ORIGINAL ARTICLE

Study of Hepatic functions and Prevalence of Hepatitis B surface Antigenaemia in Nigerian children with human immunodeficiency virus infection

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Abstract

Background: *HIV and hepatitis B virus (HBV) co-infected patients have a significantly increased risk of dying from liver disease especially after starting treatment with highly active antiretroviral therapy. We aim to determine the prevalence of hepatitis B surface antigenaemia in HIV-infected children and their significance in relation to hepatic functions.*

Method: *Two hundred and eighty four HIV-infected children aged between 4 mouths to 15 years attending the Paediatric infectious disease clinic of University of Maiduguri Teaching Hospital (UMTH) Maiduguri, Nigeria from September 2007 to December 2007 were the subject for this study. Two hundred and seventy six HIV-negative children with served as age and sex-matched controls. They underwent investigations to evaluate the liver function (serum alanine transferase (ALT), alkaline phosphotase (ALP) and bilirubin) and the prevalence of hepatitis B surface antigen (HBsAg) using ELISA technique.*

Results: *Prevalence of HBsAg of 19% and 9.4% was observed among HIV-infected children controls (p= 0.004). Serum ALT and bilirubin concentrations were significantly higher in the HIV-infected group compared to the controls, (p<0.05). HIV-infected children with HBs antigenaemia had significantly higher ALT and ALP concentrations compared to those without HBs antigenaemia (p<0.05).*

Conclusion: *These findings point to the high risk of HBV infection and continual paranchymal damage in HIV-infected children before commencing ART. Vaccination against HBV should eliminate this risk. Ideally HBV serology should be evaluated before starting ART to help guide therapeutic decision-making.*

Key words: *Hepatic functions, Hepatitis B surface Antigen, HIV-infected children.*

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Introduction

Diseases of the hepatobiliary system as evidenced by jaundice, hepatomegaly and deranged liver function tests constitute a major problem in patients with human immunodeficiency virus (HIV) infection.[1-2] Liver diseases in HIV-infected patients can occur due to HIV itself, hepatotropic viruses (e.g. hepatitis B and C viruses), sepsis, hepatic tuberculosis, malnutrition malignancies or due to the effects of antiretroviral therapy (ART).[1-3] An estimated one-third of deaths in HIV-infected patients are directly or indirectly related to liver diseases and liver enzymes abnormalities have been reported in 20-93% of HIV-infected population.[4]

Due to common routes of transmission, geographical region and risk group, HIV and HBV infections frequently occur as concomitant infections and are major public health problems in sub-Saharan Africa.[1,2,5] More recently, it was reported that HIV and HBV co-infected patients have a significantly increased risk of dying from liver disease. This risk was found to increase after starting treatment for HIV using highly active antiretroviral therapy (HAART).[6] In addition; there have been reports of hepatotoxicity [7] and reactivation [8,9] of HBV infection in co-infected individuals, when using HAART. This led us to study the prevalence of hepatitis B surface antigenaemia in children with HIV infection and their significance in relation to hepatic functions prior to initiation of ART.

Materials and Methods

Two hundred and eighty four newly diagnosed HIV-infected children, ART-naive attending the paediatric infectious disease unit at the University of Maiduguri Teaching Hospital (UMTH) Maiduguri, Nigeria, from September 2007 to December 2007 were the subject of this study. They represented the HIV-infected children in north-eastern Nigeria. Two hundred and seventy six apparently normal, HIV-negative children served as age and sex-matched controls. Children with hepatitis

C virus infection and those on isoniazide were excluded from the study. The study was approved by the UMTH ethical committee. Parents'/caregivers' written consent were also obtained for participation in the study after pre-test counselling.

All the study children were subjected to thorough history taking, with special emphasis on previous history of jaundice, injections, blood transfusions and history of medication (such as ART and anti-tuberculosis). Detail clinical examination was performed, and size of liver and spleen were recorded. Blood samples were collected for estimation of liver enzymes (serum alanine transferase (ALT), alkaline phosphotase (ALP)) and bilirubin concentrations. Based on liver enzyme results, bilirubin levels and considering the upper limits of normal, patients were classified into having established liver disease or normal. All the serum samples of the study population were tested for the presence of hepatitis B surface antigen (HBsAg) using ELISA technique (Wellcozyme HBsAg commercial kits) according to manufacturer's protocol.

Data were analysed using the *t*-test for comparison between study groups when data were normally distributed and Wilcoxon test when they were not. Values were expressed as mean ±standard deviation. A p value of <0.05 was considered significant. Tables were used appropriately for illustration.

Results

Fifty four out of the 284 HIV-infected children were HBsAg positive (19%), while 26 out of 276 controls were HBsAg positive (9.4%) (p= 0.004). Table I shows the liver functions and HBsAg status of HIV-infected children and controls. Serum bilirubin ALP and ALT concentrations were significantly higher in the HIV-infected group compared to the controls, (p<0.05). Comparison of liver functions between two groups of HIV-infected children with and without HBs antigenaemia is showed in table II. HIV-infected children with HBs antigenaemia had significantly higher ALT and ALP concentrations compared to those without HBs antigenaemia (p<0.05).

Table I: Liver functions and HBs antigenaemia in the study population (mean ±SD)

	Age (Years)	Bilirubin (µmol/l)	ALT (IU/l)	ALPHBsAg (IU/l)	positive
HIV-infected (n=284)	4.02±3.42	21.6±3.0˙	15.2±5.1˙	61±6.154 (19%)˙	
Controls (n=276)	4.10±3.25	16.1±2.2	10.9±1.472±7.326 (9.4%)		

˙=*P <0.05*

Table II: Liver functions in HIV-infected children with and without HBs antigenaemia

(Mean ±SD)

	Bilirubin (µmol/l)	ALT (IU/l)	ALP (IU/l)
HBsAg positive (n=54)	22.9±2.1˙	16.7±3.3˙	84±5.1˙
HBsAg negative (n=230)	19.7±1.0	14.6±3.5	60±2.8

˙=*P <0.05*

Discussion

This study shows that HBsAg sero-positivity was greater among HIV-infected children than HIV negative controls. This is consistent with findings of Treitinger *et al*,[10] and Mustapha *et al* [11]. The fact that HIV and HBV share common modes of transmission (predominantly blood and blood products, high risk sexual behaviours and mother-to-child transmission) contributes to the significant association between HBV and HIV.[1,2,10,11]

An elevated serum ALT, ALP and bilirubin concentrations in HIV-infected children compared to control children denotes the presence of mild chronic hepatocellular dysfunction which may be due to HIV itself, hepatotropic viruses, or due to the toxicities of ART.[1, 2] All patients in this study were antiretroviral-naïve. When the liver enzymes (ALT & ALP) and bilirubin concentrations in HIV-infected children were compared among HBsAg positive and HBsAg negative groups, it was found to be significantly higher in the former group indicating that HIV-infected children with positive HBsAg have more deterioration of live function. This findings is in agreement with other result which indicates that HIV infection has been found to exacerbate liver disease, with a previous study reporting death from liver failure in four of five HIV-positive HBV carriers, compared with two of six HIV-negative HBV carriers.[12] More recently, it was reported that HIV and HBV co-infected patients have a significantly increased risk of dying from liver disease. This risk was found to increase after starting treatment for HIV using HAART.[6] Unfortunately, in most resource limited setting patients are not routinely investigated for HVB infection prior to initiation of HAART and most first line ART regimes include lamivudine and if HBV-HIV co-infection is present, acquisition of HBV resistance to lamivudine is high.[6]

In conclusion, these findings point to the high risk of HBV infection and continual paranchymal damage in HBV-HIV co-infected children before initiation of ART. In such a situation, missed diagnosis of HBV-HIV co-

infection would further worsen the already relatively unfavourable prognosis of children with HIV/AIDS in sub-Saharan countries. Ideally HBV serology should be evaluated before starting ART to help guide therapeutic decision-making.

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