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Prevalence of hepatitis- B virus infection among HIV patients in Ikole Ekiti, South – Western, Nigeria

OO Opaleye[1], AS Oluremi[1]*, DO Ogbolu[2], BA Babalola[3], T Shittu[4], AA Adesiyan[2]

[1]Department of Medical Microbiology and Parasitology, Lautech, Nigeria
[2]Biomedical Science Department, Lautech, Nigeria
[3]Specialist Hospital, Ikole Ekiti, Nigeria
[4]Medical laboratory Science Department, Lautech Teaching Hospital, Ogbomoso, Nigeria

ABSTRACT

Infections from HIV, Hepatitis B virus constitute a major public health challenge in sub-Saharan Africa, and there are evidences to suggest that there is faster progression of HIV in those co-infected with either HBV. The aim of this study was to determine the prevalence of HBV infections among HIV-infected patients, and describe the socio-demographic features and correlates of HIV and HBV co-infected patients at Specialists Hospital, Ekiti, Nigeria. One hundred and fifty eight (158) HIV individuals who consented to the study were tested for HBV using Diaspot HBsAg kit (Screening test) and Biorex Diagnostic ELISA kit (Confirmatory test) between November 2012 and April, 2013. CD4 counts were also analysed with Aldrich Sigma kit and flow cytometery respectively. P value < 0.05 was considered to be significant. Prevalence rates of Hepatitis B infections among HIV obtained were 5.7%. Individuals who were 51 years or younger were the most affected HBV co-infection was more common among females than males (3.8%: 1.8%, res, $P = 0.0004$). Out of 9 patients, 8 patients (88.9%) fell within the age range 30-49 years which implies the high prevalence of HIV among labour force while 1 patient (11.1%) fell within the range of 50-60 years .Mean serum ALT and AST among participants with HIV alone were (42.0, 38.3) International Units (IU), but were significantly higher (57.6, 43.7) International Units (IU) for those with HIV/HBV co-infection, $P = (0.048, 0.032)$.Mean CD_4 count for HIV/HBV co-infected participants (389 cell/mm^3) was significantly higher than that for participants with HIV alone (230 cell/mm^3), $P = 0.024$ **Conclusion:** Co-infection with hepatitis B virus is common among HIV-infected patients in our setting and this further reaffirms the need for routine baseline screening for this marker, as it is a major consideration in the initiation and choice of highly active antiretroviral therapy. Furthermore, those found to be negative should be immunized with HBV vaccine to improve the prognosis of their HIV status.

Keywords: Hepatitis B, Hepatitis C, HIV, Nigeria, Prevalence.

Introduction

There are estimated 34.2 million people living with HIV/AIDS worldwide, and sub-Saharan Africa remains the region most affected by the global Acquired Immunodeficiency Syndrome (AIDS) pandemic [1]. On the other hand Hepatitis B virus (HBV) constitutes a major public health challenge in this same region of the world with prevalence of >8% of the population.

**Correspondence*
Adeolu Sunday Oluremi,
Medical microbiology and Parasitology,
LAUTECH, Ogbomoso, Nigeria
Email: adsunday2012@gmail.com

Epidemiologically HIV and HBV have common routes of transmission, hence the frequent occurrence of their co-infections.

Additionally, HIV immunosuppression may be associated with reactivation of HBV infection in persons who have lost detectable HBsAg, or HBeAg, or developing AIDS [2] or re-infection in patients who have lost protective anti-HBs or are progressing to AIDS [3]. Human Immunodeficiency Virus (HIV) is a lentivirus that infects cells of the human immune system and destroys or impairs their function. Infection with this virus results in the progressive deterioration of the immune system, leading to 'immune deficiency [5].While hepatitis is the inflammation of the liver; it

may be caused by exposure to certain chemicals, autoimmune diseases, or by bacterial infections but is often caused by one of several viruses [6].The hepatitis B virus can be transmitted through contact with infected blood and other body fluids and is transmitted from person to person through unprotected sexual intercourse with an infected person, sharing infected needles, or other sharp agents that break the skin [6]. Hepatitis B virus and HIV have been associated with reduced survival, increase risk of progress to liver disease and hepatotoxicity associated with anti-retroviral therapy. Hepatitis B virus and HIV share the same routes of transmission; as a consequence, infection with HBV is expected in HIV infected patients. Hepatitis B virus (HBV) infection is one of the most common infections in the world, with approximately 2 billion people infected [7]

HBV exhibits a mutation rate more than 10-fold higher than other DNA viruses and more closely resembles the replication characteristics of RNA viruses like HIV [8]. This leads to a high mutation rate and constant production of new viral variants, even in the absence of antiviral treatment. The rate at which nucleotide substitutions develop varies at different stages of infection. The natural evolutionary rate for the HBV genome in chronic hepatitis B is approximately 1.4 - 3.2 x 10-5 substitutions per site per year, which is approximately the same as retroviruses (10−5) but 104 times higher than DNA genomes [9] The high mutations lead to complex mixtures of genetic variants, also known as "quasispecies," which result from this high-level, low-fidelity replication, and circulate in various reservoirs specific to each virus.

Under the selective pressure of antiviral therapy that does not profoundly suppress viral replication; drug-resistant strains are selected for as the dominant species, with the potential loss of virological suppression. Both viruses have rapid development of drug-resistant viral variants during suboptimal therapy, and it's because of both the high rate of replication and turnover of virus (HIV produces ~ 10 billion new viral particles per day while HSV produces at least 10 times that number in each infected individual) [10] and the high error rate of the HIV reverse transcriptase and HBV polymerase enzymes. As a result of similar polymerase enzyme, HBV and HIV share a number of antiviral drugs, and hence the development of similar antiviral resistance patterns during antiviral therapy. There is overwhelming evidence that HIV co-infection impacts very negatively in the modification of the natural history of HBV infections [4]. However, there has not been any convincing evidence that showed HBV to impact the course of HIV disease [11]. Other studies have also suggested HBV protein (HBx) being responsible in super inducing ongoing HIV replication and HIV long-term repeated transcription by synergizing with tat-protein and T-cell activation signals. These findings indicate that HBx could promote faster progression to AIDS in HBV/HIV-co-infected individuals. Studies from the pre-HAART era did not demonstrate a significant impact of HBV carriage on HIV disease progression [12]. While HBV does not seem to influence HIV disease progression, there is overwhelming evidence that HIV impacts very negatively on the HBV natural infections. This includes: (i) Increase in progression to HBV chronic carriage; (ii) Reduced persistence of anti-HBs and anti-HBc; (iii) Increased HBV infectivity (iv) Increased transmission of HBV; and (v) Impact on liver disease and (vi)occult hepatitis B infections diagnosis [4]. Studies have shown that HIV/AIDS individuals co-infected with HBV are less likely to clear acute HBV infection spontaneously, resulting to chronic infection. This study therefore aims to determine the prevalence and demographics characteristics of HBV infection among HIV infected individuals in Ikole Ekiti, Nigeria.

Materials and methods

The study was conducted in IHVN Clinic, Specialist Clinic, Ikole Ekiti, and Medical Microbiology and Parasitology Laboratory, Laboratory complex, Osogbo, Nigeria. Ethical approval was obtained from Permanent Secretary, Ministry of Health, Ekiti State. A total of 158 consecutive patients with HIV infection seen at the Specialist Hospital, Ikole Ekiti, Nigeria were selected for the study. Information was obtained with the aid of an interviewer-administered questionnaire. Status of serological markers for HIV and HBV (HBsAg) were determined using Enzyme-linked Immunosorbent Assay (ELISA).HIV screening was done using the national algorithm; i.e., using DETERMINE ^{TM} (manufactured by ABBOTT CO LTD, MINATO-KU, JAPAN) and STAT PAK ^{TM} (manufactured by CHEMBIO DIAGNOSTIC SYSTEMS INC, USA) techniques and a third test GENIE II test served as a tie breaker if there were discordant results with the first two tests. HBsAg test was done using First Response HBsAg Card Test, manufactured by PMC Medical (India) Pvt. Ltd. Kachigam Daman (UT) 396215, India. CD_4 Count Estimations were done using Cyflow SL-Green, manufactured by Patex, Germany. Study centre is Medical Microbiology and Parasitology Laboratory, Laboratory complex, LAUTECH, Osogbo, Nigeria. Data were analysed using statistical package within the Microsoft Excel and SPSS software to determine the effect of sex, age, CD4 count and Liver enzymes on the

data obtained. P < 0.05 was considered to be significant.

Results

Among the study subjects, there were fourty males (25.3%) and One hundred and eighteen females (74.7%) as shown in table 4.1. These patients aged between 3-82 years with mean age was 35 years. One hundred and twenty four (83.2%) patients fell within the age range 30-49 which implies the high prevalence of HIV among adult. Mean and median CD4 T lymphocyte count of the study participants were 210/mm^3 and 142/mm^3 respectively.

HBsAg is the main serological marker for diagnosis of HBV infection as it indicates either an active or chronic state, this study detected nine patients were positive for HBsAg and later confirmed with ELISA and therefore the prevalence of HBV infection was 5.7%. Among the study subjects, there were 3 males (1.9%) and 6 females (3.8%). These patients aged between 28-54 years, mean age was 35.5 years and median age was 36 years. Out of 9 patients, 8 patients (88.9%) fell within the age range 30-49 years which implies the high prevalence of HIV among adult while 1 patient (11.1%) fell within the range of 50-60 years.

The entire patients had normal ALT and AST except one. Five (3.2%), 3 (1.9%) and 1 (0.6%) fell within the CD4 of greater than 500, 200-499 and < 200 cells/mm^3 respectively as shown in table 1. Table 4.1also showed the distribution of the human immunodeficiency virus (HIV) infected in study participant as per Centers for Diseases Control (CDC) classification for HIV infected adults and adolescents with the mean CD4 lymphocyte count in each category. Fifty four patients (36.2%) had CD4 count of more than 500 cell/mm^3, 68 patients (45.6%) had CD4 count ranging from 7- 56 cells/mm^3 and 27 patients (18.2%) had CD4 count of less than 200 cells/mm^3.

Table 4.1: The baseline characteristics of HBV negative and positive patients

Parameters	HBV -Ve(149)	HBV +ve (9)	All patient(158)
Sex			
Male	37(24.8%)	3(33.3%)	40
Female	112(75.2%)	6(66.7%)	118
Age			
<20	8(5.4%)	0	8
20-29	1(0.67 %)	0	1
30-49	124(83.3 %)	8(88.9%)	132
>50	16(10.7 %)	1(11.1 %)	0
Mean	35yrs	36yrs	35.5yrs
Range	3-82yrs	28-54yrs	3-82yrs
CD4			
>500	54((36.2 %)	5(55.6 %)	59
200-499	68(45.6%)	3(33.3%)	71
<200	27(18.2 %)	1(11.1 %)	28

Table 4.2: Classified alaline transaminase (ALT) and aspartate transaminase (AST) of the patients into three (3) groups. 143 (95.6%) had normal ALT and 6 (4.4%) had raised ALT while 130 (87.5%) showed normal AST and 19 (12.8%) showed higher AST

Parameters	HBV –Ve (149)	HBV +Ve (9)	All Patients
ALT(IU/L)			
<7	3(2.01%)	1(11.1%)	4
7-56	140(94.0%)	8(88.9%)	148
>56	5(4.02%)	1	6
AST(IU/L)			
1-4	0	0	0
5-40	130(87.25%)	9(100%)	148
>40	19	0	19

The distribution of the study participants according to the 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS among Adolescents and Adults were as shown in Table 4 3. Sixteen (10.7%) of patients were of age greater than 50 years, 8 (5.4%) of teenager and no children was affected. All 158 serum samples was confirmed HIV positive.

Table 4.3: The distribution of the human immunodeficiency virus (HIV) infected in study participant as per Centers for Diseases Control (CDC) classification for HIV infected adults

Category	CD_4	No of Patients	Mean CD4 count
1	T cells >500cells/mm^3	59	118.36
2	T cell 200-499cells/mm^3	71	32.24
3	T cells <200 cells/mm^3	28	32.11

Mean serum ALT and AST level among participants with HIV alone were (42.0, 38.2) International Units (IU), and this was significantly higher (57.6, 43.0) International Units (IU) for those with HIV/HBV co-infection, P = (0.048, 0.032).The mean CD_4 count for HIV/HBV co-infected participants (259.7 cell/mm^3) was significantly higher than that for participants with HIV alone (230.0 cell/mm^3), P = 0.024.

Table 4.4: Compares the liver enzymes and CD4 count of the HIV with HIV- HBV coinfected patients

Characteristic (mean)	HIV only, n=149	HIV/ HBV, n=9	P value
Age (years)	34	39	0.34
ALT (IU/L)	220	389	0.024
AST (IU/L)	42.0	57.6	0.048
CD4 (cell/mm^3)	38.2	43	0.032

HIV: Human immunodeficiency virus, HBV: Hepatitis B virus, ALT: Alanine transaminase, AST: Aspartate Transaminase

Discussion

From this study, the prevalence of HBV co-infections among HIV infected individuals in Ikole Ekiti, Ekiti State; South-Western, Nigeria is 5.7%. The observed prevalence rate of 5.7% in HIV infected individuals attending the IHVN clinic may be due to rural location of the site of the study but it is however an indication of the rising prevalence of HBV infection in this environment. This 5.7% value reported in this study is lower than the 9.7% by Ejele *et al* in the Niger Delta area of Nigeria, 11.9% reported by Otegbayo *et al*. (2008) in Ibadan, 16.7% reported by Idoko *et al* in Jos and 25.0% by Uneke *et al*. (2005) among HIV-infected in Nigeria.

The differences in prevalence in these studies could be attributed to differences in patient selection. Gender-specific prevalence showed that females had higher seropositivity for HIV- HBV co-infections (3.8%) than their male counterparts with (1.9%) prevalence. This observation however, disagrees with the report by Mehmet *et al*. (2005) in which males had higher prevalence rate than females in both rural and urban areas with observation that male sex was an important risk factor for HBV positivity. The statistically significant difference in HIV- HBV co-infections between males and females in the present study suggests that they were not equally exposed to HBV-HIV in corroboration to earlier findings [13].

A prevalence of 5.7% was found among HIV patients attending Specialist hospital, Ikole Ekiti, Nigeria were seropositive for hepatitis B virus which may probably be a pointer to the fact that HBV infection is the major threat to the HIV infected patients as a result increase hepatotoxicity after initiation of antiretroviral therapy. Therefore, HIV infected patients should be screened for as well as vaccinated against HBV infection prior to the initiation of antiretroviral therapy. There should also be more awareness and campaign on HBV infection prevention.

Baseline ALT was significantly higher among HIV/HBV co-infected participants compared to those with HIV alone and this is in agreement with the findings of Zhou *et al*., 2007 [14]. There was an

elevation of liver enzymes among all the patient groups. The mean level was highest for those co-infected with hepatitis B. This finding is corroborated by a study in Lagos [15]. In that study, liver enzymes were significantly higher in HIV patients than in controls, as well as higher in HIV patients who were also positive for hepatitis B surface antigen compared to those not co-infected. This finding highlighted some challenges being encountered in treating patients who were co-infected, especially regarding the choice of HAART regimen, how to prevent further hepatic damage, and when to initiate HAART, especially in resource-limited settings with limited ARV options [15].

A statistically significant relationship was found between the mean CD_4 count and HBsAg serological status of the participants. Individuals with HIV/HBV co-infection had the highest mean value of CD_4 count ($P = 0.024$) when compared with participants with HIV alone. Previous investigators reported variable findings, with some corroborating findings similar to this study. However, the implication of this finding may relate to HAART-associated hepatotoxicity which is commonly seen in patients with relatively higher baseline CD_4count, for instance HAART-naïve women with baseline CD_4 count > 250/mm^3 and HAART-naïve men with CD_4 count > 400/mm^3 are at increased risk of hepatotoxicity when started on Nevirapine-based HAART. The mechanism of HAART-related hepatotoxicity in patients with HIV/HBV co-infection is mainly by immune reconstitution and some authors have identified an increase in CD_4 count of >50/mm^3after initiating HAART as an independent risk factor for hepatotoxicity[16].

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