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Triple Infections of HBV, *Plasmodium falciparum* and *Helicobacter pylori* among people living with HIV presenting at a tertiary Hospital in Bayelsa State, Nigeria

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Abstract: Background: The study determined the prevalence of triple infections of HBV, *Plasmodium falciparum* and *Helicobacter pylori* amongst people living with HIV presenting at a tertiary hospital in Bayelsa, Nigeria. **Method:** Two hundred (200) people living with HIV-1 were enrolled in the study. ELISA technique was used to screen for HBsAg while rapid diagnostic tests were used for *Plasmodium falciparum* and *Helicobacter pylori*. **Results:** Triple infections of HBV/PF/HP were 0.5%. Higher HBV/PF/HP triple infection rates occurred only among PLWH who were females (0.7%), within the age group 31-50 (0.8%), single marital group (1.2%), non-formal educational background (1.4%), unemployed occupational group (1.0%), CD4 counts of >350 cells/µl (0.8%), and viral loads of 40-1000 copies/ml (0.7%). **Conclusion:** The study has demonstrated that among HIV-1 positive individuals presenting at a teaching hospital in Bayelsa, Nigeria, triple infections with the hepatitis B virus, *Plasmodium falciparum*, and *Helicobacter pylori* are common. This calls for concerted efforts in the management of people living with HIV-1 in Bayelsa, Nigeria.

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1. Introduction

HIV/AIDS is still a global pandemic and is still spreading throughout the world (Okonko et al., 2020a). As a catastrophe of social and medical significance, HIV comes with dire consequences (Onoja et al., 2012). The percentage of the general population living with HIV is known as the HIV prevalence (UNAIDS, 2018; Nkuize et al., 2023). The UNAIDS model (UNAIDS, 2019; Nkuize et al., 2023) previously described the methodology for determining

HIV prevalence. In summary, existing epidemiological data for nations where HIV transmission is epidemic in the general population come from nationally representative communitybased surveys and pregnant women attending prenatal clinics (Nkuize et al., 2023). In individuals living with

HIV who have compromised immune systems, opportunistic infections (OIs) are more common and severe, and co-infection also poses a significant additional difficulty as it influences the rate at which the illness advances to AIDS (Okonko et al., 2020a). Major public health issues are infections with HBV, HCV, and HIV (Okonko et al., 2012a,b). It is anticipated that millions of people in sub-Saharan Africa have hepatitis B and/or C viruses, as both are endemic there (Okonko et al., 2015). Hepatitis B is one

of the main viral hepatitis cases that has been reported as a worldwide public health concern (Okonko & Udeze, 2011; Sule et al., 2010, 2011; Okonko et al., 2012c,d,e). Despite extensive attempts to eradicate these pathogens via teaching, diagnostic, and vaccination programs, hepatitis B, which is caused by HBV, is still a global public health apprehension (Okonko et al., 2012d). HBV infection is the most dangerous form of viral hepatitis (Ojo et al., 2013a) and a major global public health concern, particularly in Africa and the Western Pacific area (WHO, 2017). As to the 2017 global hepatitis report, around 0.88 million fatalities globally are attributed to consequences of chronic HBV infection, and 257 million individuals, or 3.5% of the total population, are expected to be living with HBV infection (WHO, 2017).

The two primary worldwide public health hazards that impede development in low- and middle-income countries are HIV and malaria (Ejike et al., 2020a,b; John et al., 2020). Malaria is one of the most prevalent and deadly widespread of all parasitic diseases in the world (Ibekwe et al., 2009; Okonko et al., 2009; 2012f,g). With over 3000 fatalities every day, malaria continues to be one of the world's most common causes of illness and mortality (Okonko et al., 2009, 2010a, 2012e,f). In sub-Saharan Africa, *Plasmodium falciparum* infection poses a severe risk to public health (Oyeyemi & Amugo, 2015). In most endemic locations, *P. falciparum* and the hepatitis B virus coexist in individuals living with HIV-1 (Oyeyemi & Amugo, 2015). Also, 350 million persons globally are thought to be chronic carriers of HBV, even though the precise infection status remains unknown (WHO, 2008; Liaw & Chu, 2009; Oyeyemi & Amugo, 2015).

HIV and *Helicobacter pylori* are pandemic infections with varying rates of geographic prevalence (Nkuize et al., 2023). The bacterial pathogen *H. pylori* is the cause of several diseases, including stomach cancer, chronic gastritis and peptic illness (Marshall & Warren, 1984; Conteduca et al., 2013; Burgard et al., 2019; Crowe, 2019; Choi et al., 2020; Nkuize et al., 2023). Similar to *H. pylori* infection, pre-neoplastic lesions and gastric cancer (GC) have different prevalence rates in different populations at the continental or subcontinental level, as demonstrated in Europe and China (Venneman et al., 2018; Lu et al., 2022; Nkuize et al., 2023). The African paradox, which is distinguished by a high frequency of *H. pylori* infection and a low frequency of GC, is an exception to this rule (Smith et al., 2022; Nkuize et al., 2023). Global analysis reveals that 59.2% of people on the planet have *H. pylori* infection (Hooi et al., 2017). However, projections of HIV infection worldwide in 2022 (UNAIDS, 2018; Nkuize et al., 2023) show that 38 million individuals were living with HIV (PLWHIV).

To ascertain potential correlations between these triple infectious agents, additional epidemiological information regarding their simultaneous occurrence is required. In light of this, this investigation established the coexistence of *H. pylori*, *P. falciparum*, and the hepatitis B virus in individuals living with HIV-1 who were attending a tertiary hospital in Bayelsa State, Nigeria.

2. Materials and methods

2.1. Study Design and Population This study was cross-sectional in design. The ethical conduct of the work was approved by the Bayelsa State Ethics Committee at NDUTH. The patient's demographic information and past medical records were acquired using standardised questionnaires. The 200 HIV-1 patients included in this study were all members of the cohort of eligible patients who were HIV-positive. On the other hand, all subjects whose data were incomplete were excluded from the study.

2.2. Laboratory Analysis

Plasma was analysed for the presence of *H. pylori*, *Plasmodium falciparum*, and HBsAg at the University of Port Harcourt's Virus & Genomics Research Unit of the Department of Microbiology.

2.2.1. HBsAg Serological Analysis The HBsAg content of plasma samples was measured using a Bio-Rad ELISA kit. The manufacturer's instructions were followed for conducting the analysis. Interpretation was done by the manufacturer's instructions. The results were interpreted using the sample OD450nm to cut-off value ratio and the following values: S/CO <0.9 is considered unfavourable, 0.9–1.1 is considered uncertain, and >1.1 is considered favourable.

2.2.2. Serological Analysis of *Plasmodium falciparum*

Blood samples were tested using the SD Bioline RDT kit (Standard Diagnostics Pvt. Ltd., India) to check for the malaria *Plasmodium falciparum* Antigen. Every laboratory test was carried out following the manufacturer's instructions and with the use of quality controls through standard operating procedures.

2.2.3. Serological Analysis of *Helicobacter pylori*

One stage ANTI-FTP was used to do a parallel test for the Helicobacter pylori antibodies. The tests were carried out in compliance with the kit manufacturer's instructions.

Table 1: Co-infections of HIV/HBsAg/Plasmodium falciparum/Helicobacter pylori and Socio-Demographic/Clinical Features of HIV-Infected Individuals

Variables	No. Tested (%)	No. positive for HIV/HBV/PF/HP (%)
Sex		
Male	33.5	0.0
Female	66.5	0.7
Age (years)		
≤ 30	17.0	0.0
31-50	61.5	0.8
≥ 51	22.0	0.0
Marital Status		
Married	50.5	0.0
Single	40.5	1.2
Others	9.5	0.0
Educational Status		
Primary	8.0	0.0
Secondary	23.0	0.0
Tertiary	34.0	0.0
Non-formal	35.0	1.4
Occupation		
Unemployed	47.5	1.0
Business	5.0	0.0
Civil Servants	15.5	0.0
Artisans	1.0	0.0
Farmers	2.0	0.0
Traders	0.5	0.0
Self-employed	8.0	0.0
Students	18.5	0.0
Undisclosed	2.0	0.0
CD4 (Cells/ul)		
≤ 200	34.0	0.0
200- 349	6.0	0.0
≥ 350	60.0	0.8
Viral Load (Copies/ml)		
≤ 40	16.0	0.0
40-1000	68.0	0.7
≥ 1001	16.0	0.0
TOTAL	**100.0**	**0.5**

2.2.4. CD4 and Viral Load Analysis Following the manufacturer's instructions, each participant's CD4 count was determined using a Partec flow cytometer (Partec GmbH, Germany), and their viral load was determined using Abbott Real-Time Polymerase Chain Reaction (PCR) equipment.

2.3. Data analysis

To evaluate the data, Microsoft Excel version 16.0 (Microsoft, USA) was utilised. The statistical significance of every analysis was determined using Fisher's exact test at a 5% significance threshold.

3. Results

Of the 200 participants studied, 0.5% had coinfections with HIV/HBsAg/ *Plasmodium falciparum* (PF) and *Helicobacter pylori* (HP). Based on sex, only females (0.7%) had multiple co-infections of HIV/HBsAg/*Plasmodium falciparum* (PF) and *Helicobacter pylori*. Based on age groups, HIV/HBsAg/PF/HP coinfections were present only in the age group 31-50 years (0.8%). Also, based on marital status, the HIV/HBsAg/PF/HP coinfections were only present in single marital status (1.2%) as indicated in Table 1.

In terms of educational background, only those with non-formal educational backgrounds (1.4%) had HIV/HBsAg/PF/HP coinfections. As regards occupational status, only participants who were unemployed occupational group (1.0%) had HIV/HBsAg/PF/HP coinfections. Looking at their CD4 counts, only participants with CD4 counts of >350 cells/µl (0.8%) had HIV/HBsAg/PF/HP coinfections. For viral load assay, only participants with a viral load of 40-1000 copies/ml (0.7%) had HIV/HBsAg/PF/HP coinfections as indicated in Table 1.

4. Discussion

This study determined the coexistence of hepatitis B virus, malaria *P. falciparum* and *H. pylori* among people living with HIV-1 attending a tertiary hospital located in Bayelsa State, Nigeria. According to Nkuize et al. (2023), there is variation in the prevalence rates of pandemic illnesses such as HIV and *Helicobacter pylori* across different regions. Similar to *H. pylori* infection prevalence, pre-neoplastic lesions and gastric cancer (GC) vary with population at the continental or subcontinental level, as observed in Europe and China (Lu et al., 2022; Nkuize et al., 2023; Venneman et al., 2018). The African paradox is an anomaly to this rule, as evidenced by its low frequency of GC and high prevalence of H. pylori infection (Smith et al., 2022; Nkuize et al., 2023). According to a global analysis, 59.2% of people on the planet are infected with *H. pylori* (Hooi et al., 2017). Conversely, predictions of the number of people living with HIV (PLWHIV) in 2022 (UNAIDS, 2018; Nkuize et al., 2023) show that HIV is also a global infection. More epidemiological information about their simultaneous existence is required to ascertain any potential connections between these four pathogens. Thus, among individuals living with HIV-1 attending a tertiary hospital in Bayelsa State, Nigeria, this study established the coexistence of the hepatitis B virus, *P. falciparum*, and *H. pylori*.

Previously, most studies have concentrated on determining either the co-infection prevalence of HIV/HBV (Tremeau-Bravard et al., 2012; Hamza et al., 2013; Udeze et al., 2015; Aaron et al., 2021; Innocent-Adiele et al., 2021; Omatola et al., 2020a; Okonko et al., 2010b, 2013, 2020b,c, 2023a,b,c,d,e; Elenwo et al., 2023; Ugwu et al., 2023a,b) or HIV/Malaria (Okonko et al., 2012f,g; Ejike et al., 2020a,b; John et al., 2020; Okonko et al., 2019, 2021; Innocent-Adiele et al., 2023a) or HIV/*H. pylori* (Ahaotu et al., 2023; Alubi et al., 2023; InnocentAdiele et al., 2023b; Okonko & Barine, 2023), or HBV/Malaria (Aernan et al., 2011; Dabo et al., 2015; Baeka et al., 2017; Kotepui & Kotepui, 2020; Omatola et al., 2019, 2020b; Omatola & Okolo, 2021; Cookey et al., 2021, 2022; Afolabi & Bakare, 2022; Okonko et al., 2022, 2023a,b,c) or HIV/HBV/Malaria (Okonko et al., 2021; 2023b), none of have looked at the coinfections HIV/HBV/Malaria/*H. pylori* in the country, especially in this region of Nigeria. The 0.5% reported in this study may look very low but its impact may not be insignificant, as most of these pathogens are implicated in cancer (De Flora et al., 2015).

Cancer is primarily caused by chronic infections and infestations (De Flora et al., 2015). According to their research, 15% of all human malignancies are thought to be caused by *Helicobacter pylori*, HPV, HBV, and HCV (De Flora et al., 2015). The current data may highlight a gap in our knowledge of the epidemiology of these many co-infections and point to separate epidemiological variables functioning in the nation. It has been established that co-infection with *H. pylori*, HBV, and malaria in individuals living with HIV affects the course of either or all of these infections, hepatitis, malaria, or both (Affia et al., 2024).

4. Conclusion

According to the study, individuals with HIV-1 who present to a teaching hospital in Bayelsa, Nigeria, had

triple infections with the hepatitis B virus, *Plasmodium falciparum*, and *Helicobacter pylori*. This calls for concerted efforts in the management of people living with HIV-1 in Bayelsa, Nigeria.

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