Full Length Research paper

A survey of hepatitis B and C virus prevalence in human immunodeficiency virus positive patients in a tertiary health institution in North Eastern Nigeria

Ballah Akawu Denue¹*, Babajide Ajayi², Abubakar Usman Abja³, Abubakar Abdullahi Bukar⁴, Cecilia Akawu⁵, Ernest Ekong⁶ and Mohammed Bashir Alkali⁷

¹Department of Medicine, University of Maiduguri Teaching Hospital, Maiduguri, Borno State Nigeria.
 ²Department of Immunology University of Maiduguri Teaching Hospital, Maiduguri, Borno State Nigeria.
 ³Department of Haematology University of Maiduguri Teaching Hospital, Maiduguri, Borno State Nigeria.
 ⁴Department of Haematology University of Maiduguri Teaching Hospital, Maiduguri, Borno State Nigeria.
 ⁵Department of Geography University of Maiduguri, Maiduguri, Borno State Nigeria.
 ⁶AIDS Preventive Initiative in Nigeria (APIN), Nigeria.
 ⁷Department of Medicine University of Maiduguri Teaching Hospital.

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Co-infection of hepatotropic virus(es), with HIV has been associated with a reduced survival rate, an increased risk of progression to severe liver disease, and an increased risk of hepatotoxicity associated with active antiretroviral therapy. Information regarding prevalence of HBV and HCV co-infection with HIV in Nigeria is limited. This study was designed to determine the seroprevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV), and the impact of co-infection on baseline serum alanine transaminase (ALT), CD4+ T lymphocyte (CD4) count, and plasma HIV-RNA (viral load) in a cohort of HIV-infected Nigerians. Patients confirmed to be positive for HIV infection by Western blot analysis were consecutively recruited into the study from Infectious Disease Clinic, General Out-patient Department and Medical Wards of University of Maiduguri Teaching Hospital, Nigeria. Demographic data and pre-treatment laboratory results (hepatitis B surface antigen (HBsAg), and HCV antibodies (anti-HCV), ALT, CD4 count and viral load) were analysed. A total of 569 HIV-infected patients (male: female ratio, 1:1.4) were consecutively recruited. HBsAg was present in 12.3%; anti- HCV in 0.5% and both markers was not present in any patients. HBsAg prevalence was 12.3% in both male and females, while anti-HCV was detected in 0.8% in males and 0.3% females. HIV-infected patients alone had a higher mean baseline CD4 count compared to those without anti- HCV or HBsAg (181 vs. 117 cells/mm³, respectively; p = 0.01). Serum ALT was higher among patients co-infected with HBsAg or anti-HCV than only HIV infected (37 vs. 34 International Units (IU), respectively p = 0.1). The high frequency of HBsAg confirms the need for routine screening for these markers in HIV-infected patients in our setting. CD4 count was significantly lower, in patients with prior exposure to hepatitis B or C, while ALT was slightly higher among those positive for HBV or C infection. These findings are pointer to the importance of testing for HBV and HCV in all HIV-infected persons in our setting.

Key words: Hepatitis B, hepatitis C, CD4, HIV.

INTRODUCTION

Chronic viral hepatitis due to hepatitis B virus (HBV) and hepatitis C virus (HCV), as well as infection with human

immunodeficiency virus (HIV) are global public health problems (Alter, 1997; World Health Organization, 1998 Geneva:; Soriano et al., 2004). It has been estimated that about 2 billion people have been infected with hepatitis B virus (HBV) and 350 million have chronic lifelong infection. The prevalence of hepatitis C virus (HCV) is

^{*}Corresponding author. E-mail: d_akawu@yahoo.co.uk.

is also high and it is estimated that about 170 million people are chronically infected while 3 to 4 million people are newly infected every year (http/www.who.int/media centre/fact sheet/fs 164/en/accessed; Merican et al., 2000) A considerable proportion of these patients will progress onto cirrhosis and hepato-cellular carcinoma (Guan et al., 1995; Furusyo et al., 2002).

Worldwide, HIV is responsible for 38.6 million infections estimated at the end of 2005 as (http://www.unaids.org/en/HIV data/2011GlobalReport/). An estimated one-third of deaths in HIV patients are directly or indirectly related to liver disease. Liver diseases in HIV infected persons can occur due to hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfections, chronic alcoholism, hepatic tuberculosis, or due to the effects of antiretroviral therapy (ART) (Kumarasamy et al., 2005; Rathi et al., 1997).

Since the principal routes for HIV transmission are similar to that followed by the hepatotropic viruses, as a consequence, infections with HBV and HCV are expected in HIV infected patients. Co-infections of HBV and HCV with HIV have been associated with reduced survival, increased risk of progression to liver disease and increased risk of hepatotoxicity associated with antiretroviral therapy. The reported co-infection rates of HBV and HCV in HIV patients have been variable worldwide depending on the geographic regions, risk groups and the type of exposure involved (Alter, 2006; Rockstroh, 2003: Dodig and Tavill, 2001; Tien. 2005; Sungkanuparph et al., 2004). In Europe and USA, HIV-HBV coinfection has been seen in 6 to 14% (Alter, 2006; Rockstroh, 2003) of all patients while HIV-HCV coinfection has been variably reported ranging from 25 to almost 50% (Dodig and Tavill, 2001; Tien, 2005) of these patients. Evidence of exposure to HBV and HCV has been found in 8.7 and 7.8%, respectively, of HIV patients from Thailand (Sungkanuparph et al., 2004) in Southeast Asia. The HIV sero-prevalence in adult Nigerians is estimated at 5%. Viral hepatitis and HIV/AIDS having become so intertwined have constituted a major public health problem in the country. However in spite of this, very little information on viral hepatitis and HIV-coinfection is available. The few reports documented were on HBV-HIV co-infection (Halim et al., 1992; Baba et al., 1998) and HIV /HBV-HCV co-infection in low risk group (Egah et al., 2007). With this background, we set out to determine the prevalence of hepatitis B and C virus infections in HIV-positive patients coming to a tertiary care hospital located in North Eastern Nigeria.

PATIENTS AND METHOD

Study area

The study was conducted in the Department of Medicine, University of Maiduguri Teaching Hospital, Borno State. This is a 500 bedded hospital designated as a Centre of Excellence for infectious diseases and provides primary, secondary and tertiary services for the North Eastern part of Nigeria. It also caters for the neighbouring countries such as Cameroon, Niger and Chad Republics. Maiduguri, the capital of Borno State, is situated in the North Eastern Nigeria and the largest settlement near the Lake Chad, located on the fringe of the Sahara desert between longitude 11°8E and 14°4' E and latitudes 10°2'N 13°4'N.

Study participants

Patients confirmed to be positive for HIV infection by Western blot analysis were recruited into the study from Infectious Disease Clinic, General Out-patient Department and Medical Wards of the Hospital from January to December 2010. Informed consent was obtained from each participant with the assurance that all information would be treated with utmost confidentiality. Using a structured, pre-evaluated questionnaire, information was obtained on demographic, clinical manifestation, blood transfusion, sexual behaviour and intravenous drug use. Seroprevalence of HBsAg and Anti-HCV antibodies in apparently, HIV-negative blood donors and those that presented for pre-marital HIV counselling and testing during the same period was also analysed for comparision with the prevalence of hepatitis markers in HIV positive individuals.

Viral diagnosis

Five millilitres of blood were obtained from each participants, the blood were allowed to clot and spun at 1000 xg for 10 min. The serum samples were separated into 2 ml cryorials containers and stored at -20°C until required for testing. The coded samples were anonymously tested using enzyme linked immunosorbent assay kits at a later date for the presence of HBsAg and HCV antibodies (DIA, PRO, Diagostic Bioprobes Sri, via columella no 20128 milano-Italy).

RESULT

A total of 569 patients were consecutively recruited into the study comprising 235 (41.5%) males and 333 (58.5%) females, with male to female ratio of 1:1.4. The mean age of both sexes was 34.2 ± 10.1 (14 to 81) years. Male patients were older than females, 37.7 ± 10.8 (14 to 81) and 31.8 ± 8.7 (14 to 72) years respectively (p<0.05). The presumed mode of acquiring HIV infection was through heterosexual contact in all the participants.

Data was available for 291 prospective blood donors during the same period. It was presumed that these blood donors represent the general population and they are exposed to similar risk as the general population. There were 249 males and 42 females. The mean age of the donors was 27.8±5.9 (18 to 52).

Prevalence of viral co-infection in HIV positives

The frequency of HBsAg co-infection in HIV+ cohort as reflected in Table 1, was 12.3% (70 in 569) compared to HCV antibody prevalence of 0.5% (3 in 569) with P value < 0.05. Triple infection with both HBsAg and HCV was not seen in any HIV patient.

Variable	HBsAq {n(%)}	HCV {n(%)}
HIV patients (n=569)	70 (12.3)	3 (0.5)
Males (n=236)	29 (12.3)	2 (0.8)
Females (n=333)	41 (12.3)	1 (0.3)
Controls (n= 291	15 (5.2)	4 (1.4)
Males (n=249)	12 (4.8)	4 (1.6)
Females (n=42)	3 (7.1)	0 (0)

 $\ensuremath{\text{Table 1.}}$ Seroprevalence of HBsAg and anti-HCV antibodies in HIV positive patients.



Figure 1. Age-related distribution of HBsAg and HCV in HIV positive patients.

The frequency of HBsAg co-infection in blood donors was 5.2% (15 in 291) compared to HCV antibody prevalence of 1.4% (4 in291) with P < 0.05) as depicted in Table 1. Co-infection of infection with both HBsAg and HCV was not seen in any blood donor.

Taking the prevalence's of co-infection in HIV-positive with hepatitis viruses based on gender into accounts, HIV/HBV co-infection was the same in both sexes, it was seen in 29 of 236 (12.3%) males and in 41 of 333 (12.3%) females respectively (P>0.05). HIV co-infection with HCV antibody was seen in 2 of 236 (0.8%) males and in only 1 of 333 (0.3%) females.

The frequency of HBsAg was 4.8% (12 of 249) and 7.1% (3 of 42) in male and female blood donors

respectively; the prevalence of HCVab was 1.6% in males and 0% in females.

Figure 1 shows age related prevalence of HIV coinfection with HBsAg and HCV antibodies. Individuals of age group 10 to 19 years had the highest prevalence of HBsAg (21.4%). This was followed by those of age-group 60 to 69 years (16.7%) and 14.4% in age group 40 to 49 years, while age-group 40 to 49 years has the highest prevalence of HCVab with 0.8% followed by age-groups 20 to 29 and 30 to 39 years with prevalence's of 0.6% and 0.4% respectively.

Table 2 shows immuno-virological parameter of the participants. The mean CD4 count for the HBsAg/HCVab negative was 181 cells/µl and it was significantly higher

Biochemical characteristics	HIV+	HIV+/HBsAg+/HCVab	p-value
ALT	34.7±12.5	37.3±9.6	0.2
Immunological characteristics			
Mean CD4+T-cells(cells/µl)	181.34 ± 70.8	117±82.23	0.01
Virological characteristics (copies/ml)	314561.43±4881.93	617272.38±1045.33	0.03

Table 2. Biochemical, immunological and virological characteristics of patients.

ALT, CD4 and viral load are expressed in mean values.

than those of the positive (117 cells/ μ l) (p < 0.05). On the contrary, the viral load of HBsAg/HCV negative had significantly lower values than HIV monoinfection (P<0.05). ALT levels did not show any significant difference between the two groups of patients (P>0.05).

DISCUSSION

According to WHO estimates, the global burden of HIV, HCV and HBV is 33.2 million, 170 million and 400 million. respectively. Knowledge of the prevalence and distribution of blood borne viruses and sexually transmitted diseases (STDs) in different parts of the world, and particularly in Africa, is important for the planning of preventive measures and the development of vaccination programmes. More females than males presented for care during the study period, but majority of blood donors were males, all the females were pregnant autologus donors. This gender inequality in presentation for therapy is consistent with the sex distribution documented in the majority of treatment centres particularly in the first decade of antiretroviral therapy. A potential explanation for more females at our centre is that women present for care after positive HIV test on their sick children, death of their husband, or perhaps they are more sensitive to changes in their health and may be socially conditioned to seek and receive assistance for their sickness. This, however, does not translate to more women are infected with HIV in our population, as study in Nigeria actually found that more men were afflicted with HIV/AIDS (Ola et al., 2005).

When asked about the risk factors concerning the viral infections, none of the study subjects reported the history of intravenous drug use or multiple sexual partnership. It is well known that HIV/HBV co-infection is linked most often to sexual intercourse (both heterosexual and men who have sex with men (MSM), followed by IDU, while HIV/HCV co-infection has predominantly been associated with a non-sexual parenteral route of transmission of blood or blood products, particularly IDU (Thomas et al., 1994; Gilson et al., 1997; Kellerman et al., 2003; Rodríguez-Méndez et al., 2000; Sherman et al., 2002). In our study, absence of triple HIV/HCV co-infection as none of the

subjects reported the history of intravenous drug use, neither was needle tract was noticed in their limbs. These results are in agreement with previous reports that HCV is not efficiently transmitted by perinatal or sexual exposure, which are major modes of transmission for HBV and HIV (Kellerman et al., 2003; Rodríguez-Méndez et al., 2000; Sherman et al., 2002). HCV is predominantly found in persons who have had percutaneous exposure to blood products and IDU in particular (Wasley and Alter, 2000). Studies had demonstrated that IDU is the most important factor associated with triple infections with HIV/HBV/HCV in urban HIV-infected populations. It has been reported that the prevalence of HIV-HCV coinfection among IDUs can surpass 90%, highlighting the need for special attention to populations with IDU for screening viral co-infections with HIV and HBV/HCV (Maier and Wu, 2002; Aceijas and Rhodes, 2007).

The co-infection prevalence of 12.3% for HIV and HBV is a pointer to the fact that HBV is a major threat to HIV/AIDS patients in Nigeria, as reported in other parts of the world (Weber et al., 2006) The HBV co-infection rate in this study is similar to prevalence of 11.9% documented in southwestern part of Nigeria,(Otegbayo et al., 2008) but higher than the 9.7% reported in healthy urban population Northern region (Sirisena et al., 2002) but lower than the 25.9% reported in HIV positive in the same region (Uneke et al., 2005). The factors driving these regional differences are unclear. No gender difference in prevalence of HBV was observed in this study. This finding is in contrast with higher prevalence in male, that observed that a high proportion of HBV infections in sub-Saharan Africa is acquired vertically or horizontally (from family members and other children) before the age of 5 years (Davis et al., 1989). Since boys have a predilection for aggressive sports and plays that may result in injury with bleeding, they may be more predisposed to horizontal HBV transmission. Further, societal acceptance of multiple sexual partners for men may contribute to the higher HBV prevalence among HIV-infected men (Zhou et al., 2007).

Anti-HCV co-infection was detected in 0.5% of the patients in this study. In an earlier study, HCV co-infection based on plasma HCV RNA quantification was detected in 8.2% of HIV-infected patients in Northern Nigeria (Agwale et al., 2004). However, cross-study

comparisons may be misleading because of the differences in HCV detection techniques. Quantifiable plasma HCV RNA is present only in patients with active HCV replication. In contrast, anti-HCV can be detected in patients with previous HCV exposure, including those with ongoing HCV replication and those whose immune responses curtailed viral replication. There may be very rare cases of falsely negative anti-HCV in patients with advanced immunosuppression (Mphahlele et al., 2006; Bonacini et al., 2001). In the current study, although the absolute number (n = 3) was relatively small for analysis, the rates of anti-HCV detection were comparable in males (0.8%) and females (0.3%). Although the association between HCV positivity and CD4 count shows conflicting reports (Greub et al., 2000; Anderson et al., 2004; Hershow et al., 2005) It would appear that the immunological status of monoinfection is higher than HBV/HCVab coinfection, as evidenced by the higher CD4 counts in HIV monoinfected than HIV-coinfected with HBV/HCVab. Contrary to observations made Idoko et al in the North-central (Idoko et al., 2009) and Ortegbayo et al in South-western part of Nigeria (Otegbayo et al., 2011). The viral load was higher in HBV/HCVab than HIV monoinfected. The mean values of transaminases (ALT) among HBV/HCVab coinfected patients, was similar to HIV monoinfected in this study.

HCV by itself has not been shown conclusively to be an independent risk factor for more rapid CD4 decline, although it has been associated with increased occurrence of AIDS-defining events (Rockstroh et al., 2005; Stebbing et al., 2005). Studies enrolling a larger number of subjects are needed to elucidate these potential associations further. The limitations of this study are that plasma HCV-RNA was not quantified in patients who had anti-HCV, making it impossible to distinguish active HCV infection from those that have spontaneously cleared the infection.

Conclusion

The high frequency of HBsAg confirms the need for routine screening for these markers in HIV-infected patients in our setting. Significantly lower CD4 and higher viral load, was observed in patients with prior exposure to hepatitis B or C, while ALT was similar among those positive for HBsAg/HCVab and HIV mono-infection. These findings underscore the importance of testing for HBV and HCV in all HIV-infected persons in our setting.

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