Research Article

Serological Markers for Hepatitis B Virus among HIV Individuals in Ogbomoso, Oyo State, Nigeria

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Abstract | Human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) co-infection have been associated with reduced survival, increased risk of liver disease and hepatotoxicity despite undergoing antiretroviral therapy (ART). This study aims to determine the prevalence of serological markers of HBV based on serological markers among infected individuals with HIV. Ninety-three sera samples of HIV positive individuals were collected by Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital- HIV/AIDS Supporting and Counselling Unit, Ogbomoso. The collected samples were analyzed for enumeration of CD4+ cells and presence of HBV. The selected three HBV serological markers were HBsAg, HBeAg and HBcAb while using a third generation ELISA kit for screening. The mean CD4+ count and age were 479.12 ± 23.48 cells/µl and 48.56 ± 1.27 years, respectively. Only six samples out of ninety-three HIV-positive samples were positive to HBsAg while fifty-four samples (58.1%) were positive for HBcAb however, HBeAg marker was negative among all samples. Interestingly, the prevalence of the HBV infection was more in females (66.6%) compared to the male counterparts (33.3%) within the overall screening. In conclusion, the current study describes the prevalence of HBV infection amongst HIV-positive individuals in Ogbomoso. The high prevalence of HBcAb confirmed that Ogbomoso district is highly endemic with HBV infection. Likewise, HBV vaccination in HIV-infected patients is encouraged with careful monitoring for liver function, particularly those under ART.

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Introduction

Infection caused by Hepatitis B virus (HBV) represent a major health challenge (Henry et al., 2016). About 2 billion persons are infected worldwide and more than 400 million are chronic carriers (Naga, 2017). Additionally, about 34.2 million people have been estimated to be living with HIV/AIDS worldwide with sub-Saharan Africa remaining the most affected region globally (Olufemi et al., 2009) .

Epidemiologically, Human immunodeficiency virus (HIV) and HBV have common routes of transmission, hence the frequent occurrence of co-infections (Opaleye et al., 2014). The main transmission for infection is believed to be sexual, vertical and intrafamilial routes (Toscano and Correa, 2017). However, majority of infection in adolescents

and young adults are acquired sexually or through percutaneous exposure (Laufer et al., 2010).

Infections caused by HIV results in progressive deterioration of the immune system resulting in reactivation or re-infection with HBV in individuals who have undetectable HBsAg, HBeAg or developing AIDS (Odenyo et al., 2000; Alter, 2006)

HIV and HBV co-infection have been associated with reduced survival, increased risk of liver disease and hepatotoxicity associated with antiretroviral therapy (ART) (Manegold et al., 2001; Thio, 2009). Previous studies have identified less likely clearance of HBV infection amongst HIV/AIDS co-infected leading to chronic infection (Marion, 2007). HIV and HBV infections are prevalent in Africa, however, there is dearth information on the prevalence of HIV/HBV co-infection. This study aims to determine the demographic characteristics and prevalence of HBV infection among HIV positive patients who were screened individually between the period of July and November, 2017 in Ogbomoso, South-Western Nigeria .

Materials and Methods

Sampling data

The study was conducted in Ogbomoso district, Oyo State, Nigeria between July and November 2017. The study population consisted of ninety-three HIV-positive outpatients. Informed consent was obtained from each participant and ethical approval was obtained from the Ethics Committee, Ministry of Health, Ogbomoso Local Government, Oyo State. A self-designed semi-structured questionnaire was used to obtain the sociodemographic data and risk factors associated with HBV infection. Some individual variations such as age, sex, and history of exposure to antiretroviral drugs like Lamivudine and/or Tenofovir were collected.

Blood collection and ELISA

Following pre-test counseling and attainment of consent, blood samples were obtained and retested for HIV by immuno-chromatographically using the HIV 1/2 STAT-PAK® Assay Dipstick (CHEMBIO Diagnostic Systems, Medford, NY-USA). Positive sera samples were confirmed for HIV by the enumeration of CD4+ cells using the Automated Cytometer with sensitivity 98-100% and specificity 97-99.5%. Samples were then screened for HBsAg, HBeAg and HBcAb using third generation Enzyme-linked Immunosorbent Assay (ELISA) kits (Melsin Medical Co., Limited, China) according to the manufacturer's instruction.

Statistical analysis

Statistical package of SPSS version 2 was used for analyzing data. Mean and standard deviation were used to summarize continuous variables while frequency and percentage were used for categorical variables. Pearson Chi-square test was used to make comparisons for the categorical variables. The level of significance was set at 95% confidence interval with $p \leq 0.05$.

Results and Discussion

A total of 93 HIV-positive individuals including sixty females (64.5%) and thirty-three males (35.5%). The HIV-positive individuals were aged between 11 and 80 years with the mean age 48.56 ± 1.27 years. The mean CD4+ count was 479.12 ±23.48 cells/µl. The highest prevalence was found in the age range between 41-50 years (31.2%) while the lowest were in the age ranges between 11-20 (1.1%) and 21-30 (1.1%) years, respectively (Table 1). Out of the ninety-samples, 64.5% (60/93) showed positive results for serological markers of HBV; Six samples (6.5%) were positive for HBsAg while 54 (58.1%) were positive for HBcAb and none was positive to HBeAg which is contrary to previous studies that recorded the same results (Otegbayo et al., 2008). This however, was also discovered for HDV by (Paul et al., 2018).

The serological markers used for HBV infection in this study were HBsAg, HBcAb and HBeAg. Among the examined samples, six (6.5%) samples were positive for HBsAg while 54 (58.1%) were positive for HBcAb. None of the samples were positive for HBeAg (Table 2). The 6.5% recorded for HBsAg in this study is higher than the 5.7% recorded in Ekiti (Opaleye et al., 2014) and lower that the 9.7% in Niger Delta (Ejele et al., 2004), 11.9% in Ibadan (Otegbayo et al., 2008), 15% in North-Eastern Nigeria (Olokoba et al., 2008) and 16.7% in Jos (Idoko et al., 2009). The prevalence recorded in this study is higher than 2.3% in Kaduna (Aba and Aminu, 2016) and lower than a 5.8% recorded in Owerri (Nwolisa et al., 2013). The geographical variation, differences in cultural practices, sexual behaviour and practices as well as differences

in the test methods employed in detection can play an important role in the disease epidemiology and surveillance.

Table 1: *Demographic characteristics of the study population.*

Variables		Frequency	Percentage
Age (years)	11-20	1	1.1
	21-30	1	1.1
	31-40	24	25.8
	41-50	29	31.2
	51-60	24	25.8
	61-70	8	8.6
	71-80	6	6.5
Sex	Female	60	64.5
	Male	33	35.5
$CD4^+$ Count (cells/µl)	≤ 200	8	8.6
	201-400	28	30.1
	401-600	30	32.3
	601-800	18	19.4
	801-1000	6	6.5
	≥ 1001	3	3.2

Table 2: *Seroprevalence of HBV markers among the study subjects.*

Markers	HBsAg Status	HbcAb Status	HBeAg Status
Reactive (%)	6 (6.5)	54 (58.1)	0 (0.0)
Non-reactive (%)	87 (93.5)	39 (41.9)	93 (100.0)
Total (%)	93 (100)	93 (100)	93 (100.0)

HIV infected individuals with low immunity are mostly unable to mount a response to the core and surface antigen making them to persist longer than HIV non-infected population (Christopher and Chloe, 2007) hence high prevalence (54%) recorded for HBcAb as the presence of HBcAb indicates previous or current infection with HBV (Sirisena et al., 2002).

Also, four females (66.6%) and 2 males (33.3%) were positive to HBsAg however, this difference was not statistically significant (ρ = 0.909). Out of the six HBsAg-positive samples, three (50.0%) were fallen within the age range 51-60 years while the lowest was within the group 31-40 (16.6%). The difference in the age groups was also not statistically significant (ρ = 0.152). Individuals who had CD4+ count between 401-600 cells/µl had the highest seropositivity (66.6%) while those between 601-800 cells/µl had the least seropositivity (5.6%) that was statistically non-significant difference (P = 0.367) (Table 3). Even though age has been identified to be a major determinant of HBV incidence and its, however, from this study, HBsAg detection was not significantly associated with age (P = 0.836) even though the highest prevalence was among the patient aged between 51 and 60 years. The age-specific prevalence in this study is in contrast with the findings of (Olokoba et al., 2011; Aba and Aminu, 2016) who reported that the highest prevalence was recorded in the age range 21 and 35 years. Also, our results are similar to the findings of (Manjula et al., 2018) that mentioned age factor in individuals was >40 years. The difference might be ascribed to high sexual activities in the studied patients.

Table 3: *Relationship of HBsAg positivity with the considered variables.*

Variable	Level	Positive (6)	Negative (87)	χ^2	*P-value*
Age (years)	11-20	0 (0.0)	1 (1.1)	2.775	0.836
	21-30	0 (0.0)	1 (1.1)		
	31-40	1 (16.6)	23 (26.4)		
	41-50	2 (33.3)	27 (31.0)		
	51-60	3 (50.0)	21 (24.1)		
	61-70	0 (0.0)	8 (9.2)		
	≥ 71	0 (0.0)	6 (6.9)		
Sex	Female	4 (66.6)	56 (64.4)	0.013	0.909
	Male	2 (33.3)	31 (35.6)		
CD4+ count (cells/µl)	≤ 200	1 (16.6)	7 (8.4)	5.415	0.367
	201-400	0 (0.0)	28 (32.2)		
	401-600	4 (66.6)	26 (29.9)		
	601-800	1 (16.6)	17 (19.5)		
	801-1000	0 (0.0)	6 (6.9)		
	≥ 1000	0 (0.0)	3 (3.4)		

As shown in Table 4, 54 (58.1%) were positive to HBcAb. Out of the 54 patients, 36 (66.6%) were females while 19 were males (33.3%). However, this difference was not significant statistically (ρ = 0.610). The prevalence of co-infection with HBV and HIV was higher in females (6.6%) than males (33.3%), which in accordance with previous findings by (Oluyinka et al., 2017), however HBV infection was not significantly associated with sex (P > 0.05). Also, these findings are similar to report study by (Opaleye et al., 2014) and Azhani and Stephane, 2017). The main reasons might be attributed to gender inequalities, reduced socio-

economic status, increased sexual violence as well as increased biological, cultural and structural risk factors amongst females rather males (Mabala, 2006). In contrast, these results disagree with previous findings by (Mehmet et al., 2005; Manjula et al., 2018) who stated that HIV-positive males were coinfected with either HBV or HCV with higher rate than females.

Table 4: *Relationship of HBcAb positivity with the considered variables.*

Variable	Level	HBcAb Status		χ^2	*P-value*
		Positive (54)	Negative (39)		
Age (years)	11-20	1 (1.9)	0 (0.0)	6.267	0.394
	21-30	1 (1.9)	0 (0.0)		
	31-40	11 (20.4)	13 (33.3)		
	41-50	18 (33.3)	11 (28.2)		
	51-60	15 (27.7)	9 (23.1)		
	61-70	3 (5.5)	5 (12.8)		
	≥ 71	5 (9.3)	1 (2.6)		
Sex	Female	36 (66.6)	24 (61.5)	0.260	0.610
	Male	18 (33.3)	15 (38.5)		
CD4+ count (cells/µl)	≤ 200	6 (11.1)	2 (5.1)	5.361	0.373
	201-400	18 (33.3)	10 (25.6)		
	401-600	19 (35.2)	11 (28.2)		
	601-800	8 (14.8)	10 (25.6)		
	801-1000	2 (3.7)	4 (10.3)		
	≥ 1000	1 (1.9)	2 (5.1)		

Participants in age range 41-50 years had the highest positive subjects (18/54; 33.3%) while the lowest (1.9%) was within the groups 11-20 and 21-30, respectively. The difference in the age groups was also not found to be significant statistically (p = 0.394). From the findings of this study, HBcAb infection was not significantly associated with age (P = 0.394) even though the highest prevalence (33.3%) was among the patient aged between 41 and 50 years, high prevalence amongst this age group might be as a result of sexual and socio-cultural practices common within this age group.

Subjects with CD4+ count between 401-600 cells/µl had the highest seropositivity (19/30; 35.2%) while those between ≤ 200 and 1001-1200 cells/µl had the least seropositivity (1.9%). No statistical significant difference was found (P = 0.373). Statistical analysis revealed that there is no statistical significant association between acquiring HBV infection and CD4 count on the basis of age with gender exclusion (P > 0.05) and this in accordance with previous findings reported by (Digban et al., 2017; Manjula et al., 2018) However the prevalence of HBV and HIV co-infection revealed higher CD4 count within the range 401-600 cells/µl.

None of the patients were positive to HBeAg, hence, a reduced risk of vertical transmission of HBV infection through perinatal route (Roingeard et al., 1993).

Conclusions and Recommendations

This study describes the prevalence of HBV infection amongst HIV-positive patients in Ogbomoso. Nigeria. High prevalence of HBV infection was reported more in females than males based on HBcAb marker detection. Our results confirm that Ogbomoso district is endemic with HBV infection that highlights the need for routine screening of HBV markers in HIV-infected patients. Likewise, HBV vaccination in HIV-infected patients should be encouraged with careful monitoring for liver function, particularly those under ART as liver diseases have been said to be major cause of mortality among HIV/AIDS patients, thereby accounting for 15-17% of HIV-associated mortality worldwide.

Authors Contribution

All authors contribute equally in study design, sample collection,laboratory analysis, funding, manuscript drafting and editing,and all approved the final draft of the manuscript.

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