



Original Research Article

Study of Hepatitis B virus and Hepatitis D virus infection in HIV infected patients and its correlation with CD4 counts in a tertiary care hospital

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ABSTRACT

Keywords

Hepatitis B virus and Hepatitis D virus
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Hepatitis B virus is one of the world's most important infectious diseases, with one third of the world's population having been infected. It is important to identify HBV/HDV co-infections to reduce the morbidity and improve quality of life in HIV positive patients. The present study was performed to find out Hepatitis B virus and Hepatitis D virus infection in HIV infected patients and its correlation with CD4 counts in a tertiary care hospital. Total number of HIV patients included in the study were three thousand one hundred and forty two (3142). Out of these hundred and six (106) were positive for HBsAg. CD4 counts range was 20-1217 cells/mm³ and mean CD4 count was 342 cells/mm³. One patient had chronic hepatitis D infection as IgG HDVAb was positive in serum. The present study emphasize that a uniform protocol should be formed to screen every HIV/AIDS patient and their co-partners for Hepatitis B and hepatitis D virus for early detection and management of these co-infection beside HIV for better prognosis and survival of these patients.

Introduction

Hepatitis B virus is one of the world's most important infectious diseases, with one third of the world's population having been infected, approximately 400 million being chronically infected and one million dying of the complications of HBV infection each year¹. It has been estimated that ~5% of HBV carriers are also coinfecting with HDV, resulting in ~15 million persons infected with HDV worldwide².

Co-infections with viral hepatitis in individuals living with HIV or acquired immunodeficiency syndrome (AIDS) are of great concern due to their association with unfavorable outcomes and failure of antiretroviral therapy³.

It is important to identify HBV/HDV co-infections to reduce the morbidity and improve quality of life in HIV positive

patients. The literature regarding the prevalence of co-infection with HBV and HDV in HIV infected patients in India is sparse. Hence, the present study was performed to find out hepatitis B virus and Hepatitis D virus infection in HIV infected patients and its correlation with CD4 counts in a tertiary care hospital.

Materials and Methods

Study was conducted in the department of Microbiology of P.G.I.M.E.R and Dr. Ram Manohar Lohia Hospital, New Delhi. Study was performed over a period of one year from December 2011 to November 2012. Inclusion criteria was patients positive for HIV and giving consent for the investigations. 6 ml of the blood was collected from confirmed HIV-positive patients into plain and EDTA (ethylenediamine tetraacetic acid) vacutainer tubes. Serum was separated from the plain vacutainer and used for serological testing. Blood in EDTA vacutainer was used for CD4 counts testing.

Testing for hepatitis B surface antigen (HBsAg) was performed using Monolisa HBs Ag ULTRA, Bio-Rad, France. All HBsAg positive samples were further tested for HBeAg (HbeAg- Wantai, Beijing, China), IgM HBcAb (Wantai, Beijing, China), total (IgM+IgG) HBcAb (Wantai, Beijing, China), total (IgM+IgG) HBeAb (Wantai, Beijing, China). IgG anti-HDV (Wantai, Beijing, China) was also detected using ELISA technique. CD4 count was performed using FACS Calibur, BD.

Results and Discussion

Demographic profile

Total number of HIV patients included in the study were three thousand one hundred

and forty two (3142). Out of these hundred and six (106) were positive for HBsAg. So, the percentage of HIV positive patients who were infected with hepatitis B virus infection was found to be 3.37 %. Amongst, 106 HBsAg positive patients, 88 were male and 18 were female. The age ranges of the HIV positive patients was found to be 22-65 years. Average age was 36 years. Amongst 106 patients, 86 patients were on ART. All 106 patients had heterosexual mode of transmission.

CD4 counts range was 20-1217 cells/mm³ and mean CD4 count was 342 cells/mm³. Patients were further divided into groups (<200, 200-350, >350-500 and >500) based on their CD4 counts. (Table 1). Average CD4 count for various serological markers of hepatitis B and hepatitis D is calculated (Table 2)

Serological staging of Hepatitis B positive patients

Acute hepatitis B infection - Acute hepatitis B virus infection was present in 10 patients. These patients were positive for HBsAg and IgM HBcAb.

- Acute hepatitis B infection with high infectivity- It was present in 2 patients. These were positive for HBeAg also.
- Acute hepatitis B infection with low infectivity- It was present in 8 patients. These were negative for HBeAg.

Chronic hepatitis B infection- Chronic hepatitis B infection was present in 96 patients. These patients were positive for HBsAg and IgG HBcAb.

- Chronic hepatitis B infection with high infectivity- It was present in 37 patients. These patients were positive for HBeAg.

- Chronic hepatitis B infection with low infectivity- It was present in 59 patients. 28 of these patients were positive for HBeAb and rest 31 were negative for HBeAb.

Serological staging of hepatitis D positive patients

One patient had Chronic hepatitis D infection as IgG HDVAb was positive in serum. He was negative for HBeAg.

Prevalance

Amongst the 3142 HIV positive patients studied, the prevalence of HBsAg was found to be 3.37 %. This is comparable to prevalence of 2.61% in a study done in New Delhi⁴. Some other studies have suggested a slightly higher prevalence of 5.3%⁵ and 9.9%⁶ in New Delhi. In a study done in Maharashtra, the prevalence was found to be 2.99%⁷ while it was 1.7% in a study done in UP⁸. In a study done in Lucknow prevalence was 2.25%⁹.

Worldwide, prevalence was found to be 3.7% in a study done in Brazil¹⁰ while it was 5.6% in Scotland¹¹. 9.2% prevalence was reported from Tanzania¹² and 6.4% from Japan¹³. In China¹⁴ prevalence was reported to be 7.2% in a study while in Nigeria¹⁵ prevalence was found to be 7.9% in a study. Our study showed a prevalence of 0.94% HDV infection among HBsAg positive patients in HIV patients. In Northern India, the prevalence of hepatitis D in HBsAg-positive individuals from New Delhi was reported to be 8.1% in patients with severe liver diseases in 1996¹⁶ and 10.6% in patients with HBV-related liver diseases in 2005 in Central India¹⁷. A study in Indore showed higher prevalence of 5.7% in patients with chronic liver disease, 1.9% in those with acute viral hepatitis and 15% in those with hepatic failure¹⁸. In Kolkata, the

prevalence was found to be 3.3% among HBsAg positive jaundice patients in 1998¹⁹. Another study from Ludhiana showed a prevalence of 10% in HBsAg-positive liver disease patients²⁰.

The prevalence of anti-HDV in chronic HBsAg/HIV carriers in Euro- SIDA was 14.5% and hepatitis D was predominated in intravenous drug users²¹. In another study done in Western Iran, high HDV prevalence of 31.57% in HIV/HBV co-infected individuals was found²². An Italian multicenter survey, carried out in 2006 among HBsAg-positive patients, yielded an anti-HDV prevalence of 8.1%²³. With a 5.9% prevalence of hepatitis D in HBsAg-positive patients, Switzerland has been found to be less affected than most other European countries²⁴. In 2003, a study was conducted in which 194 HBsAg-positive Korean patients were tested for anti-HDV, out of which, seven (3.6%) tested positive. Six of these patients had HCC (hepatocellular carcinoma) and one had cholangiocarcinoma. Therefore, HDV was mainly associated with patients with HCC in that study. The reason behind high prevalence of HDV infection in other studies may be because they had done study on patients with liver disease including cirrhosis, liver failure and HCC. Studies done on patients with cirrhosis, liver failure HCC and intra venous drug abusers had indicated high prevalence. In our study, none of the patient had any history of cirrohosis, liver failure, HCC and intravenous drug abuse. So, the prevalence is found to be low in our study.

Staging of hepatitis B among HIV infected patients

Acute hepatitis B infection was seen in 10 (9.43%) patients. Out of which 2 (20%) had high infectivity as they were positive for

HBeAg. Rest of 8 (80%) patients had low infectivity as they were negative for HBeAg. Chronic hepatitis B infection was seen in 96 (90.5%) patients. These patients were further divided into chronic hepatitis B with HBeAg positive (37 patients, 38.5%) and chronic hepatitis B with HBeAg negative (59 patients, 61.5%). Chronic hepatitis B with HBeAg were considered with high infectivity while chronic B with HBeAg negative were considered with low infectivity. In a study 26.1% of chronic carriers were HBeAg positive²⁵ while other study demonstrated 47.3% of chronic carriers were HBeAg positive²⁶. In a study done in Nigeria 30.8% of chronic carriers were HBeAg positive²⁷.

Average CD4 cell count was 342 cells/mm³ and range was 20-1217 cells/mm³. In this study average CD4 counts amongst HBeAg positive patients was found to be lower than average CD4 counts among HBeAg negative patients (270 cells /mm³ v/s 324 cells /mm³). In one study CD4 counts of HBeAg negative patients was found to higher than HBeAg positive patients (189.4 v/s 113.11 cells /mm³)²⁶ while in other study done in Nigeria CD4 counts of HBeAg negative patients was also found to higher than HBeAg positive patients (119 v/s 80 cells /mm³)²⁷. In another study CD4 counts of HBeAg negative patients was also higher than HBeAg positive patients (417 v/s 355 cells /mm³)²⁸. Only one patient had IgG HDV and his CD4 count was 32 cells /mm³. In one study average CD4 counts of HDV and HBV/HIV co-infected patients was found to be 281 cells /mm³²¹ while in another study it was found to be 100 cells /mm³²⁹.

HIV and HBV

The degree of immunodeficiency represents an important factor in the progression of hepatitis among individuals co-infected with

HBV and/or HDV³⁰. In addition to increased mortality, HIV co-infection accelerates the progression of hepatitis B and increases the risk of cirrhosis³¹. Patients with AIDS apparently are less likely to clear HBV infection after exposure or more likely to reactivate latent HBV infection or both³².

HBV co-infection in HIV disease considerably complicates its diagnosis and management³². In HIV infected patients, chronic HBV has an unfavorable course compared with those who do not, and the risk of liver-associated mortality is significantly increased³¹. Therefore, prevention is vital and HBV infection is preventable by vaccination. It is anticipated that the natural history of HBV will change in sub-Saharan Africa as more countries introduce infant vaccination; this is likely to influence the rate of HBV-HIV co-infection in the future³³.

HBV and HDV

Infection by HDV can be caused either as a coinfection in individuals with HBV or as a superinfection in chronic HBV carriers. Because the HBsAg carriers permit a continuous replication of HDV, HDV may play a role in the development of fulminant hepatitis and accelerate the progression of chronic liver damage in both HIV-uninfected³⁴ and HIV-infected patients³⁵ with chronic HBV infection. Another important feature of chronic hepatitis D is that it can give rise to hepatocellular carcinoma in the infected individuals³⁶

The present study emphasize that a uniform protocol should be formed to screen every HIV/AIDS patient and their co-partners for Hepatitis B and hepatitis D virus for early detection and management of these co-infection beside HIV for better prognosis and survival of these patients.

Table.1 CD4 counts range of hepatitis B virus infection in HIV infected patients

CD4 counts range	Male	Female	Total
<200	24	3	27
200-350	24	3	27
>350-500	26	6	32
>500	14	6	20
Total	88	18	106

Table.2 CD4 counts in HBV-HIV co-infected individuals with respect to various serological markers of hepatitis B and hepatitis D

Presence of serological marker	Average CD4 counts(cells/mm ³)
HBeAg	270
(IgM+IgG) HBeAb	324
IgM HBcAb	370
(IgM+IgG) HBcAb	331
IgG HDVAb	32

Table.3 Serological staging of hepatitis B positive patients

Acute hepatitis B infection (n=10)	High infectivity	2(20%)
	Low infectivity	8(80%)
Chronic hepatitis B infection(n=96)	High infectivity	37(38.5%)
	Low infectivity	59(61.5%)

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