Original Article

Hepatitis B and C virus co-infection in Nigerian patients with HIV infection

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Abstract

Introduction: We set out to determine the seroprevalence of hepatitis B and hepatitis C viruses among human immunodeficiency virus infected individuals and its impact on pattern of presentation.

Methodology: A serological study for hepatitis B and hepatitis C viruses was performed on 260 HIV-positive individuals. These patients were tested for the presence of hepatitis B surface antigen and anti-hepatitis C virus (HCV) antibody.

Results: Thirty (11.5%) patients tested positive for hepatitis B surface antigen, six (2.3%) tested positive for anti-hepatitis C virus antibody, four (1.5%) were positive for both hepatitis B surface antigen and anti-hepatitis C virus and the overall prevalence was 15.4% . Individuals younger than 40 years of age were more affected, and the odds ratio of a female being co-infected was 1.2, 25% versus 75% p value = 0.03. The prevalence of HIV and hepatitis co-infection rises with age except for hepatitis C. There was no significant difference in the mean levels of liver enzymes (AST, ALT) among the various groups. The groups differ significantly in their mean CD4 count: it was lowest for those co-infected with hepatitis B and hepatitis C; 106 cells/mm^3, 171 cells/mm^3 for those with HIV alone; and the highest value of 260cells/mm^3 was obtained in those who tested positive for anti-HCV. Scarification marks and multiple blood transfusions were more common among those infected. There was no case of intravenous drug abuse identified.

Conclusion: This low frequency of HIV/HCV co-infection is probably due to the uncommon intravenous drug abuse in this population. Co-infection with hepatitis B virus is common among our HIV-infected patients and should be a major consideration in the initiation and choice of therapy.

Keywords: hepatitis B virus; hepatitis C virus; Human immunodeficiency virus; Risk factors, presentation.

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Introduction

The hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are devastating viruses that share certain epidemiological characteristics such as risk populations and transmission routes. This puts HIV positive individuals at risk of co-infection with either hepatitis B or hepatitis C viruses, or both. For HIV and HCV co-infection (HIV/HCV), the seroprevalence rate ranges from eight to thirty percent among HIV-infected individuals [1-3]. For HIV and HBV co-infection (HIV/HBV), the seroprevalence ranges from 6.3% to as high as 39% [4-6].

Another important issue is the interaction between HIV and HBV or HCV. HIV/HBV and HIV/HCV co-infection have a negative impact on liver disease caused by these viruses [7-8]. For example, HCV accelerate the evolution and progression of liver disease in HIV-infected individuals [8,9]. HIV/HBV co-infected patients are at an increased risk of developing cirrhosis, having higher levels of HBV replication, having lower rates of spontaneous resolution of the HBV infection, and having a higher risk of reactivation of previous infections [7,10-11]. HCV and HBV infections also increase the toxicity to antiretroviral medications [7].

Whether HBV or HVC affects HIV progression has been a matter of much debate. However, there are

evidences to suggest that there is faster progression of HIV, even to AIDS-defining illness, in those co-infected with either HBV or HCV [12-13]. With the advent of highly active antiretroviral therapy (HAART) and the possibility for HIV patients to live longer, clinicians are more likely to be confronted with issues relating to co-infection and the management challenges they present, especially in resource-limited settings.

Despite widespread evidence that suggests increasing prevalence of HBV/HIV and HCV/HIV co-infections, there has been no published report about the frequency of infections in HIV-positive patients in our hospital, which is a major treatment center. The objectives of this study were i) to determine the frequency of serologic evidence of HBV and HCV infection among a cohort of HIV infected patients; ii) to explore risk factors associated with the presence of markers for these viruses; and iii) to investigate the effects of these viruses on the pattern of presentation of HIV.

Materials and Methods

Study population

This is a prospective and retrospective study among HIV-positive individuals seen at the adult HIV clinic at the National Hospital in Abuja, Nigeria. In Nigeria, about 3.1% of adults between the ages of 15 and 49 are living with HIV/AIDS [14]. The National Hospital is a major treatment and referral center in the Federal Capital City (FCT). The adult HIV clinic received support from the President Emergency Plan for AIDS Relief (PEPFAR) through the Institute of Human Virology in Nigeria.

Case records of 160 patients whose names were randomly selected from the clinic register were retrieved and reviewed for analysis. In addition, 100 newly diagnosed HIV-positive patients were also recruited after informed consent. Information obtained from the case notes included socio-demographic characteristics, risk factors, and results of serological markers for HIV. For HBV the marker was hepatitis B surface antigen (HBsAg) and for HCV the marker was anti-HCV.

HIV was diagnosed using the rapid capillus method (Des Jarlis, 1984) and confirmed by the method of Determine. HBsAg and anti-HCV was determined using ELISA kit (second generation type). In addition, results of other tests, such as CD4 count, full blood count, liver enzymes, and lipid profiles, were retrieved and analyzed.

Statistical analysis

For data collection and analysis, SPSS version 11 (Chicago IL, USA) were used. Descriptive statistics are presented with mean and standard deviations (SD) or proportions, for continuous or categorical variables, respectively.

Analysis of variance was used to test association between means of different variables within the different groups.

Results

Socio-demographic characteristics of study subjects

The subjects were divided into two groups: those with HIV alone and those with HIV and also hepatitis B, hepatitis C, or both. As shown, the majority of the patients were in the 30-39 age group, representing 54% and 75% of patients with HIV alone and those co-infected with any of the other viruses, respectively. There were more females in both categories, and a larger proportion of the females were co-infected with hepatitis B, hepatitis C, or both and co-infected with HIV with an odds ratio of 1.2, $p < 0.03$. These data are shown in Table 1.

Married men and women constitute the largest proportion of those affected, while a larger proportion of widows/widowers were infected with both viruses.

Almost equal numbers of individuals in both categories were smokers. However, more patients (32%) who were not co-infected consumed alcohol. As shown, 75% of those who were not co-infected had a positive history of multiple sexual partners (MSP) and unprotected sex compared with 50% in the other category. However, a larger proportion of those co-infected had a history of scarification marks (50%) and multiple blood transfusions (25%). There were no cases of IV drug abuse in any of the groups.

Prevalence of hepatitis infection in HIV

Table 2 shows the prevalence of hepatitis B, hepatitis C, and both among the study subjects based on age, sex, and clinical staging of disease. Of the 260 of those who were HIV positive, thirty were seropositive for HBsAg, six were positive for anti-HCV antibody, and four were positive for both HBsAg and anti-HVC. This gives a prevalence rate of 11.5% for HIV and hepatitis B co-infection, 2.3% for HIV and hepatitis C co-infection, and 1.5% for triple infection including all three viruses. The overall prevalence of both HBV and HCV among the patients was 15.4%.

The prevalence of HIV/HBV/HCV (triple infection) and HIV/HCV co-infection was 100% in those aged less than 40 years. For males and females, the prevalence of HBsAg was 50% each. However, the prevalence of HIV/HCV and HIV/HBV/HCV infection among women was 100%. Based on clinical staging, the prevalence of HIV/HBV co-infection was 17% in those with clinical stage 3 and 84% in those with clinical stage 4. All those with clinical stage 4 had HIV/HBV/HCV co-infection, while the prevalence was 50% for HIV/HCV and 83% for HIV/HBV co-infections in clinical stage 4.

Table 1. Socio-demographic characteristics of study subjects.

Characters	HIV alone n = 220(%)	HIV/Hepatitis co-infected n = 40(%)	Total
Age Group			
20-29	60(27)	5(12.5)	65
30-39	120(54)	30(75)	150
40-49	30(13.6)	5(12.5)	35
50-59	10(4.5)	-	10
Sex			
M	65(29.6)	10(25)	75
***F**	155(70.5)	30(75)	185
Marital Status			
Married	125(56.8)	25(62.5)	150
Single	65(29.5)	5(12.5)	70
Widow/Widower	30(13.6)	10(25)	40
Smoking			
Yes	60(27)	10(25)	70
Alcohol			
Yes	70(31.8)	10(25)	80
Risk Factors			
Unprotected sex	170(75)	20(50)	190
Multiple blood transfusion	30(13.6)	10(25)	40
Scarification marks	60(27)	20(50)	80
IV Drug Abuse	-	-	-

*Odds ratio 1.2,p=0.03.

Characteristics of HIV infection in HIV/Hepatitis coinfection

As shown in Table 3, even though the mean age was lowest for those with HIV/HBV/HCV co-infection and highest for those co-infected with HCV, there was no statistically significant difference between the mean age of the four groups, p value = 0.3. Similarly, the mean weight was highest for those infected with HIV alone, followed by subjects who were co-infected with HBV, and lowest for those infected with all the three viruses. This finding was not statistically significant either, p value = 0.1.

Of subjects with HIV alone, 78% reported history of MSP and unprotected sexual intercourse, while 80% of those co-infected with hepatitis B, 78% of those co-infected with HCV, and 76% of those co-infected with both HB and HCV reported history of MSP. The highest occurrence of multiple blood transfusions was found in those with HIV/HCV and HIV/HBV, 90% and 76% respectively. The lowest prevalence of blood transfusion of 67% was recorded in subjects with HIV alone. Similarly, subjects with HIV/HCV co-infection and HIV/HCV/HBV co-infections had a higher report of scarification marks, 90% and 71% respectively. About 56% of those infected with HIV alone and 65% of those with HIV/HBV also reported scarification marks, respectively.

As shown, there was no statistically significant association between the mean PCV, mean low density lipoprotein (LDL), mean high density lipoprotein, (HDL), mean aspartate aminotransferase

(AST), and alanine amino transferase (ALT) between the groups, p value = 0.39, 0.2, 0.5, 0.2, 0.1, respectively. However, the groups differ significantly only in the mean CD4 count.

As shown, subjects with HIV/HBV/HCV co-infection had the lowest mean CD4 count (106 cells/mm^3), while subjects with only HCV co-infection had the highest value of 260 cells/mm^3. Subjects with HIV alone and those with HIV/HBV co-infection had a mean CD4 count of 171 cells/mm^3 and 121 cells/mm^3, respectively. The P value was 0.03.

Discussion

This study included data on 260 patients seen in an urban center in Nigeria. The prevalence of hepatitis B in this cohort of HIV-positive patients was 11.5%. It was three percent for HIV/HCV

Table 2. Prevalence of hepatitis B and C co-infection with HIV.

Characteristics	**HIV alone n = 220 (%)**	**HIV/HBV n = 30(%)**	**HIV/HCV n = 6 (%)**	**HIV/HBV/HCV n = 4 (%)**	**Total**
Age (years)					
< 40	180 (81)	25 (83)	5 (100)	4 (100)	215
40 and above	40 (19)	5 (17)	-	-	45
Sex					
M	65 (29.5)	15 (50)	-	-	80
F	155 (70.4)	15 (50)	5 (100)	4 (100)	180
Clinical staging					
1	10 (5)	-	-	-	10
2	20 (9)	-	-	-	20
3	55 (25)	5 (17)	3 (60)	-	63
4	135 (61)	25 (83)	2 (40)	4 (100)	167

Table 3. Characteristics of HIV infection in co-infected patients.

Characters	**HIV only n = 220**	**HIV/HBV n = 30**	**HIV/HCV n = 5**	**HIV/HBV/HCV n = 4**	**P value**
Clinical **features**					
Mean age	34.8 ± 7.7	35.1 ± 5.2	36 ± 2.3	31 ± 4	0.3
Mean weight	59.6 ± 13.2	57 ± 4.9	42 ± 3.5	40 ± 4.5	0.1
Risk factors					
% MSP	78	80	78	76	
% Unscreened blood transfusion	67	70	90	76	
% Scarification marks	56	65	90	71	
Laboratory features					
Mean PCV	32.8 ± 5.4	36.5 ±7	43 ± 6.7	34 ± 5.7	0.39
Mean CD4	171 ± 127	127.6 ±97	260.3 ± 23.4	106 ±56	003
Mean LDL	93 ± 38.5	62 ± 51.8	43 ± 11	50 ± 10	0.2
Mean HDL	31.9 ± 23.8	20.3 ± 3.7	52 ± 26	50 ± 25	0.5
Mean AST	30.3 ±21.2	64.8 ± 33.7	34 ± 7	25 ± 2.5	0.2
Mean ALT	50.7 ±45.2	72.6 ± 23.7	85 ± 12	43 ± 3.5	0.1

Note: ANOVA was used to test for association. Significance level < 0.05. MSP (multiple sexual partners) PCV (Packed Cell Volume), CD4 (T lymphocyte count CD4 subset of T Lymphocytes), AST (aspartate aminotransferase), ALT (alanine amino transferase), HDL (high density lipoprotein) and LDL (low density lipoprotein).

co-infection, and the combined prevalence was 16.1% for HIV/HBV/HCV co-infection. Individuals less than 40 years old, females, widows, and widowers were most affected.

The prevalence rates for HIV/HBV co-infection and for HIV/HBV/HCV obtained in this study are higher than the 5.7% and 1.8%, respectively, reported among Brazilian patients [15]. The prevalence of hepatitis B found in this study is also higher than the 6.3% reported among HIV patients in Jos, Nigeria [4]. However, the anti-HVC seroprevalent rate was higher in the studies in Brazil (17%) [6]. Our findings are also similar to findings in Ibadan, Nigeria [16]. In a study in Japan, the seroprevalence rate of HIV/HCV infection was 19% [2]. All these may be a reflection of the seroprevalent rate and the risks in these populations. As discovered in the Brazilian study, IV drug abuse was reported in more than 50% of those with HIV/HCV. This was not the case in our study, as there was no reported case of IV drug abuse. This may still partially explain the difference in our findings. Major risk factors identified for co-infection with all three viruses were multiple and unprotected sexual exposure, multiple blood transfusions, and scarification marks.
However, a higher percentage of those with HIV/HCV co-infection had additional risk factors, especially scarification marks.

The prevalence of HIV was highest in those younger than 40 years (81%). In those co-infected, the prevalence of HIV/HBV, HIV/HCV and HIV/HBV/HCV in those younger than 40 years was 83%, 100%, and 100%, respectively. As revealed by this study, 50% of males and females were HIV/HBV co-infected; however, the prevalence of HIV/HCV in females was 100%. The interaction between HIV and HCV has been well documented, especially as it relates to transmission of HCV/HIV; co-infection increases vertical transmission of HCV, leading to increasing incidence of HCV in newborn babies [9]. This has grave public health consequences. Screening for the two viruses should be routinely done during the antenatal care services because, as suggested by this study, women are at an increased risk of HIV/HBV/HCV co-infection, with an odds ratio of more than one. HIV-positive women should be encouraged to have both HBV and HCV screenings done.

Another finding of this study is that the prevalence of hepatitis co-infection with HIV increases with progression in clinical staging of HIV. For instance, the prevalence of hepatitis B infection in stage 3 was 17%, and in stage 4, it was 83%. A similar pattern of incidence of HIV/HBC co-infection with disease progression was observed in a study in India [17]. The same pattern was observed in those co-infected with both hepatitis B and hepatitis C. This finding may be a reflection of pattern of disease presentation among this cohort of patients. This is supported by the fact that a similar pattern was noticed among individuals infected with HIV alone. However, this was not the case for hepatitis C co-infection. In hepatitis C infection, the prevalence was highest at stage 3 (60%) and lowest (40%) for stage 4. The reason for this is not clear at present, but it could be related to the duration of hepatitis infection or the strength of the immune suppression.

As found in this study, there was an elevation of liver enzymes among all the patient groups, though there was no significant association. The mean level was highest for those co-infected with hepatitis B, followed by those co-infected with hepatitis C, and lowest for those co-infected with both viruses. This finding is corroborated by a study in Lagos [18]. 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 to be encountered in treating patients who were co-infected, especially regarding which HAART regimen to use, how to prevent further hepatic damage, and when to initiate HAART, especially in resource-limited settings with limited ARV options. For example, PIs have no effect on HCV and may cause progressive elevation of AST and ALT [8,9,13]. Additionally, HIV worsens HCV infection, leading to severe fibrosis, cirrhosis and, ultimately, death from liver disease [8,9].

A statistically significant association was found between the mean CD4 count and the hepatitis serological status of the subjects. As shown, individuals with HIV/HCV have the highest mean value of CD4 count, followed by those with HIV alone, while those with HIV/HBV/HCV have the lowest value. This finding of higher mean CD4 count in those with HIV/HCV corroborates our initial finding that those with HIV/HCV tend to present at earlier stages of the disease when immunity may still be strong. This finding of a higher CD4 count in those co-infected with HCV has been observed in a previous work in Jos, Nigeria [19]. In that study, it was shown that there was an increased chance of detecting anti-HVC in the sera of HIV patients whose

immune status is better than those severely immunocompromised.

This study has some limitations. First, because it was a cross-sectional study, it was unable to adequately establish a causal relationship between time of exposure and subsequent infections. Second, it was conducted in a tertiary hospital (a referral center for HIV) and not in a community setting. However, the results can be used to plan for the clinical care of patients with HIV infection.

We have shown that HIV/HBV, HIV/HCV and HIV/HBV/HCV co-infections occur in our environment at rates that are comparable with those of other communities, and the seroprevalence rate may be higher than that among health care workers, who may also be at risk of the hepatitis viruses [20]. Because of the shared transmission pathways, synergistic effects of these viruses and the impact of HBV and HCV on presentation, morbidity, and mortality of HIV, screening for HCV should be included in the armamentarium of investigations to be done pre-HAART. Screening for HBsAg must be ensured, especially in young/middle-aged persons, in widowed/divorced persons, in individuals with a previous history of blood transfusion or scarification marks, and in females.

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