



## A Tale of Two Viruses: Seroepidemiological and a Cross-Sectional Insights into HIV/HBV Coinfection in Selected Hospitals in Rivers State, Nigeria

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### ABSTRACT

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**Background:** Hepatitis B virus (HBV), a circular DNA virus with humans serving as the only reservoir, remains a worldwide public health problem. The similarity in transmission routes for HBV and HIV makes co-infection very common. Thus, this study aimed at unveiling the seroepidemiological patterns of HBV coinfections among HIV-infected individuals in some selected hospitals in Rivers State, Nigeria.

**Materials and methods:** A cross-sectional study was conducted on 350 HIV-infected individuals attending ART clinics at selected hospitals in Rivers State, Nigeria. Sociodemographic data were collected based on interviewer-based questionnaires, and clinical history was obtained from participants' medical records. Serological analysis for HBsAg was done using the ELISA method.

**Results:** Of the 350 HIV-infected patients, 9(2.6%) were positive for HBsAg. The majority of HIV/HBV coinfecting participants were in age groups  $\geq 41$  (3.7%), females (2.9%), singles (3.0%), tertiary education holders (3.5%), and business owners (1.1%). Furthermore, immunological and virological markers analysis revealed that HBV seropositivity is more common with patients having a CD4 count of 350-499 cells/mm<sup>3</sup> (6.2%) and viral loads as a target not detected (TND) with 5.4%.

**Conclusion:** This study observed an HIV/HBV coinfection rate of 2.6% which has further confirmed the persistence of HIV/HBV co-infection in Rivers State, Nigeria. Ongoing and persistent public health interventions among the study population are thereby advocated.

### KEYWORDS:

Antibodies, Coinfection, HCV, HIV, Rivers State, Nigeria

### INTRODUCTION

One of the frequent complications in HIV-infected patients is dual infection with HBV and coinfection with hepatitis B is common among HIV-infected individuals (Okonko et al., 2022). Hepatitis B and HIV infections are significant public health problems in sub-Saharan Africa, and research suggests that co-infected individuals with either HBV or HIV experience a higher rate of HIV progression (Ugwu et al., 2023a). HBV and HIV infections are major global health problems in Sub-Saharan Africa (Im et al., 2022; Okonko &

Shaibu, 2023), with over 2% of the population infected with HIV and at least 8% infected with hepatitis B (Matthews et al., 2014; Ihongbe et al., 2022).

HBV infection is a significant global public health issue (Cookey et al., 2022; Okonko et al., 2023a). Globally, it is estimated that 5%–10% of people living with HIV are co-infected with hepatitis B virus (HBV), while HIV/HBV frequency in sub-Saharan Africa varied from 0.0% to 28.4% (Stabinski et al., 2015; Cyrille et al., 2019; Adesegun et al., 2020; Oti et al., 2021; Ihongbe et al., 2022). The global prevalence of hepatitis B virus (HBV) infection among people infected with human immunodeficiency virus (HIV) is 7.4%, according to the World Health Organization (2019), and about 1% of people infected with HBV (2.7 million people) are also infected with HIV (Rai et al., 2007; Ihongbe et al., 2022). A fifth of the current global population is

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estimated to be seropositive for HBsAg (Sharma et al., 2005; Akindigh et al., 2019).

Nigeria has one of the highest chronic viral hepatitis disease burdens in the world (Cookey et al., 2022; Okonko et al., 2023a). The prevalence of HIV/HBV co-infection in Nigeria is reported to range between 10% and 70 % (Omatola et al., 2019; Ugwu et al., 2023b). As of 2013, an estimated 13.6% of the Nigerian population had been reported to be chronic carriers of HBsAg (Musa et al., 2015; Akindigh et al., 2019). Consequently, the burden of disease is considered to be high, as evidenced by the high incidence of morbidity and mortality associated with the virus (Lok, 2005; Akindigh et al., 2019).

Co-infection with HIV and HBV viruses causes complex interactions (Ihongbe et al., 2022). Coinfection of HBV with HIV is associated with significant morbidity and mortality globally (Okonko et al., 2023b). HBV infection poses hazards to antiretroviral therapy (ART)-related liver damage, limits CD4 recovery, accelerates immunologic progression, and increases morbidity and mortality in HIV-infected patients (Wandeler et al., 2013; Ihongbe et al., 2022). Although co-infection with HBV has been linked to higher HIV RNA turnover, increased liver morbidity, and complex HIV pathology, it is not typically considered in the therapy of HIV infection (Wandeler et al., 2013; Ihongbe et al., 2022). Thus, this study aimed at unveiling the seroepidemiological patterns of HBV coinfections among HIV-infected individuals in some selected hospitals in Rivers State, Nigeria.

## MATERIALS AND METHODS

### Study Area

The study was carried out in selected areas of Rivers State in Nigeria, in an urban setting with a population of 7,034,973.

### Study population

The study population included male and female individuals living with HIV that attend ART clinics at the Rivers State University Teaching Hospital, Military Hospital and Modern Primary Health Care Center, Rumuji. Three hundred and fifty (350) HIV-infected individuals were selected and participated in the study. Individuals included in the study were males and females confirmed and documented as being positive for HIV infection that are on ART. While individuals who decline and HIV negatives were not included in the study. A random sampling irrespective of age, gender and ethnicity was done to ensure that sampling was representative of Rivers State, Nigeria. Socio-demographic data such as age, sex, marital status, education and occupation and clinical data for every participant were obtained using a questionnaire.

### Sample Collection and Preparation

Blood samples (about 5ml) were aseptically collected from the participants during routine investigations, after obtaining written informed consent from the participants. The samples were collected into sterile EDTA bottles and plasma samples were obtained after centrifugation. Samples were appropriately labelled and stored in two aliquots at -20°C and -80°C until analysis.

### Serological Analysis of Hepatitis B Surface Antigen (HBsAg)

Serum samples were analyzed for HBsAg using the ELISA kit (DIA.PRO Diagnostic Bioprobes, Italy). The tests were performed according to the manufacturer's instructions.

### Data analysis

Data were systematically analyzed as appropriate. The chi-Square test was done using SPSS (Statistical Package for Social Sciences) software.

## RESULTS

Table 1 shows the HIV/HBV coinfection rates relating to their sociodemographic characteristics, immunological and virological markers. Of the 350 HIV-infected patients, 9(2.6%) were positive for HBsAg. The majority of HIV/HBV coinfecting participants were in age groups  $\geq 41$  (3.7%), females (2.9%), singles (3.0%), tertiary education holders (3.5%), and business owners (1.1%) as shown in Table 1. Furthermore, immunological and virological markers analysis revealed that HBV seropositivity is more common with patients having a CD4 count of 350-499 cells/mm<sup>3</sup> (6.2%) and viral loads as a target not detected (TND) with 5.4% as shown in Table 1.

**Table 1: HIV/HBV Coinfection relating to their sociodemographic characteristics, immunological and virological markers**

Variables	Number tested	HBV +ve	%HBV +ve	Chi-square test
<b>Age (years)</b>				
$\leq 20$	35	0	0.0	
21 -40	206	5	2.4	
$\geq 41$	109	4	3.7	
<b>Sex</b>				
Males	147	3	2.0	
Females	203	6	2.9	
<b>Marital Status</b>				
Married	227	3	2.0	
singles	123	6	3.0	

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<b>Educational Status</b>			
Primary	54	0	0.0
Secondary	190	6	3.2
Tertiary	86	3	3.5
None	20	0	0.0
<b>Occupations</b>			
Student	48	2	0.6
Business owner	191	4	1.1
Working class	145	3	0.9
<b>CD4 (Cells/mm<sup>3</sup>)</b>			
<200-349	162	3	1.9
350-499	65	4	6.2
>500 above	123	2	1.6
<b>Viral load (Copies/ml)</b>			
TND	111	6	5.4
<40	79	1	1.3
40-1000	73	1	1.4
>1000	92	1	1.1
<b>TOTAL</b>	<b>350</b>	<b>9</b>	<b>2.6</b>

### DISCUSSION

This study aimed at unveiling the seroepidemiological patterns of HBV coinfections among HIV-infected individuals in some selected hospitals in Rivers State, Nigeria. We observed a serological prevalence of 2.6% among these HIV-infected individuals. This observed result is much lower than the 14.0% reported from Rivers State, Nigeria in 2022 (Okonko et al., 2022) and 6.6% from another of our studies earlier on in Rivers State, Nigeria (Okonko et al., 2023b). The reported value here is much lower than the 17.7% reported from Awka, Anambra State, Nigeria (Ugwu et al., 2023a) and 40.9% in Onitsha, Anambra State, Nigeria (Ugwu et al., 2023b). Our observed 2.6% is also lower than the 14.7% reported in Gombe State, Nigeria (Precious et al., 2022), 10.87% reported in Japan (Demarchi et al., 2022), 10.5% in Ethiopia (Gedefie et al., 2023), the 9.2% in Jos, Plateau State, Nigeria (Akindigh et al., 2019), the 9.20% in Gambia (Bittaye et al., 2019), the 8.8% in Addis Ababa (Seyoum et al., 2022), the 8.6% in Ethiopia (Goa et al., 2019), the 7.8% in Southeast, Nigeria (Nnakenyi et al., 2020), the 7.6% in Southeast Nigeria (Oditia et al., 2023), the 6.7% in Port Harcourt, Nigeria (Okonko et al., 2015), the 6.3% in Uyo, Akwa Ibom State, Nigeria (Innocent-Adiele et al., 2021), the 6.1% in Tanzania (Nyalika, 2021), the 6.0% in the northern Nigerian communities (Adesegun et al., 2020), the 5.5% in Keffi, Central Nigeria (Oti et al., 2021), the 4.83% in Douala, Cameroon (Cyrille et al., 2019), the 4.0% in Banik et al.

(2022), the 3.62% in Nepal (Bhattarai et al., 2018), the 3.6% in Ogun State (Ihongbe et al., 2022), the 3.5% in Anyigba, Kogi State, Nigeria (Omatola et al., 2019).

This 2.6% prevalence of HBV reported here is much lower than the WHO's threshold for high-endemic areas (WHO, 2010; Okonko et al., 2022). Nigeria is ranked as one of the countries that are hyper-endemic for HBV infection (> 8%) (Ajuwon et al., 2021; WHO, 2021; Okonko et al., 2022). However, the 2.6% we reported here is comparable to the findings of other similar studies in Nigeria and overseas. It tallies with the global prevalence of HIV/HBV co-infection, which varies from 1.13% to 59.0% (Lawal et al., 2020; Ugwu et al., 2023b). The 2.6% reported here is similar to the 2.0% reported from Yenagoa, Bayelsa State, Nigeria (Okonko & Shaibu, 2023), the 2.0% and 2.1% in Port Harcourt, respectively (Okonko et al., 2020; Aaron et al., 2021), the 2.1% in Lagos, Nigeria (Odukoya et al., 2022), the 3.1% reported previously in Port Harcourt, Rivers State, Nigeria (Cookey et al., 2021) and the 2.5% from Ibadan, Nigeria (Okonko et al., 2012). It is higher than the 1.0% reported in our previous study from Warri, Delta State, Nigeria (Okonko et al., 2023a). These reports which show differences in regional prevalence may point to different epidemiological factors at work in different parts of the country and reveal a gap in our current understanding of the epidemiology of HIV/HBV co-infection. Moreover, this is probably the reason why there are variations in HIV prevalence and the frequency of HIV co-infection with HBV/HCV (Oluremi et al., 2021; Tassachew et al., 2022). National surveillance systems to provide a full picture of the co-infection landscape are urgently needed to identify epidemiological trends over time to make sure suitable prevention measures are deployed (Akindigh et al., 2019).

Among these HIV/HBV co-infected patients, the prevalence was higher among age groups  $\geq 41$ . This observation supports that of Bhattarai et al. (2018), Akindigh et al. (2019), Cyrille et al. (2019), Gedefie et al. (2023), Okonko and Shaibu (2023) and Okonko et al. (2022, 2023b), who also reported a higher prevalence within the age group 41 and above. However, the observation in this study deviated from that of another previous study in Nigeria and overseas (Adesegun et al., 2020; Mutisya et al., 2021; Oti et al., 2021; Ihongbe et al., 2022; Cookey et al., 2022; Oditia et al., 2023; Okonko et al., 2023a; Ugwu et al., 2023a, b), where a higher prevalence occurred among age group  $\leq 41$  years.

Among these HIV/HBV coinfecting participants, the prevalence of HIV/HBV co-infection was also higher among the females (2.9%) than their male counterparts (2.0%), which corresponds with other previous studies in Nigeria (Adesegun et al., 2020; Nnakenyi et al., 2020; Cookey et al., 2022; Okonko et al., 2022; Precious et al., 2022; Gedefie et

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al., 2023; Okonko & Shaibu, 2023; Okonko et al., 2023a, b, Ugwu et al., 2023a) where a higher prevalence was reported among females than males. However, this observation also contradicted the work by Bhattarai et al. (2018) and Ugwu et al. (2023b), where the co-infection was higher in males.

In terms of marital status, HIV/HBV coinfecting singles had the highest prevalence. This observation contradicted previous studies in Nigeria and abroad (Adesegun et al., 2020; Oti et al., 2021; Okonko et al., 2022, 2023a; Okonko & Shaibu, 2023; Ugwu et al., 2023a) who reported the highest prevalence in the married participants and some among the separated/divorced or widowed. However, the findings of this study on marital status-specific coinfection correspond with other previous reports in Nigeria and overseas (Bhattarai et al., 2018; Cooney et al., 2022; Ihongbe et al., 2022; Okonko et al., 2023b; Ugwu et al., 2023b).

HIV/HBV coinfection in relation to their educational profiles indicated that those with tertiary education backgrounds were more in proportion. This finding contrasted other similar studies (Bhattarai et al., 2018; Adesegun et al., 2020; Oti et al., 2021; Okonko et al., 2022; Ugwu et al., 2023a,b) reported in Nigeria. However, this observation supports other previous studies (Ihongbe et al., 2022; Okonko & Shaibu, 2023) in Nigeria.

HIV/HBV coinfection in relation to their occupational categories indicated that business owners constituted a higher HIV/HBV coinfection rate (1.1%), closely followed by the working class (0.9%) compared to students (0.6%). This observation corresponds to Okonko et al. (2022) in a previous study in Port Harcourt, Nigeria where self-employed dominated. This observation, however, deviates from the findings of other similar and previous studies (Adesegun et al., 2020; Oti et al., 2021; Okonko & Shaibu, 2023; Okonko et al., 2023a; Ugwu et al., 2023a, b), where higher coinfection rates were reported mostly in students, civil servants in some cases, among others.

Additionally, in terms of CD4 status, a higher HIV/HBV coinfection rate was observed in patients with a CD4 count of 350-499 cells/mm<sup>3</sup>. Similar observations were made in previous studies in Nigeria and overseas (Opaleye et al., 2014). Although, other studies reported higher rates in patients with <200 cells/mm<sup>3</sup> (Ojide et al., 2015; Boateng et al., 2019; Nnakenyi et al., 2020; Okonko et al., 2020; Innocent-Adiele et al., 2021; Okonko & Shaibu, 2023; Ugwu et al., 2023a), 200-350 cells/μl (Ugwu et al., 2023b) while Okonko et al. (2023b) reported higher coinfection rates among participants with CD4 counts 500 & above. This finding may not correspond with the proposition that coinfection deteriorates the immune status leading to poorer

outcomes (Nnakenyi et al., 2020). This study may also observe a reverse from the claims that individuals with a CD4 cell count of less than 200 cells/mm<sup>3</sup> have a 16.2 times higher risk of liver-related deaths than those with a CD4 count of greater than 350 cells/mm<sup>3</sup> (Falade-Nwulia et al., 2012; Boateng et al., 2019; Nnakenyi et al., 2020).

Furthermore, the viral loads of the HIV/HBV coinfecting participants did not follow any definite patterns. A higher co-infection rate occurred among coinfecting patients with targets not detected (5.4%) which was followed by those with 40-1000 copies/ml (1.4%). This finding is comparable to that of other studies (Okonko et al., 2023b; Ugwu et al., 2023a). However, this assertion is at variance with some studies in Nigeria (Okonko et al., 2020; Innocent-Adiele et al., 2021; Precious et al., 2022; Okonko & Shaibu, 2023; Ugwu et al., 2023b).

### CONCLUSION

This study observed an HIV/HBV coinfection rate of 2.6% which has further confirmed the persistence of HIV/HBV co-infection in Rivers State, Nigeria. Ongoing and persistent public health interventions among the study population are thereby advocated.

### Conflict of interest

None declared.

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