bringing about the ease of coinfection especially in HIV and HBV endemic areas such as Nigeria which account for a very significant population of infected people in Sub-Saharan Africa.[22] The World Health Organization (WHO) however, recommends screening these viruses before antiretroviral therapy is initiated.[23]

This study therefore sought to determine the serological evidence of HBV, HCV and HEV among ART-naïve HIV-1infected individuals in Port Harcourt, Nigeria.

II. MATERIALS AND METHODS

2.1. Study Area

To have a sample representative of Rivers state, sampling was done in a hospital that provided health care services to an entire population of the state. This sampling location was the University of Port Harcourt Teaching Hospital (UPTH) in Port Harcourt, Rivers State, Nigeria.

2.2. Study Design

This study involved the serological analysis of HBV, HCV and HEV among ART-naïve HIV-1 infected individuals in Port Harcourt, Rivers State, Nigeria. The patients' data were obtained and demographically sectioned according to their age, gender, occupational and marital status using a questionnaire and this information was handled with the utmost discretion.

2.3. Study Population

The study population comprised of a segment of HIV patients who attended the University of Port Harcourt Teaching Hospital for medical aid. This, however, has an appreciable representative of ART-naïve HIV-1 infected individuals in Rivers State.Consecutive sampling of ART-naïve HIV-1 infected individuals was done in the healthcare facility mentioned above to total 106; this ensured sampling that was representative of the state. A sampling of 106 HIV-1 infected ART-naive were randomly done irrespective of age, gender and tribe from their registers in the hospital.

2.4. Ethical Considerations

This study was performed in compliance with regulations concerning human subject research as required by the University of Port Harcourt Research Ethics Committee (UPH/R&D/REC/04) and the University of Port Harcourt Teaching Hospital (UPTH) Research Ethics Committee (UPTH/ADM/90/S.II/VOL.X/628).

2.5. Sample Collection and Preparation

After obtaining written informed consents from the participants, blood samples (about 5ml) were aseptically collected during routine investigations so that the participants were not bled twice. The samples were collected into sterile EDTA bottles and plasma samples obtained by centrifugation. Samples were correctlylabelled and stored in two aliquots at -20°C and -80^{O}C before carrying out other laboratory procedures.

2.6. Serological Analysis

The serum samples were examined for HBsAg, HCV antibody and HEV-IgG and IgM using the ELISA kit (manufactured by DIA.PRO Diagnostic Bioprobes, Milano – Italy) and the ELISA tests were carried out according to the manufacturer's instructions.

2.7. CD4 T Cell CountEnumeration

PartecCyFlow® Counter (Partec GmbH, Munster, Germany) was used to obtain the CD4 T cell count on the EDTA-treated blood samples as specified by the manufacturer.

2.8. HIV-1 Viral Load Testing (Abbott Real-Time Assay)

Plasma viral load (PVL) was obtained using the Abbott Real-Time HIV assay US Protocol.

2.9. Data Analysis

All statistical analysis was performed using the SPSS v20.0 software. Results of the study were presented using descriptive statistics; and where appropriate, inferential statistics (CHI-squared test and t-test), was used to establish significant differences or associations between study variables. A p-value of 0.05 was used as an indicator of significance.

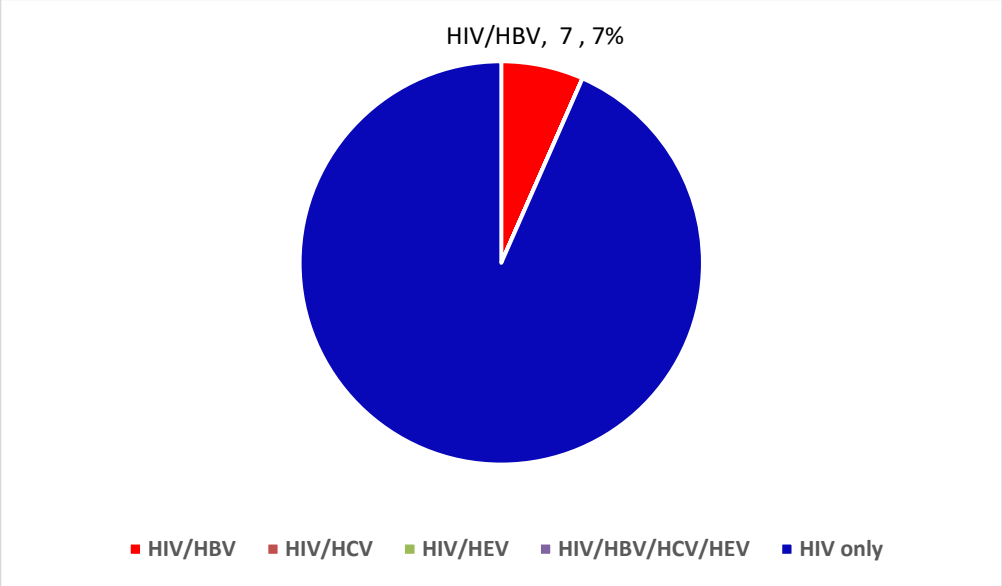
III. RESULT

3.1. Patient Characteristics

The age range of the 106 ART-naïve HIV-1 infected individuals who participated in the study was 18-70 years with a mean of 45.7 years. About 27.4% of them were in the 36-45 years age range (Table 1). The male: female ratio in the present study was 1: 0.92 (Table 1). Over 50.0% of the ART-naïve HIV-1 infected individuals were married (52.8%, n=56)(Table 1). The CD_4^+ (cells/µl) count of ART-naïve HIV-1 infected individuals used in this study ranged from 26 – 830 cells/µl (Table 2). The plasma viral load level ranged <40 – 1,429,707copies/mL (Table 2).

3.2. HIV Coinfection with Hepatitis Viruses

Serological evidence of HIVwith hepatitis viruses in this study was determined to be 6.6% for HBsAg, 0.0% for anti-HCV antibody and 0.0% for anti-HEV IgM antibody (Figure 1).



3.3. Age-specific Serological Evidence of HBV

A higher prevalence of HBV occurred among age groups 36-45 years (10.3%) than in other age groups. This was followed by ages 26–35 (9.1%) and 56-65 (8.3%) while other age groups had the least prevalence (0.0%).However, these differences were not statistically associated (P > 0.05) as shown in Table 1.

3.4. Sex-specific Serological Evidence of HBV

Higher serological evidence of HBVwas observed among females (7.8%) than in males (7.1%). The study showed no significant difference (P>0.05) between sex and HBV amongst ART-naïve HIV-1 infected individuals (Table 1).

3.5. Marital Status-specific Serological Evidence of HBV

A significant difference (P<0.05) exists between marital status and HBV amongst ART-naïve HIV-1 infected individuals. Higher serological evidence of HBV occurred among individuals who were widow/widower (12.5%) than in singles (7.1%) and married (5.4%) ART-naïve HIV-1 infected individuals (Table 1).

Table 1: Patient status and Serological Evidence of HBV characteristics

Variables	No. (%)	HIV/ HBV (%)
Age (years)		
16-25	3(2.8)	0(0.0)
26-35	22(20.8)	2(9.1)

36-45	29(27.4)	3(10.3)
46-55	26(24.5)	0(0.0)
56-65	24(22.6)	2(8.3)
66 and above	2(1.9)	0(0.0)
Sex		
Males	55(51.9)	3(7.1)
Females	51(48.1)	4(7.8)
Marital Status		
Single	42(39.6)	3(7.1)
Married	56(52.8)	3(5.4)
Widow/Widower	8(7.5)	1(12.5)
Total	**106(100.0)**	**7(6.6)**

3.7. Immunological and Virological Markers-specific seroprevalence

Higher serological evidence of HBV was observed among HIV-1 patients with CD_4^+ T cell count≥500 cells/µl (12.1%) and the least prevalence occurred in those with CD_4^+ T cell count<200 cells/µl. No HIV/HBV coinfection was found among those with a CD_4^+ T cell count 350-499 cells/µl (Table 2). Higher serological evidence of HBVwas observed among HIV-1 patients with viral loads (VL) less than 40 copies/mL and none was positive for HCV and HEV (Table 2).

Table 2: Serological Evidence of HBV in relation to immunological and Virological Markers

Markers	**No. (%)**	**HIV/ HBV (%)**
CD4 counts (cells/µl)		
Less than 200	15(14.2)	1(6.7)
200-349	24(22.6)	2(8.3)
350-499	34(32.1)	0(0.0)
500 and above	33(31.1)	4(12.1)
Viral load (copies/mL)		
Less than 40	7(6.6)	4(57.1)
40 – 500	7(6.6)	1(14.3)
>500 - 10000	46(43.4)	2(4.3)
>10000 -1,429,707	46 (43.4)	0(0.0)
Target not detected	0(0.0)	0(0.0)
Target detected but <40copies/ml	7(6.6)	4(57.1)
Target detected and quantifiable	47(44.3)	2(3.8)
Total	**106(100.0)**	**7(6.6)**

IV. DISCUSSION

Regardless widespread evidence that suggests increasing prevalence of HBV/HIV and HCV/HIV co-infection, there is still a dearth of information regarding frequency of infections in ART-naïve HIV-1 infected individuals in Rivers State, Nigeria. This study sought to obtain the frequency of serologic evidence of HBV infection among a cohort of ART drug naïve HIV-1 infected individuals and to observe associated risk factors with the presence of markers for these viruses. In this study, the serological evidence of HBV, HCV and HEV amongst ART-naïve HIV-1 infected individuals was 6.6%, 0.0% and 0.0%, respectively.

The 0.0% reported for both HCV and HEV were not out of place as previous studies have reported same in Port Harcourt, Nigeria[24-26], except for Aaron et al. which reported 1.0% for HCV in their study.[24]

This 6.6% observed for HBV is lower by half of the findings of Alo et al.[27] who had a general prevalence of 12.2% from 965 patients in Sokoto. This finding disagrees with the findings of Kathryn et al.[28] who reported 10% prevalence in Africa. It is also differing from the findings of Otegbayo et al.[29] who reported (11.9%) in Ibadan, Lesi, et al.[30] with 9.2% and Oyesile-Balogun[31] who also reported (31.9%) in Lagos State respectively because more people have become enlightened properly about the virus. Elsewhere in the HIV clinic in the National Hospital of Tropical Diseases (NHTD), Vũ Huy et al.had a general prevalence of 8.4%[32] while Mustapha and Jibrin analyzed 200 HIV patients in Gombe State, obtaining a 26.5% prevalence.[33] The fact that all of these findings are relatively higher depicts that HIV and HBV coinfection is endemic in Nigeria.

This 6.6% reported in this study for HBsAg is far lower than the 30.6% value reported by Ojo et al. and Ogwu-Richard et al.[3,5] It is also lower than the 25.0% reported by Uneke et al. among HIV-infected patients in Jos, Nigeria.[6]It is lower than the 28.4% reported among HIV positive donors in Ikeja, Nigeria.[17] Some previous reports of HIV/HBV coinfection of 15.0% in Maiduguri[34], 20.6% in Keffi[20], 28.7% in Jos[35], 30.4% in Ilorin[36], 70.5% in Kano[10], 33.8% in India[37], 9.2% in Lagos[30], 9.7% in Niger Delta[8], and 8.7% in Thailand[38] are, however, higher than observed 6.6% reported in this study. However, 6.6% reported in this study is more than the 1.4% in Osogbo[39]. Differences in size of samples, and sensitivity and specificity of test kits may be responsible for the differences in prevalence figures in this group of patients[15]. The differences in prevalence in these studies could be attributed to differences in patient selection[3,5] infection rate in this study is comparable to the 6.6% in Nasarawa[40], the 6.0% reported in South Africa[15] and the values reported in the HIV seronegative population, which indicates an endemic infection by the HBV the Nigerian population.[3,5,41,42]In comparison with prior studies performed in Nigeria, this figure reported among the cohort is less than 15.5% reported in Benin City[15], 11.9% reported in Ibadan[2], 20.6% documented in North Central Nigeria[20], 25.9% in Jos[6], and 28.4% in Lagos.[17]It is higher than 2.7% in Ado Ekiti.[43] But figures as high as 51.9% and 70.5% have equally been documented in Lagos[9] and Kano[10], respectively, both being the most populated and highly commercially active cities in Nigeria. Our finding is also lower than the 17.3% reported in Tanzania.[44]

The result in the age range difference of HBVserological evidence in this study hada total of 106 samples was between 18-70 years with a mean of 45.7. HBV/HIV serological evidence was found most prevalent within individuals who fell within the 36-45 age group with (10.3%) seroprevalence while no prevalence was found within those in the age range of 18-25, 46-55 and 66-70 respectively. This corresponds with the reported findings of Adewole et al. who reported then that, the prevalence was more in patients below the age of 45 years in Abuja[45] and also the findings of Ekanem et al. who recorded the highest prevalence of 19% within 40-49 years patients in Uyo.[46]However, this study is in disagreement with the study of Forbi and other researchers who had more prevalence of 44.0% within the age of 51-60 in Jos.[47]Ojide et al. also reported 0.0% prevalence of HBV in patients >60 years.[15] Opaleye et al. also reported no age-related (p>0.05) HIV/HBV coinfection in their study, although, age group 21-35 years had slightly higher HIV/HBV coinfections rate (1.8%) than age group 36-50 years with 1.6% HIV/HBV coinfections rate.[39]Ojide et al. reported that age-specific prevalence of HBV coinfection from their study was higher in the younger patients (<20-50 years) than their older counterpart (51 to>60 years).[15] This may be becauseyounger patients are more likely exposed to risky behaviours than the older ones.[15]

The present study showed no significant difference (P>0.05) between sex and HBVserological evidence amongst ART-naïve HIV-1 infected individuals. Higher serological evidence of HBV was observed among females (7.8%) than in males (7.1%). This agrees favourably with that of Opaleye et al. who also reported that females (2.3%) were more affected than males (0.0%).[39] However, this present finding deviated from previous studies which reported that male HIV-infected patients were affected more by HBV and females by HCV.[15]The dissimilar finding was reported in Lagos, Nigeria[9] and Tanzania.[44] Balogun et al. in their study reported that the prevalence of HBV/HIV co-infection was found to be higher among male study subjects (37.5%) than females (24.3%).[17]This finding contradictsthe findings of Ekanem et al. who reported 55.2% in males and 44.8% in females in the University of Uyo Teaching Hospital, Nigeria.[46] Similarly, the study disagrees with the results of Forbi et al. who reported 56.8% in male against 43.32% in females who were coinfected in Nasarawa State.[20] The findings in this study concurs with the findings of Adewole et al. who reported 2.5% in male and 7.5% in females who were coinfected in FCT Abuja.[45]This present finding differs from previous reports from Jos, North Central Nigeria[17,35] and India.[17,37] This observation could possibly be due to women being more likely to have multiple sex partners and also practice unprotected sex in a polygamous setting. There are, however, conflicting reports regarding male or female predominance for co-infection with either of these viruses (HBV, HCV and HEV).[20,30,48] The reason for this is not obvious, but may be due to the epidemiological differences in the different study populations and variations in methodology.[15]

The result of marital status in serological evidence in this study reveals that over 50.0% of the ART-naïve HIV-1 infected individuals were married (52.8%) and 3 persons (5.4%) of them also tested positive to HBV, while 42 (39.6%) were single with 3 (7.1%) patients infected with HBV; while 7.5% of the total 106 individuals were either widows, widowers or divorcees and just 1 (12.5%) among them had HBV. This totally agrees with Vũ Huy et al.[32] who analyzed 724 patients with the married having the highest occurrence with 75%, followed by those who were never married (13.5%) and the lowest being the widows and divorced with 1.5% prevalence; but it disagrees with the work of Olayinka et al.[49] who out of 965 patients tested, the singles came highest with 19.6%, then the married (12.7%), widows (8.3%), divorced/separated (7.1%) while those grouped into others came lowest with 5.0% prevalence. This could be as a result of the fact that marriage is a major risk factors in sexually transmitted diseases together with other factors such as sexual intercourse when menstruating, genital ulcer and some other pelvic

inflammatory diseases (PID)[50].A significant difference (P<0.05) exists between marital status and HBV/HIV coinfections amongst ART drug naïve HIV-1 infected individuals. Higher seropositivity of HIV and HBV co-infection was observed among individuals who are widow/widower (12.5%) than in singles (7.1%) and married (5.4%) HIV-1 infected individuals. In a study by Opaleye et al.,only widows/widowers (33.3%) had the highest HIV/HBV dual infection rates.[39]

Higher serological evidence of HBV was observed among ART-naïve HIV-1 patients with CD_4^+ T cell count 500 cells/µl and above (12.1%). No HIV/HBV coinfection was found among those with CD_4^+ T cell count 350-499 cells/µl. The result is a study by Oladipo et al. suggests that patients whose CD4 count range between 100-350 cells/ mm^3 are at risk of HEV infection.[51,52] Also, patients with CD4+ cell count ≤200 cell/µl had a higher HBsAg seroprevalence of 18.4% compared to 12.5% recorded for those with CD4+ cell count >200 cell/µl in a similar study by Ojide et al.[15] Regarding clinical stage and CD4+ cell count, the prevalence of both HIV/HBV and HIV/HCV was higher in stages 3-4 and CD4+ <200 cell/µl, respectively, than observed in stages 1-2 and CD4+ ≥200 cell/µl. These higher prevalence rates observed in these groups are, however, not statistically significant. This is similar to findings from other studies.[53,54]

Higher serological evidence of HBV was observed among ART-naïve HIV-1 patients with viral loads (VL) less than 40 copies/mL.Co-infection with HBV and HCV among HIV/AIDS patients is still a problem in our environment.[15]In order to detect these viruses early among HIV/AIDS patients and ensure they are properly managed; it is necessary to screen for these viruses regularly.[15]Although coinfection with HBV from this study is high. This is understandably so since this viruson its own is not only endemic in our environment but also share similar routes of transmission with HIV. Similar to previous studies, this study confirms that HIV and HBV coinfection is endemic in our environment and therefore highlights the need to strengthen efforts to get HIV infected individuals routinely screened as suggested by expert guidelines developed in United State and Europe.[55] Such guidelines, if adopted, will lead to early detection of cases of co-infection, proper adjustment of management strategies and better outcome.[15]

V. CONCLUSION

The seroprevalence in the current study may reflect the true burden of disease in the study area (Port Harcourt, Rivers State) since only hospital-based cases were considered. From the studies, high serological evidence of HBV infection in married ART-naïve HIV-1 infected individuals and those that fall within the age range of 36 to 45 years indicates that the means of transmission is through unprotected sex and therefore propel the need for health public enlightenment shedding lighter on their sexual lives. Also, results from the present study may not apply to the entire country, as there were some differences with some published studies from other parts of Nigeria. Notwithstanding, this study adds to the baseline serological evidence data on HBV/HIV co-morbidity for future studies.

IV. RECOMMENDATIONS

The high serological evidence of HBV among ART-naïve HIV-1 infected individuals promote the calls for screening for HBV before commencing ART and the inclusion of agent(s) more dually effective against HIV and HBV in the ART nucleoside backbone. It is therefore recommended that all patients infected with HIV be screened for HBV and possible co-infections upon enrollment into care and before highly active antiretroviral therapy (HAART) is initiated to obtain a better drug combination to each individual. Individuals who are HIV/HBV coinfected should always be informed about routes of transmission and methods to prevent further spread of the viruses. HIV-infected individuals who tested negative for HBV should receive HBV vaccination in order to prevent future infection. Also, efforts designed to grow the coverage and completeness of HBV vaccination via the consolidation of the Nigerian Expanded Program on Immunization cannot be overstated. Moreover, longitudinal study on the impact of HIV and HBV co-infection on HIV and HBV viral replication, hepatotoxicity over time and immune recovery is needed and also recommended.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Author IOO conceived and designed the study, conducted research, provided research materials, and collected and organized data. TIC, BJO, CCA, HCIA and MTB managed the laboratory analyses, analyzed and interpreted data. *Author* IOO and *Author* TIC wrote initial and final draft of article, and provided logistic support. Author IOO managed the literature searches and wrote the first draft of the manuscript. *Author IOOsupervised the whole study which, Author MTB used as part of her B.Sc. Project in the Department of Microbiology, University of Port Harcourt, Nigeria.* All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this study. 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 have, therefore, been performed following the ethical standards laid down in the 1964 Declaration of Helsinki.

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