



## DUAL POSITIVITY OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND HEPATITIS B VIRUS (HBV) IN THE HIGHLY INFECTED POPULATION OF RIVERS STATE, NIGERIA

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**Background:** One of the frequent complications in HIV-infected patients is dual infection with HBV. Screening for HBV in such a high-risk population becomes pertinent to develop and establishing effective and timely therapeutic plans. The study aimed at determining the prevalence of HIV/HBV dual infections in the highly infected population of Rivers State and the association between HIV/HBV dual infection and the socio-demographic factors among these populations. **Methods:** One hundred eighty-two HIV-infected patients attending the Retroviral Clinic of the University of Port Harcourt Teaching Hospital (UPTH), Rivers State, Nigeria, were recruited for this study. Five millilitres of blood samples were collected, and the resultant sera were analyzed for HBsAg using the ELISA kits manufactured by DIA. Serological analysis was performed according to the manufacturer's instructions. Variables tested include sex, age group and marital status. **PRO** Diagnostic Bioprobes, Milano, Italy. **Results:** Of the 94 patients investigated, 13(14.0%) were seropositive for HIV/HBV dual infections, while 81 (86.0%) had HIV only. Of the dual infection of HIV/HBV, 15.3% were females than males (11.4%). At the same time, higher HIV mono-infection occurred in males (88.6%) than females (84.7%). The age-related dual infection rate was observed, as the dual infection rate decrease with age increase. A higher HIV/HBV dual infection rate in the age group 31-40 years (15.2%) compared to other age groups. For HIV only, higher prevalence occurred in ages 51 years and above (90.0%). A higher dual infection rate occurred in the married group (15.7%) than in the singles (11.6%). However, the reverse was observed for HIV only, with the highest prevalence among the singles (88.4%). Patients with secondary levels of education had a higher dual infection rate (18.9%) compared to tertiary (12.5%) and primary education (9.1%). Those with no formal education had a zero prevalence for HIV/HBV dual infection and the highest prevalence (100.0%) for HIV only. Concerning occupation, a higher HIV/HBV dual infection rate occurred among the self-employed group (16.7%) than the employed (11.4%) and the unemployed groups (9.1%). However, the reverse was observed for HIV only, with the highest prevalence among the unemployed groups (90.9%). Furthermore, no significant associations ( $p>0.05$ ) existed between sex, age, marital status, educational background and occupational status of the patients, and dual infections of HIV and HBV. **Conclusion:** Our study showed that dual positivity of HBV and HIV is common in Rivers State, Nigeria. The findings of this study provide critical data to assess the impact of current prevention and control strategies in Nigeria.

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**Keywords:** Dual positivity, HIV, HBV, Nigeria

### INTRODUCTION

Hepatitis B virus (HBV) is a Hepadnavirus that infects liver cells and is responsible for an estimated 820,000 deaths in 2019; for example, from the subsequent development of hepatocellular carcinomas (HCC) (WHO, 2021; Ajuwon et al., 2021). An estimated 3.6% of the global population is affected by chronic HBV infection (GBDCN, 2010; GBDMCDC, 2013; Ajuwon et al., 2021). The Hepatitis B virus (HBV) is an infectious disease of global significance, causing a significant health burden in Africa due to complications associated with infection, such as cirrhosis and liver cancer (Ajuwon et al., 2021).

Dual infection with hepatitis B is common among HIV-infected individuals. There is a heavy burden of HIV-HBV and HIV- HCV dual infections in many regions of the developing world, Nigeria inclusive (Balogun et al., 2012). Available data suggest that 15-60% of the average population in many African countries may be seropositive for one or more of the serological markers of the hepatitis B virus. This region's high prevalence of HBV infection is thought to be due to horizontal transmission during childhood. Individuals coinfecting with HIV and HBV are more likely to develop chronic hepatitis B and are at increased risk for liver-related mortality (Balogun et al., 2012).

Early epidemiological studies have suggested a high variation in the estimates of HBV prevalence between countries and subgroups of the population in SSA (Ajuwon et al., 2021). These variations are often explained by methodological differences (Jacobs et al., 1997; Belo, 2000; Ajuwon et al., 2021).

In Africa, approximately 60 million people live with chronic HBV infection, with an estimated prevalence of 6.2% (WHO, 2019; Ajuwon et al., 2021). New infection rates are highest among children, and transmission predominantly occurs via perinatal routes (Ajuwon et al., 2021). The global prevalence of chronic HBV infection among children under five declined from 5% in the pre-vaccine era (the 1980s to early 2000s) to less than 1% in 2019 (Indolfi et al., 2019; WHO, 2021; Ajuwon et al., 2021). However, more than two decades after vaccine introduction, which has been criticized for reducing infections in children, the overall population prevalence of HBV infection remains high across many settings in SSA (> 8%) (Schweitzer et al., 2015; Ott et al., 2017; Ajuwon et al., 2021).

In Africa, Nigeria is ranked as one of the countries that are hyper-endemic for HBV infection (> 8%) (Kramvis & Kew, 2007; WHO, 2021; Ajuwon et al., 2021). Approximately nine in ten Nigerians who live with chronic HBV are unaware of their infection status and are missing from the global public health statistics due to a lack of resources, awareness, and political will to address Nigeria's HBV plight (FMoH, 2016; WHA, 2018; Hepatitis Foundation, 2020; Ajuwon et al., 2021). Consequently, Nigeria has one of the highest rates of HBV-attributable cancer in West Africa, with an age-standardized incidence estimate of 2.6 to < 5.1 cases per 100,000 person-years (IARC, 2018; de Martel et al., 2020; Ajuwon et al., 2021).

In Nigeria, which is considered a high prevalence country, estimates of HBV cases are inconsistent; therefore, additional clarity is required to manage HBV-associated public health challenges (Ajuwon et al., 2021). Thus, the study aimed to determine the prevalence of HIV/HBV dual infections among HIV-positive patients at the University of Port Harcourt Teaching Hospital (UPTH) Port Harcourt; and the association between HIV/HBV dual infection and the socio-demographic factors among these patients.

## MATERIAL AND METHODS

### 2.1. Study Population

The target population was 91 confirmed HIV-infected patients attending the ART clinic for their routine check-ups at the University of Port Harcourt teaching hospital (UPTH) within the study period.

### 2.2 Study Area

The study was conducted in the ART clinic of the University of Port Harcourt teaching hospital (UPTH), Port Harcourt, Nigeria.

### 2.3 Sample Collection

About 5ml blood sample was aseptically collected by venipuncture from each participant into anticoagulant EDTA bottles. The blood samples were left to clot, after which the plasma was then pipetted into sterile Eppendorf tubes and stored at -20°C until ready for use.

### 2.6 Serological Analysis of HBsAg

PRO Diagnostic Bioprobes, Milano – Italy. Serum samples were analyzed for HBsAg using the ELISA kit manufactured by DIA. ELISA tests were performed according to the manufacturer's instructions. The test results were calculated using the cut-off value determined on the mean OD450nm value of the negative control (NC) with the following formula:  $NC + 0.050 = \text{Cut-Off (Co)}$ . Test results are interpreted as the ratio of the sample OD450nm (S) and the Cut-Off value (Co), mathematically  $S/Co$ , accordingly: <0.9 as negative, 0.9-1.1 as equivocal and >1.1 as positive.

## 3. RESULTS

### 3.1. Analysis of the Total Study Population

The total number of patients included in this study was 94. The socio-demographic data for these patients were stratified and shown in Table 1. The age groups; 31 – 40 years constituted the largest population making up 71.9% (n= 46). This was followed by 21 – 30 (24.5%), 41-50 (14.9%) whereas  $\geq 51$  (10.6%). Based on gender, females have the highest proportions (62.8%) while males have 37.2%. Married patients predominated the study constituting 54.3% (n= 51) over the singles with 45.7% (n= 43). Based on educational background, 40 (42.6%) of the patients have attained the tertiary level of education. This result was closely followed by those with secondary education (39.4%, n= 37), primary level of education (11.7%) and non-formal education (6.4%). However, a close range was observed in the occupational status, with the self-employed group (51.1%) predominating the study. This was followed by the employed (37.2%) and the unemployed (11.7%) groups.

### 3.2. Overall Dual infection rate

Of the 94 patients investigated, 13(14.0%) patients were found to be seropositive for HIV/HBV dual infections, while 81 (86.0%) had HIV only (Table 1).

### 3.3. HIV/HBV Dual infection among patients concerning age

A higher HIV/HBV dual infection rate occurred in the age group 31-40 years (15.2%) compared to other age

groups. However, for HIV only, higher prevalence occurred in ages 51 years and above (90.0%).

### 3.4. HIV/HBV Dual infections among patients concerning sex

Based on sex, a higher dual infection rate occurred in females (15.3%) than the males (11.4%). While higher HIV mono-infection occurred in males (88.6%) than females (84.7%), as presented in Table 1.

**Table 1: HIV/HBV Dual infections with socio-demographic characteristics of the patients**

Variables	Groups	No. Tested (%)	HIV only		HIV/HBV Dual infection		Chi-Square Analysis
			No. Positive	%	No. Positive	%	
Age groups	21-30	23(24.5)	19	86.9	3	13.1	$X^2 = 0.208$ , df = 3, p = 0.98
	31-40	46(71.9)	35	84.7	7	15.2	
	41-50	14(14.9)	11	85.7	2	14.3	
	51 & above	10(10.6)	13	90.0	1	10.0	
Sex	Females	59(62.8)	50	84.7	9	15.3	$X^2 = 0.270$ , df = 1, p = 0.60
	Males	35(37.2)	31	88.6	4	11.4	
Marital status	Married	51(54.3)	43	84.3	8	15.7	$X^2 = 0.322$ , df = 1, p = 0.57
	Singles	43(45.7)	38	88.4	5	11.6	
Education	Primary	11(11.7)	10	90.9	1	9.1	$X^2 = 2.03$ , df = 3, p = 0.57
	Secondary	37(39.4)	29	81.1	7	18.9	
	Tertiary	40(42.6)	35	87.5	5	12.5	
	None	6(6.4)	6	100.0	0	0.0	
Occupation	Employed	35(37.2)	32	88.6	4	11.4	$X^2 = 0.701$ , df = 2, p = 0.70
	Self-Employed	48(51.1)	35	83.3	8	16.7	
	Unemployed	11(11.7)	10	90.9	1	9.1	
<b>Total</b>		<b>94 (100.0)</b>	<b>81</b>	<b>86.0</b>	<b>13</b>	<b>14.0</b>	

### 3.5. HIV/HBV dual infection among patients concerning marital status

Of the 94 patients investigated and stratified into two groups based on marital status, a higher dual infection rate occurred in the married group (15.7%) than in the singles (11.6%). However, the reverse was observed for HIV only (Table 1), with the highest prevalence among the singles (88.4%).

### 3.6. HIV/HBV dual infection among patients concerning educational background

Of the 94 patients tested, patients with secondary levels of education had a higher dual infection rate (18.9%) compared to tertiary (12.5%) and primary education (9.1%). Those with no formal education had a zero prevalence for HIV/HBV dual infection and the highest prevalence (100.0%) for HIV only (Table 1).

### 3.7. HIV/HBV dual infection among patients concerning occupation

Of the 94 patients examined and stratified into three groups based on occupation, a higher HIV/HBV dual infection rate occurred among the self-employed group (16.7%) than the employed (11.4%) and the unemployed groups (9.1%). However, the reverse was observed for HIV only, with the highest prevalence among the unemployed groups (90.9%). This is presented in Table 1.

## 4. DISCUSSION

Dual infections of HIV with HBV affect change number of patients worldwide (Nelson, 2002). Hepatitis B virus infection is associated with significant morbidity and mortality in patients with HIV infection (Piliero & Faragon, 2002; Thio et al., 2002). Although very few dual infections studies have been conducted in Africa since sub-Saharan Africa is home to about 29.4 million HIV-infected people, high HIV/HBV dual infections are expected. However, the

results are contradictory. It could also result from a higher frequency of exposure to risk factors associated with the virus, such as sharing a needle and other instruments used in manicures and pedicures, having unprotected sex, and occupational behaviour (Lesi et al., 2007). This study aimed to determine the prevalence of HIV/HBV dual infections among HIV-positive patients at the University of Port Harcourt Teaching Hospital (UPTH) Port Harcourt and the association between HIV/HBV dual infection and the socio-demographic factors among these patients.

From the result recorded in this study, the prevalence of HIV- HBV dual infections among HIV-positive patients in Port Harcourt, Rivers State, Nigeria, is 14.0%. This prevalence is higher than the WHO's threshold for high-endemic areas. This 14.0% value reported in this study is lower than the 25.0% reported by Uneke et al. (2005) among HIV-infected patients in Jos, Plateau State, Nigeria. However, the value is higher than reported in previous Nigeria studies. It is higher than the 6.7% reported by Okonko et al. (2015) in Port Harcourt and the 3.1% by Cookey et al. (2021) in Port Harcourt. Opaleye et al. (2010) reported a prevalence rate of 5.4% in Osun State, Nigeria. It is also higher than the 3.6% by Ihongbe et al. (2022) in Ogun State, Nigeria and is inconsistent with the 3.6% reported in Borno State, Nigeria by Bello et al. (2011). It also in disagrees with the 3.5% reported by Omatola et al. (2019) in Kogi state, Nigeria. It is also dissimilar to the 3.6% reported by Smit et al. (2004) in the Netherlands, 3.2% by Rai et al. (2004) in Japan, 3% by Lodenyio et al. (2000) in Johannesburg, and 3.7% by de Almeida et al. (2006) in Brazil. Lower prevalence was earlier reported among HIV-positive patients, 2.7% in Nigeria (Mbaawuaga et al., 2014), 1.2% in Tanzania (Telatela et al., 2007), 1.13% in Mali (Touunkara et al., 2009), 1.8%, and 2.6% in Iran (Moradi et al., 2011). Okonko et al. (2012) also reported 2.5% HBV/HIV coinfection among apparently healthy children in Ibadan, Nigeria. The differences in prevalence in these studies could be attributed to differences in patient selection and probably geographical locations.

HBV prevalence among patients with HIV was estimated to be 9.9% and 7.7% among HIV-positive pregnant women (Ajuwon et al., 2021), although this rate is lower than the 14.0% reported in our study. The value reported here is higher than the 12.5% reported in a study by Hamza et al. (2013) and the 11.5% prevalence obtained from a health facility in North central Nigeria (Tremeau-Bravard et al., 2012). Additionally, this study revealed a higher prevalence than the 7.0% reported among HIV-positive pregnant women (Ajuwon et al., 2021). These results suggest that the burden of HBV and HIV dual infection is significant in the Nigerian population. This may lead

to higher levels of detectable virus (Gilson et al., 1997), accelerated cirrhosis (Salmon-Ceron et al., 2005) and an increased likelihood of developing HCC (Clifford et al., 2008) in the already immune-compromised sub-population (Ajuwon et al., 2021).

Of the 94 patients investigated, 14.0% were seropositive for HIV/HBV dual infections, while 86.0% had HIV only. Dual infections with HBV increase the risk for hepatotoxicity of HAART and the likelihood of onset of an AIDS-defining illness compared with infection with HIV-1 alone (Greub, 2000; Feld et al., 2005; Forbi et al., 2007). However, HIV dual infections with HBV have been recognized worldwide in individuals exposed to blood-borne. In Nigeria, a country where HBV and HIV prevalence is high, HBV coinfection occurs in 10% to 70% of HIV-infected individuals (Ejele et al., 2004; Iwalokun et al., 2006; Nwokedi et al., 2006; Otegbayo et al., 2008; Idoko et al., 2009).

This study's dual infection rate (14.0%) was lower than the 30.6% value reported by Ojo et al. (2013). It is also lower than the 28.4% reported among HIV-positive donors in Ikeja, Nigeria (Balogun et al., 2012). This study's experimental HIV/HBV dual infections (14.0%) are comparable with previously reported figures in different parts of Nigeria and outside. Some previous reports of HIV/HBV dual infections of 12.1% in HIV-positive pregnant women in Jos, North Central Nigeria (Okoye et al., 2015), 7.7% in Nigerian children (Sadoh et al., 2011), 10.0% in children in Enugu, South-East Nigeria (Davidson et al., 2016), 7.8% in HIV-positive children in Benue State, North Central (Anigilaje et al., 2013), 28.4% among HIV-positive in South West Nigeria (Balogun et al., 2010), 4.20% in HIV-positive pregnant women in South West Nigeria (Ezechi et al., 2014), 4.67% among in Port Harcourt, South-South, Nigeria (Frank-Peterside et al., 2016), 10.3% in Abuja, North Central Nigeria (Ifeorah et al., 2017), 9.8% in Aba, South East (Ngwogu et al., 2016) and 1.0% in Anyigba, Kogi State, Nigeria (Omotola et al., 2019).

A dual infection rate of 14.0% was reported in patients ages 21- 67. Higher HIV/HBV dual infection rate occurred in age group 31-40 years (15.2%) compared to other age groups, 21-30 (13.1%), 41-50 (14.3%) and  $\geq 50$  (10.0%). This aligns slightly with the findings of previous studies in Nigeria. The higher dual infections rate reported among the age group 31-40 is consistent with previous studies in Ogun State, Nigeria (Ihongbe et al., 2022), Uyo, Akwa-Ibom State, Nigeria (Innocent-Adiele et al., 2021), in Abuja, Nigeria (Ogundeji, 2018), in North-West Ethiopia (Hou et al., 2005), and Cameroon (Ymele et al., 2012). This is in concurrence with previous reports by Tessema et al. (2010), Baba et al. (2000) and Ejele et al. (2005), in which higher prevalence was observed



among youths. This finding corresponds to Katamba et al. (2020), who showed that one of the correlates of HIV/HBV dual infections was age (between 20 and 39 years), and Nnakenyi et al. (2020), who reported HIV/HBV dual infections prevailed most among young adults (21 to 30 years). This may be associated with higher sexual activities within this age group, especially those within adolescent age. Ymele et al. (2012) reported that HBV infection prevalence decreased with age. Ogundeji (2018) reported that the age group of 21-40 years had the predominant HIV, HBV, and HCV prevalence in their study. Okoye et al. (2015) reported 12.1% of HIV-positive pregnant women ages 21-50 years in Jos, North Central Nigeria. Balogun et al. (2010) reported 28.4% of HIV positive > 18 years in South West, Nigeria. Ezechi et al. (2014) reported that 4.20% of HIV-positive pregnant women aged 14-44 in South West Nigeria. Frank-Peterside et al. (2016) reported 4.67% of HIV-positive > 20 years in Port Harcourt. Ifeorah et al. (2017) reported 10.3% of HIV-positive aged 1.4-67 years in Abuja, North Central, Nigeria. Ngwogu et al. (2016) reported 9.8% of HIV-positive in Aba, South East, and Omotola et al. (2019) reported 1.0% in HIV-positive ages  $\geq 15$  years in Anyigba, Kogi State, Nigeria. The present finding deviated from that of Cookey et al. (2021), who reported higher HIV/HBV dual infections among age group >59 and Omatola et al. (2020), who observed higher HIV/HBV dual infections in the ages (40-49 years). This observation deviated from other previous studies in Nigeria. Sadoh et al. (2011) reported 7.7% in Nigerian children, 2 months-17 years. Davidson et al. (2016) reported 10.0% in children 18 months – 15 years in Enugu, South-East Nigeria. Anigilaje et al. (2013) reported 7.8% of HIV-positive children, 8 months-15 years, in Benue State.

Based on sex, a higher dual infection rate occurred in females (15.3%) than in males (11.4%). In contrast, higher HIV mono-infection occurred in males (88.6%) than females (84.7%). Females predominated in this study because more females reported to the hospital for medical attention than males. It also points out that gender might be an essential epidemiological determinant of HIV/HBV dual infection among patients. This observation aligns with Cookey et al. (2021), Okonko et al. (2020), Nnakenyi et al. (2020) and Ekere et al. (2020), who also reported that most HIV-infected participants were females. On the contrary, other studies reported that males were more likely to be dually infected with HBV and HIV than females (Diwe et al., 2013; Akindigh et al., 2019). Balogun et al. (2012) also reported higher dual infections among males than females.

Of the 94 patients investigated and stratified into two groups based on marital status, married

patients predominated the study constituting 54.3% (n= 51) over the singles with 45.7% (n= 43). This observation aligned with Cookey et al. (2021). A higher dual infection rate occurred in the married group (15.7%) than in the singles (11.6%) in this study; this result deviated from a similar study by Innocent-Adiele et al. (2021) and Ihongbe et al. (2022). It also disagrees with Sirisena et al. (2002), Isa et al. (2014), Olayinka et al. (2016) Demarchi et al. (2022), who reported a higher prevalence among singles than the married. The positivity of HIV/HBV dual infections among the married groups in this study could indicate that the infection might be through unprotected heterosexual intercourse or close contact with their infected partners, as the virus can spread through body fluids (Innocent-Adiele et al., 2021). Ezegebudo et al. (2004) report that significant infection rates from HIV, HBV, and HIV-HBV coinfection were associated with marital status. The lack of association between marital status and HIV/HBV dual infections may imply that marital status is not a risk factor for HBV infection. However, marital status is an indicator to consider the sexual partner as a risk for infection since unmarried people may have many sexual partners or have unprotected sex. However, the reverse was observed for HIV only, with the highest prevalence among the singles (88.4%). This observation aligns with that of Tlou (2019), Kposowa (2013) and Shisana et al. (2004). They revealed that widowed, divorced and single individuals are at higher risk of contracting HIV infection than their married counterparts.

Of the 94 patients tested, patients with secondary levels of education had a higher dual infection rate (18.9%) compared to tertiary (12.5%) and primary education (9.1%). This finding aligns with a similar study by Ihongbe et al. (2022). They reported that HBV infection was independent of the educational level of the study subject, with secondary and tertiary education having the highest occurrence (1.8%). This observation disagrees with a similar study by Innocent-Adiele et al. (2021). They reported a higher prevalence among those with prior educational status was observed (8.3%) compared to another educational statuses: tertiary (6.9%) and secondary (4.9%); but in agreement with a study by Katamba et al. (2020) who reported that correlates of HIV and HBV dual infections were primary education (shallow level of education). Compared to the rest of the population, patients with no formal education had more excellent rates of HIV mono-infection. This observation disagrees with Omotola et al. (2020) who reported higher HBV prevalence in patients without formal education.

Of the 94 patients examined and stratified into three groups based on occupation, a higher HIV/HBV dual infection rate occurred among the self-employed

group (16.7%) than the employed (11.4%) and the unemployed groups (9.1%). However, the reverse was observed for HIV only, with the highest prevalence among the unemployed groups (90.9%). Compared to the rest of the population, homemakers (unemployed) patients had higher rates of HIV mono-infection. This result also disagrees with Omotola et al. (2020), who reported higher HBV prevalence in patients who were housewives.

However, no significant difference existed between the characteristics of these patients and HIV/HBV dual infections. This finding agrees with the results obtained from other studies (Okonko et al., 2020; Ekere et al., 2020). This observation disagrees with Innocent-Adiele et al. (2021). They reported an education-specific association with HIV-HBV coinfections in Uyo, Nigeria. Our analysis shows that HIV/HBV dual infections rate (14.0%) is high, as per the World Health Organisation's criteria for HBV endemicity ( $\geq 8\%$ ; high, 2–7%; moderate and  $< 2\%$ ; low) (Ott et al., 2012; Ajuwon et al., 2021). The findings of this study provide critical data to assess the impact of current prevention and control strategies in Nigeria (Ajuwon et al., 2021). This finding will serve as a reference for designing and implementing effective public health management programmes toward the 2030 elimination goal (Ajuwon et al., 2021). The dynamics and epidemiology of HBV infection are distinct in HIV patients, and continuing to target these individuals with the implementation of HBV screening remains very pertinent (Ajuwon et al., 2021).

## 5. CONCLUSION

This study confirms that the HIV/HBV dual infections rate in Port Harcourt, Rivers State, Nigeria is high. This study's results have highlighted that HBV/HIV dual infections are common in Port Harcourt, Nigeria. The primary way of eliminating HBV in individuals, especially HIV-infected individuals, involves intensive HBsAg screening among individuals attending antiretroviral clinics to enable early detection and treatment.

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