Co-infections of hepatitis B and C with human immunodeficiency virus among adult patients attending human immunodeficiency virus outpatients clinic in Benin City, Nigeria

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Abstract

Background: Hepatitis B and C viral co-infections with human immunodeficiency virus (HIV) are known to affect progression, management, and outcome of HIV infection. This study was aimed to access the prevalence of hepatitis B and C co-infections in HIV-infected adult patients in the University of Benin Teaching Hospital with a view of understanding the gravity of this problem in the local population.

Methods: The descriptive cross-sectional study was carried out on 342 HIV-infected adult patients on highly active antiretroviral therapy attending HIV Outpatients Clinic of University of Benin Teaching Hospital, between April and September, 2011. Patients' sera were screened for hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) using immunochromatographic-based kits. Clinical stage of HIV and CD4+ cell counts were equally evaluated. Data were analyzed using SPSS version 17.

Results: Of the 324 HIV-infected patients screened, 53 (15.5%) were positive for HBsAg, 24 (7.0%) positive for hepatitis C virus antibodies (HCV-Ab), while 2 (0.6%) were positive for both viruses. Seroprevalence of HBsAg was higher in male (17.8%) than in female (14.7%) (χ^2 = 0.49, P = 0.49), while the reverse is the case for HCV-Ab; 7.1% for female and 6.7% for male (χ^2 = 0.02, P = 0.88). Seroprevalences of HBsAg and HCV-Ab were also higher among patients in World Health Organization disease stages 3–4 and patients with CD4+ cell count ≤200 cell/μl compared to those in stages 1–2 and with CD4+ cell count >200 cell/μl.

Conclusion: Co-infection with hepatitis B virus and HCV among HIV/acquired immune deficiency syndrome (AIDS) patients is still a problem in our environment. Screening for these viruses among HIV/AIDS patients will allow for early detection and proper management.

Key words: Benin, co-infection, hepatitis B virus, hepatitis C virus, human immunodeficiency virus/acquired immune deficiency syndrome

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Introduction

Hepatitis B and C co-infection with human immunodeficiency virus (HIV) have assumed a growing concern in public health especially in Sub-Saharan Africa. The three viral infections are not only endemic in the region;[1] they equally share similar routes of transmission such as injection drug use, sexual contact, or from mother to child during pregnancy or birth. Furthermore, there

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are reports suggesting a more rapid progression of viral hepatitis caused by Hepatitis B and C viruses to end-stage liver disease and death in HIV-infected patients.[2-4] The viral hepatitis agents, on the other hand, are reported to increase HIV replication, increase highly active antiretroviral therapy (HAART) related hepatotoxicity and decrease CD4 + cell count.[5,6] Some researchers have equally opined that as antiretroviral therapy programs in this region matures and people living with HIV/acquired immune deficiency syndrome (AIDS) (PLWHA) survives longer, the morbidity and mortality associated with co-infections will become increasingly important.[7]

Globally, 34 million people were living with HIV by the end of 2011. Sub-Saharan Africa remains most severely affected, with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide.[8] In Nigeria, adult prevalence rate was estimated to be 3.7% at the end of 2011 and considering her population size of 162.2 million, an estimated 3.5 million Nigerians are living with HIV/AIDS, ranking Nigeria third among the countries with the highest HIV/AIDS burden in the world, next only to India and South Africa.[9]

Both hepatitis B virus (HBV) and hepatitis C virus (HCV) are equally endemic across African continent, Nigeria inclusive.[1] The prevalence of mono-infection for hepatitis B infection in her general population ranges from 9% to 39%,[10] more than 7% chronic carrier rate considered hyperendemic.[11] The prevalence rate of HCV in Nigeria is also considerably high ranging from 5.8% to 12.3%.[12] Due to the endemic nature of these viruses in the sub-Saharan region and the shared routes of transmission, co-infections of HIV-HBV or HIV-HCV or even the three viruses (HIV-HBV-HCV) are not uncommon. Prevalence of co-infection varies depending on the population studied. An earlier Nigerian study reported 11.9%, 4.8%, and 1% for HIV-HBV, HIV-HCV, and HIV-HBV-HCV co-infections respectively.[13] Prevalence of HIV-HBV and HIV-HCV co-infections among Nigerian prison inmates was also reported as 2.7% and 0.7%, respectively.[14] In Ruwanda, prevalence of HIV-HBV and HIV-HCV co-infections, respectively, were reported as 5.2% and 5.7%.[15] Among HIV-infected pregnant women, prevalence of 4.9% and 0.6% in Uganda; and 2.4% and 4.9% in Ruwanda were recorded for HIV-HBV and HIV-HCV, respectively.[16] The difference in prevalence is thought to be due to the differential efficacies of these viruses to the types of exposures found in the various geographical regions.[17]

Expert guidelines developed in the United States and Europe recommend screening of all HIV-infected persons for infection with HCV and HBV and appropriate management of those found to be chronically infected.[7] In Nigeria, however, HIV-infected patients are not routinely screened for hepatitis viruses. Screening for HBV and HCV are only considered following observed deranged liver enzymes. This practice will not allow for early detection of co-infections and institution of proper management of cases. Again, data on the prevalence of co-infection in our environment are still relatively scarce. This study is, therefore, aimed at determining the prevalence of HBV and HCV co-infections in HIV-infected adult patients in our environment.

Methods

This is a cross-sectional study involving 342 HIV-infected adult patients on HAART attending the HIV Outpatients Clinic of the University of Benin Teaching Hospital between April and September 2011. This hospital is a 700 bed tertiary institution located and serving as a major referral center in the southern part of Nigeria. Informed consents were sought, and consecutively consenting patients were recruited into the study. Bio data and clinical histories were obtained through interviewer-administered structured questionnaires and patients' case notes. For the purpose of this study, participants were categorized into asymptomatic (stage 1 and 2) and symptomatic (stage 3 and 4) in line with World Health Organization (WHO) clinical staging system.[18]

The HIV status of participants was already determined through their plasma samples screened with two different methods namely; Abbott determine HIV 1 and 2 kit which is an *in vitro* visually read immunoassay (Abbot Japan C. Ltd., Tokyo, Japan) and HIV 1 and 2 STATPAK Assay kit, which is an immunochromatographic test for the qualitative detection of antibodies to HIV-1 and HIV-2 in human plasma (CHEMBIO Diagnostic system, Inc., New York, USA). These tests were carried out strictly following the manufacturers' instructions. Both methods have inherent quality controls that were used to validate results. Seropositivity for the two methods was used to classify patients as HIV infected.

Five milliliters of blood was taken from each of the HIV-infected patients and shared into a sterile unanticoagulated and ethylenediaminetetraacetic acid (EDTA) bottles. The former were centrifuged, sera separated, and stored at −20°C and later analyzed for both hepatitis B surface antigen (HBsAg) and anti-HCV using commercially available Clinotech diagnostics HBsAg and anti-HCV test kits (Canada), following the manufacturer's instructions. The test kits were based on immunochromatographic principles and designed to detect HBsAg and anti-HCV qualitatively with sensitivity of 99.8% and specificity of 100%. The specimen on EDTA bottles was used for CD4+ cell count using flow cytometry.

Statistical analysis

Data were analyzed using Data were analyzed using

SPSS Statistics for Windows, Version 17.0 (Chicago, SPSS Inc.). Descriptive data were presented as mean ± standard deviation. Chi-square or Fisher's exact was used where appropriate to test the association. Statistical significance was presumed where $P < 0.05$.

Table 1: General characteristics of participants

Characteristics	Frequency (%)
Gender	
Male	90 (26.3)
Female	252 (73.7)
Age group (years)	
≤20	6 (1.8)
21-30	49 (14.3)
31-40	134 (39.2)
41-50	89 (26.0)
51-60	59 (17.3)
>60	5 (1.5)
Disease stage (WHO)	
1-2	214 (62.6)
3-4	128 (37.4)
CD4+cell count (/μl)	
≤200	174 (50.8)
>200	168 (49.2)

WHO=World Health Organization

Table 2: Seroprevalence of HBsAg, HCV-Ab, HBsAg/HCV-Ab among participants (*n*=342)

Test	Number tested	Number positive (%)	Number negative (%)
HBsAg	342	53 (15.5)	289 (84.5)
HCV-Ab	342	24 (7.0)	324 (93.0)
HBsAg/HCV-Ab	342	2 (0.6)	340 (99.4)

HCV-Ab=Hepatitis C virus antibodies; HBsAg=Hepatitis B surface antigen

Results

A total of 342 HIV-infected adult patients took part in the study comprising 90 (26.3%) males and 252 (73.7%) females giving a male to female ratio of 1:2.8. Their ages ranged between 19 and 69 with a mean age of 40 ± 10 years. 134 (39.2%) of the participants belonged to age group 31–40 years, followed by 89 (20.6%) in the age group 41–50 years, while only 5 (1.5%) were above 60 years. Following the WHO clinical staging system, 214 (62.6%) were in stages 1 and 2 and the remaining 128 (37.4%) were in stages 3 and 4. The CD4+ cell counts of 174 (50.8%) patients were ≤200/μl [Table 1].

Of the 324 HIV-infected patients screened, 53 (15.5%) were positive for HBsAg, 24 (7.0%) positive for hepatitis C virus antibodies, while 2 (0.6%) were positive for both viruses [Table 2]. Seroprevalence of HBsAg was found to be more in male (17.8%) than in female (14.7%), but this was not statistically significant ($\chi^2 = 0.49$, $P = 0.49$) as shown in Table 3. Seroprevalence of HBsAg was also found to hover within the range of 16.3–16.9% in age groups <20 years, 21–30 years, 31–40 years and 41–50 years, but dropped to 11.9% in age group 51–60 years and 0.0% in patients >60 years [Table 3]. Patients presenting with WHO disease stages 3–4 were affected more with hepatitis B infection than those with stages 1–2 (19.5% vs. 13.1%), ($\chi^2 = 2.54$, $P = 0.11$). Furthermore, patients with CD4+ cell count ≤200 cell/μl had a higher HBsAg seroprevalence of 18.4% compared to 12.5% recorded for those with CD4+ cell count >200 cell/μl ($\chi^2 = 2.20$, $P = 0.14$).

Table 4 shows the anti-HCV status of participants. Seroprevalence of anti-HCV was slightly higher in female

Table 3: HBsAg status of participants

Characteristics	HBsAg positive (%)	HBsAg negative (%)	Total	χ^2	*P*	OR
Gender						
Male	16 (17.8)	74 (82.2)	90	0.49	0.49	0.99
Female	37 (14.7)	215 (85.3)	252			
Age group (years)						
≤20	1 (16.7)	5 (83.3)	6	1.76	0.88	
21-30	8 (16.3)	41 (83.7)	49			
31-40	22 (16.4)	112 (83.6)	134			
41-50	15 (16.9)	74 (83.1)	89			
51-60	7 (11.9)	52 (88.1)	59			
>60	0 (0.0)	5 (100.0)	5			
Disease stage (WHO)						
1-2	28 (13.1)	186 (86.9)	214	2.54	0.11	1.03
3-4	25 (19.5)	103 (80.5)	128			
CD4+cell count (/μl)						
≤200	32 (18.4)	142 (81.6)	174	2.20	0.14	0.97
>200	21 (12.5)	147 (87.5)	168			

WHO=World Health Organization; OR=Odds ratio; HBsAg=Hepatitis B surface antigen

Table 4: HCV-Ab status of participants

Characteristics	HCV-Ab positive (%)	HCV-Ab negative (%)	Total	χ^2 or Fisher's exact	*P*	OR
Gender						
Male	6 (6.7)	84 (93.3)	90	0.02	0.88	1.01
Female	18 (7.1)	234 (92.9)	252			
Age group (years)						
≤20	0 (0.0)	6 (100.0)	6	4.24	0.43	
21-30	3 (6.1)	46 (93.9)	49			
31-40	13 (9.7)	121 (90.3)	134			
41-50	7 (7.9)	82 (92.1)	89			
51-60	1 (1.7)	58 (98.3)	59			
>60	0 (0.0)	5 (100.0)	5			
Disease stage (WHO)						
1-2	14 (6.5)	200 (93.5)	214	0.20	0.66	1.03
3-4	10 (7.8)	118 (92.1)	128			
CD4+cell count (/μl)						
≤200	14 (8.0)	160 (92.0)	174	0.88	0.35	0.95
>200	10 (6.0)	158 (94.0)	168			

WHO=World Health Organization; OR=Odds ratio; HCV-Ab=Hepatitis C virus antibodies

patients (7.1%) than males (6.7%) (χ^2 = 0.02, *P* = 0.88). Age group 31–40 years recorded the highest prevalence (9.7%), followed by 41–50 years (7.9%) and 21–30 years (6.1%), while patients that were ≤20 years and >60 years both recorded 0.0%. Patients presenting at stages 1–2 of WHO clinical staging had a nonsignificant lower anti-HCV seroprevalence of 6.5% than those at stages 3–4 (7.8%) (χ^2 = 0.20, *P* = 0.66), just as patients with CD4 + cell count >200 cell/μl had a lower rate of 6.0% compared to 8.0% recorded for those with ≤200 cells/μl (χ^2 = 0.88, *P* = 0.35) as shown in Table 4.

Discussion

This survey aimed at determining the prevalence of hepatitis B and C infections in HIV-infected adult patients in the University of Benin Teaching Hospital revealed that 15.5% of our patients were HBsAg positive. In comparison with earlier studies carried out in Nigeria, this figure is higher than 11.9% reported in Ibadan,[13] 6.6% in Nasarawa[14] and 2.7% in Ado Ekiti,[19] but lower than 20.6% documented in North Central Nigeria,[20] 25.9% in Jos,[21] and 28.4% in Lagos.[22] Figures as high as 51.9% and 70.5% have equally been documented in Lagos[23] and Kano,[24] respectively, both being the most populated and highly commercially active cities in Nigeria. Our finding is also comparable to 17.3% reported in Tanzania,[25] but lower than 6.0% reported in South Africa. Again from our study, 7.0% of HIV-infected patients equally harbor HCV. This is comparable to 8.2% reported in Abuja, Nigeria,[26] but contradicts 14.7% reported in Lagos,[22] no case of HIV/HCV co-infection reported among asymptomatic pregnant women attending antenatal clinic[27] and 4.4% among HIV-infected patients[12] documented in earlier studies carried out in Benin, Nigeria.

Although co-infection with HBV from this study is higher than with HCV, a recurring finding in almost all the studies in Nigeria, the prevalence of co-infection for both viruses is still considerably high. This is understandably so since these viruses on their own are not only endemic in our environment, but also sharing similar routes of transmission. Apart from confirming the endemicity of co-infections by both viruses in our environment as reported by previous researchers, our finding also underscores the need to intensify efforts to get HIV infected individuals routinely screened for both HBV and HCV in Nigeria as recommended by expert guidelines developed in United State and Europe.[7] Such guideline, if adopted, will lead to early detection of cases of co-infection, proper adjustment of management strategies and better outcome.

Dual co-infection with HBV and HCV has been documented before in similar studies. Our study revealed that 0.6% of our patients had dual co-infection, a figure comparable to 0.3% recorded in Kenya[28] and 1.0% reported in Ibadan, Nigeria.[13] Relatively higher prevalence of HIV/HBV/HCV co-infections has been documented in Lagos (3.9%)[22] and North Central Nigeria (7.2%).[20] A Tanzanian study reported 3.9% prevalence of HIV/HBV/HCV co-infections.[25] Dual co-infection with HBV and HCV in PLWHA is an interesting observation made in this study although only two case (0.6%) were detected, comprising 34-year-old male and 41-year-old female, both presenting in stage 4 with CD4+ count <100 cell/μl. Further studies involving the greater number of dual co-infection will be enriching and therefore advocated.

Male HIV-infected patients were affected more by HBV and females by HCV from our study. Similar finding was reported in Lagos, Nigeria,[23] and Tanzania.[25] There are, however, conflicting reports regarding male or female predominance for co-infection with either of these

viruses.[20,29,26] The reason for this is not obvious, but may be due to the epidemiological differences in the different study populations and variations in methodology. Age-specific prevalence of HBV co-infection from this study was higher in the younger patients (<20–50 years) than their older counterpart (51 to >60 years). This may be due to the fact that the younger patients are more likely exposed to risky behaviors than the older ones. This pattern of presentation was, however, lacking for HIV/HCV co-infection where prevalence rose with age for a while, peaked at 31–40 years before declining again.

Regarding clinical stage and CD4+ cell count, prevalence of both HIV/HBV and HIV/HCV was higher in stages 3–4 and CD4+ <200 cell/μl, respectively, than observed in stages 1–2 and CD4+ ≥200 cell/μl. These higher prevalence rates observed in these groups are, however, not statistically significant. This is similar to findings from other studies.[30,31]

Conclusion

Co-infection with HBV and HCV among HIV/AIDS patients is still a problem in our environment as 15.5% and 7.0% of these patients were seropositive for HBV and HCV respectively; and 0.6% for both viruses. Screening for these viruses among HIV/AIDS patients is, therefore, advocated as this will allow for early detection and proper management.

Limitation

The window period of the Australian antigen, time between the disappearance of HBsAg and appearance of anti-HBs was not considered in this study. IgM anti-HBc serological marker would have been very useful in detecting those in the window period, but this was not done in the study. HBV DNA would have as well equally helped in this regard but was not tested in the population due to lack of facility for the test and high cost of sending samples out for such test.

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