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## HBV INFECTION AMONG HIV-INFECTED COHORT AND HIV-NEGATIVE HOSPITAL ATTENDEES IN SOUTH WESTERN NIGERIA

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### Abstract

**Background:** Prevalence, association and probable mode of acquisition of HBV and HIV dual infections have not been fully explored. Thus, HBV intervention plan and services are sometimes exclusively targeted towards HIV-infected population. We investigated HBV infection among HIV-infected cohort in comparison with HIV-negative hospital attendees to ascertain dual infectivity pattern; thereby encouraging appropriate allotment of intervention services.

**Materials and Methods:** A total of 349 (M=141; F=208; Mean=33.98 years; Range= 0.33-80 years) plasma specimens from two virus diagnostic laboratories in south-western Nigeria were analysed. These include 182 HIV-positive and 167 HIV-negative specimens from ART and GDV laboratories respectively. The specimens were initially screened for detectable HIV antigen/antibody, and subsequently HBsAg by ELISA technique.

**Results:** Overall, HBsAg was detected in 20.92% (95% CI: 16.65-25.19%) of the patients. Also, 24.82% (95% CI: 17.69-31.95%) and 18.27% (95% CI: 13.02-23.52%) HBsAg positivity was recorded for males and females respectively. CHI square analysis showed no association (P=0.14) between gender and prevalence of HBsAg. Similarly, comparison of prevalence of HBsAg by age groups shows no significant difference (P=0.24). Overall, no significant difference (P=0.59) was observed in the prevalence of HBsAg among the HIV-infected cohort and HIV-negative hospital attendees.

**Conclusions:** Results of the study confirm endemicity and comparable rates of HBV infection independent of HIV-status.

**Key words:** ART; HBV; HIV; Nigeria; Dual positivity

### Introduction

An estimated two billion people worldwide have serologic evidence of past or present Hepatitis B virus (HBV) infection and 360 million are both chronically infected and consequently at risk for HBV-related liver disease (WHO, 2000., 2004., Wiersma et al., 2011). HBV can be transmitted by transfusion of infected blood and through unsafe practices such as carrying out healthcare procedures with contaminated instruments (Norman, 1997; Mahoney 1999). Also, perinatal and sexual exposures to HBV are highly efficient modes of transmission (Alter, 2006).

Globally, 90% of human immunodeficiency virus (HIV)-infected persons has evidence of previous HBV infection, while 5 to 15% of total cases of HIV worldwide; that is, 2-4 million are estimated to have chronic HBV co-infection (Alter, 2006). Such high prevalence has been attributed to routes of transmission shared by the two viruses. However, remarkable variation have been noted in the HIV-HBV dual infection rates depending largely on the geographic location, risk groups, the type of exposure involved and the socioeconomic condition of the particular region (Saha et al., 2011).

Although, cases of Hepatitis B and HIV infections have been well documented in Nigeria (Iwalokun et al., 2006; Otegbayo et al., 2008; Adesina et al., 2010); prevalence, association and pattern of dual infectivity in the population have not been clearly defined. Thus, existing infrastructure and government-supported services appears to be largely directed toward HIV intervention with a notion that HBV infection is more prevalent among the group as reported in the developed countries. In that way, HBV may be spreading discreetly among untargeted population. Consequently, this study was designed to investigate prevalence of Hepatitis B infection among HIV-infected cohort in comparison with HIV-negative hospital attendees to ascertain rate of infection in both groups.

### Materials and Methods

#### Study Area

Two virus diagnostic laboratories; General Diagnostic Virology (GDV) and Anti-Retroviral (ART) laboratories were selected for the study. GDV laboratory serves lying-in-ward and out-patient clinic attendees, as well as antiretroviral clinic referrals from different parts of the country, while the ART laboratory is designated for monitoring HIV-infected individuals on antiretroviral therapy. Both laboratories are attached to University Teaching Hospitals (UTH) in southwest region of Nigeria.

#### Study population

After obtaining ethical approval and informed consents, a total of 364 (182 specimens per site) blood specimens were obtained from the two selected diagnostic laboratories between September, 2010 and January, 2011. Demographic information of the selected specimens was recovered from the laboratory register. After preliminary HIV screening, a total of 15 plasma specimens with detectable HIV antigen/antibody from GDV laboratory were excluded from the study. Overall, a total of 349 {M=141; F=208; Mean age= 33.98 years [95% CI: 32.44-35.52 years]; Age range= 0.33-80 years} specimens were considered in the study analysis (Figure 1).

### Sample collection, preparation and laboratory analysis

An average of 10 blood specimens was randomly selected from each laboratory per week. These specimens were recovered from the laboratory at the end of each week between September, 2010 and January, 2011. One hundred and eighty-two blood specimens were collected from each laboratory to accumulate a total of 364 specimens from the two centers. Whole blood specimens were treated for plasma extraction by centrifugation at 500 x g for 5 minutes. Thereafter, plasma specimens were stored at -20°C until assayed. In strict compliance with the manufacturers' specifications, each plasma specimen was analyzed for the presence of HIV antigen and antibody using Genscreen Ultra HIV Ag-Ab ELISA. Subsequently, a total of 349 (182 HIV-positive from ART and 167 HIV-negative from GDV) specimens were subjected to Hepatitis B surface antigen (HBsAg) using HBsAg one DIA.PRO<sup>®</sup> Diagnostic Bioprobes srl (Via Columella n° 31 20128 Milano-Italy) test kit. Thereafter, results were interpreted strictly as described by the test kit manufacturers.

### Statistical analysis

Analysis was performed with SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL.). Results were presented using descriptive statistics. Independent t-test was used to determine similarity in gender and mean ages of different age groups. CHI-square test was used to establish association between participants' variables, and prevalence of HBV and HIV-HBV dual infections. Indicator of statistical significance was set at  $p \leq 0.05$ .

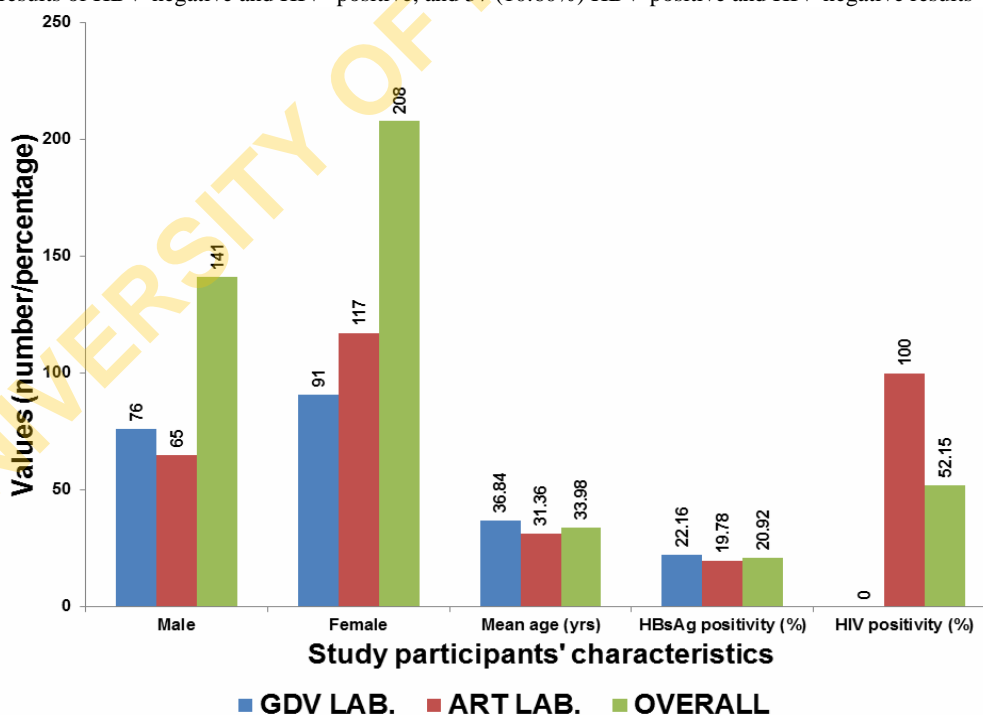
### Results

Overall, age range of the studied patients is 0.33-80 years ( $n=349$ ); mean age is 33.98 years [95% CI: 32.44-35.52 years]. Age range for males is 0.33-80 years ( $n=141$ ) with mean age of 34.82 years [95% CI: 32.03-37.61years]; and females, 0.83-80 years ( $n=208$ ) with mean age 33.41years [95% CI: 31.64-35.18]. Mean age of the males was comparable ( $P=0.40$ ) to that of the females.

Overall, prevalence of 20.92% [95% CI: 16.65-25.19%] and 52.15% [95% CI: 46.91-57.39%] was recorded for HBV and HIV infections respectively (Figure 1). The corresponding values for males are 24.82% [95% CI: 17.69-31.95%] and 46.10% [95%CI: 37.87-54.33%]; and for females 18.27% [95% CI: 13.02-23.52%] and 56.25% [95% CI: 49.51-62.99%] respectively. CHI-square analysis showed no association ( $P=0.14$ ) between gender and prevalence of HBsAg, and similarly for gender and prevalence of HIV ( $P=0.06$ ).

The patients were subsequently grouped by age into  $\leq 15$  years; 16-30 years; 31-38 years and  $\geq 39$  years. Comparison of prevalence of HBsAg by age groups { $\leq 15$  years: 6.9%,  $n=29$ ; 16-30 years: 20.4%,  $n=108$ ; 31-38 years: 22.0%,  $n=100$ ; and  $\geq 39$  years: 24.1%,  $n=112$ } showed no significant difference ( $P=0.24$ ). However, comparison of the respective HIV prevalence of the same age groups { $\leq 15$  years: 100.0%,  $n=29$ ; 16-30 years: 34.3%,  $n=108$ ; 31-38 years: 67.0%,  $n=100$ ; and  $\geq 39$  years: 43.8%,  $n=112$ ) showed high significant difference ( $P=0.001$ ).

A total of 36 (10.32%) concordant positive and 130 (37.25%) concordant negative HIV-HBV results were recorded. Also, 146 (41.84%) discordant results of HBV-negative and HIV- positive, and 37 (10.60%) HBV-positive and HIV-negative results were recorded.



**Figure 1:** Hepatitis B and human immunodeficiency viruses profiles among hospital attendees in south-western Nigeria

### HBV positivity profiles among patients attending the GDV laboratory.

In GDV laboratory, 167 patients (age range: 16-80 years, mean age: 36.84 years [95% CI: 34.52-39.16 years]) comprising 91 females (age range: 16-80 years, mean age: 35.19 years [95% CI: 31.99-38.38 years]), and 76 males (age range: 16-80 years, mean age: 38.83 years [95% CI: 35.50-42.16]) were studied. The mean age of the males and females was comparable ( $P=0.13$ ). Prevalence of HBsAg among the patients in GDV was 22.16% [95% CI: 15.86-28.46%] (Figure 1), corresponding values for males and females were 27.63% [95% CI: 17.57-37.68%] and 17.58% [95% CI: 10.03-25.40] respectively. No statistical association ( $P=0.12$ ) was observed between gender and prevalence of Hepatitis B in this location. Patients in the location were grouped into four age groups (16-19 years, 20-30 years, 31-37 years and  $\geq 38$  years). Comparison of

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prevalence of HBsAg (16-19 years: 28.57%, n=14; 20-30 years: 19.3%, n=57; 31-37 years: 27.27%, n=33; and  $\geq 38$  years: 20.63%, n=63) among the four age groups showed no significant difference ( $P=0.76$ ).

### HBV and HIV-HBV dual positivity profiles among patients attending the ART laboratory

In ART laboratory, a total of 182 patients (age range: 0.33-65 years, mean age: 31.36 years [95% CI: 29.37-33.35 years]) comprising 117 females (age range: 0.83-57 years, mean age: 32.03 years [95% CI: 30.13-33.93 years]) and 65 males (age range: 0.33-65 years, mean age: 30.14 years [95% CI: 25.74-34.54 years]) were studied. The mean age of the males and females in the location was comparable ( $P=0.44$ ). Prevalence of hepatitis B in the location was 19.78% [95% CI: 13.99-25.57%] (Figure 1). Corresponding values for males and females in the location were 21.54% [95% CI: 11.55-31.53%] and 18.80% [95% CI: 11.72-25.88%] respectively. In the study location no statistical association ( $P=0.66$ ) was observed between gender and prevalence of HBsAg. Patients in this location were also grouped into 4 (0.33-12 years, 6.90%, n=29; 20-30 years, 18.92%, n=37; 31-38 years, 19.40%, n=67;  $\geq 39$  years, 28.57%, n=49) and the prevalence of hepatitis B compared. No significant difference ( $P=0.14$ ) was observed in the prevalence of hepatitis B among the age groups.

Finally, prevalence of hepatitis B was compared between patients in GDV (exclusively HIV-negative) (22.16% [95% CI: 15.86-28.46%]) and ART (exclusively HIV-positive) (19.78% [95% CI: 13.99-25.57%]). However, no significant difference ( $P=0.59$ ) was observed between patients from the two study locations.

### Discussion

Viral hepatitis, though a major public health problem worldwide, is more prevalent in the developing countries (Johnson et al., 1986; Wiersma et al., 2011). Sub-Saharan Africa is considered to be a region of high endemicity with an average carrier rate of 10-20% in the general population. Precisely, 70 to 95% of adults in the region have at least one marker of HBV infection (Kire, 1993; Alter, 2006). Thus, HBV prevalence of 20.92% recorded in this study corroborates previously reported rates of 9 to 39% in the country (Fakunle et al., 1981; Abiodun et al., 1986; Yakubu et al., 1998; Ejele et al., 2004; Iwalokun et al., 2006; Otegbayo et al., 2008; Adesina et al., 2010).

In contrast to the report by Otegbayo et al., (2008) in a study involving HIV-infected cohort in south western Nigeria, statistical analysis showed no association ( $P=0.14$ ) between gender and prevalence of HBV infection in this study. Also, no significant difference ( $P=0.24$ ) was observed in the prevalence of HBV by age groups. However, prevalence of HIV by the same age groups showed high significant difference ( $P=0.001$ ). This might be because all the patients in the  $\leq 15$  yrs age group were HIV-positive and from the ART laboratory.

It is noteworthy that findings from this study are comparable with results of previous studies from different regions of the country (Iwalokun et al., 2006; Otegbayo et al., 2008; Fakunle et al., 1981; Abiodun et al., 1986; Yakubu et al., 1998; Ejele et al., 2004). Thus, the endemicity of viral hepatitis in the country is not debatable. However, these findings call for the need to harness current measures aimed at facilitating adequate prevention and control of HBV infection in the perceived high risk (HIV-infected) group and expand it to the entire population.

The 10.32% prevalence of concordant positive HIV-HBV observed in the study is comparable to 9.7 and 11.9% reported in previous studies by Ejele et al., (2004) and Otegbayo et al., (2008) respectively. In a previous study in Nigeria, Ejele et al., (2004) recorded different rates of HIV-HBV concordant positivity with highest value among age group 33-39 years. In contrast, no significant difference ( $p=0.99$ ) was recorded in HIV-HBV concordant positivity rates among different age groups and gender in this study. Comparable ( $P=0.59$ ) prevalence of hepatitis B was recorded in the two study centers, though the ART laboratory exclusively serve HIV-infected patients on ART while the GDV site attends to referrals from different clinics. Specifically, the study shows a high prevalence and similar distribution of HBV infection among both the HIV-positive (19.78%) and HIV-negative (22.16%) study populations. Similarly, Shimelis *et al.*, (2008) in a study among VCT and ART attendees in Addis Ababa reported that there was no significant difference in HBsAg seropositivity between HIV-positive and HIV-negative subjects. In addition, findings from several studies in sub-Saharan Africa showed that areas of high HBV endemicity reported no significant difference in prevalence of HBV among HIV-infected and HIV-seronegative populations (Oshitani et al., 1996; Rouet et al., 2004; Simpo et al., 2006).

Therefore, while the same route of acquisition of HBV and HIV could be suggested for the HIV cohort from ART laboratory, it may not be so for the HIV-negative patients from GDV laboratory who have similar HBV prevalence. Since previous studies have shown that most HIV infections in Nigeria were acquired by heterosexual mode, (Piot *et al.*, 2002; UNAIDS, 2002) it might be appropriate to state that the HIV-negative but HBV-positive patients from GDV laboratory might have acquired HBV from routes other than sexual. Thus, this also suggests that there may be more routes of exposure or acquisition of HBV infection among the group other than sexual and blood-related transmission. This might connote poor knowledge of HBV epidemiology in comparison with HIV, thus resulting in accidental acquisition of HBV via less apparent routes. For example, acquisition of HBV infection in endemic areas has been attributed largely to transmission from person to person during childhood (McMahon et al., 1985; Dusheiko et al., 1989; Kiire, 1990; Ruiz-Moreno et al., 1999; Bortolotti, 2006) rather than through sexual transmission and injecting drug use in adulthood (McQuillan et al., 1999; Stroffolini et al., 2000; Mast et al., 2005).

### Conclusions

Results of the study confirm endemicity and comparable prevalence of HBV infection among patients from the two study centers independent of their HIV status. This indicates that both study populations had comparable exposure to HBV. Therefore, HBV prevention measures should be promoted in the population regardless of HIV status. Also, existing infrastructure for government-supported HIV services should be expanded to include HBV education and management to reduce the spread of both infections. Nevertheless, due to higher morbidity and mortality in co-infected patients, providing the opportunity for HBV testing for HIV-infected people is essential.

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**Competing interest:** The authors have no competing interest.

**Author's contributions:** OMA participated in sample collection, processing, analysis and result interpretation. He also wrote the manuscript. ED participated in sample collection, processing, analysis, result interpretation and review of the manuscript. WFS was responsible for statistical analysis of the results and also participated in manuscript review. OO participated in sample collection and processing, and review of the manuscript.

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