ORIGINAL ARTICLE

INTERPRETING LIVER FUNCTION TEST IN HIV-HBV COINFECTION

Tamal Mukherjee[1], Sandeep Nanda[2], Sonia Barve[3], Ravi Gupta[4]

Authors' Affiliation: [1]Post Graduate Student; [2]Assistant Professor; [3]Associate Professor, Department of Clinical Microbiology, Medical College & Sir Sayajirao General Hospital, Baroda, Gujarat; [4]Tutor, Department of Clinical Microbiology, SN Medical College, Jodhpur
Correspondence: Tamal Mukherjee, **Email:** tamalmukherjee2007@gmail.com

ABSTRACT

Background: Liver diseases in HIV infected persons can occur due to hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infections, chronic alcoholisms, and hepatic tuberculosis or due to hepatitis caused by antiretroviral drugs. Co infection of HIV and HBV is frequently encountered with HIV having negative impact on HBV progression.

Objectives: The objectives of this study was to detect the prevalence of hepatitis B virus in HIV positive individuals and impact of HBV- HIV on liver function tests.

Materials & Methods: - Serum of 200 patients positive for HIV were screened for HBsAg by ELISA test and LFTs were performed in first, second and third week in serum of patients co infected with HIV- HBV and HBV alone.

Results: - Prevalence of HBV was found in 15 out of 200 HIV positives with maximum in age group 21-40yrs 60% of the cases. In HIV-HBV co-infected patients the amount of total Bilirubin, ALP and ALT was found to be considerably lower as compared to HBV infected persons only and the difference was statistically significant.

Conclusions: - From the present study it is fairly clear that the co-infection of HIV and HBV is an emerging problem that should be addressed immediately. Hepatic damage in case of co-infected patients should not be assessed only on the basis of serum liver enzyme estimation as their rise is not significant enough in these cases. Liver biopsy accompanied by liver function test provides a clearer picture of nacroinflammation. Such co-infected individuals also face increased risk of hepatotoxicity from anti-retroviral therapy. Individuals with HIV-HBV co-infection should have both the infections completely assessed in order to decide on the best therapeutic option for both viruses.

Keywords: HIV- HBV co-infection, Liver Function Test, Total Bilirubin, Alkaline Phosphatase, Alanine Amino Transaminase

INTRODUCTION

Diseases of the hepatobiliary system are a major problem in patients with Human Immunodeficiency Virus (HIV) infection. 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) co-infections, chronic alcoholisms, and hepatic tuberculosis or due to hepatitis caused by antiretroviral drugs. Principle routes of HIV transmission are similar to that followed by hepatotropic viruses. As a consequence, infections with HBV and HCV are expected in HIV infected patients. While HIV-HCV co-infection has predominantly been associated with non-sexual parenteral route of transmission, the HIV-HBV co-infection has been linked to both intravenous injection and sexual route of transmission [1].

Some 40 million individuals are estimated to be infected with HIV worldwide and nearly 400 million are chronic HBV carriers. Moreover HIV and HBV are endemic in the same world regions.[2] India with a whopping 5.2 million cases of HIV infection has a distinction of harboring the second highest number of this patients in the world. Within India also variable co-infection rates have been reported from region to region [1].

Co-infection with both viruses is frequently seen. Although HBV is more infectious than HIV[2]. Hepatitis B is transmitted more efficiently than HIV through sexual, vertical and percutaneous routes. HIV infection negatively impacts HBV infections by decreasing the rate of Hepatitis B surface antigen (HBsAg) clearance. HIV infection is also associated with occult hepatitis B. co-infection has also been associated with higher HBV DNA levels and increased risk of cirrhosis [3].

Recent molecular level studies suggest that the HBx gene present in hepatitis B virus contributes to a faster progression of Acquired Immuno Deficiency Syndrome (AIDS) in HIV-HBV co-infected individuals [4].

Compared to HIV negative individuals, those who are HIV positive are less likely to respond to HBV vaccine, have lower mean antibody titers and loose protective antibody levels quickly [5].

Along with the above mentioned complications, it has been observed that in most cases of HIV positive person with the absence of host defense, HBV replication in liver is non-cytotoxic and non-cytopathic [6]. The severity of inflammatory liver disease may be associated histologically or by the level of liver transaminases. Studies have found lower levels of transaminases in HIV infected HBV patients even though such patients are at increased risk of other causes of liver diseases [7].

Keeping in consideration the above mentioned facts, this study was undertaken to assess the prevalence of HBV among HIV positive individuals by detecting the presence of HBsAg in serum and to determine whether abnormalities exist in liver function test parameter in HIV-HBV co-infected persons as compared to only HBV infected persons.

MATERIALS AND METHODS

The present study was carried out in Department of Microbiology, Medical College, Vadodara. Patients attending clinics at SSG hospital, Baroda were tested for HIV based on clinical suspicion after pre-test counseling and informed consent. Only the confirmed HIV positive serum samples were included in this study and were tested for hepatitis B surface antigen (HBsAg). The study period was from October 2006 to August 2007. The patients were segregated according to different age groups and suspected mode of transmission. High risk behavior included practices like visit to CSW, homosexual behavior etc. Liver function test was performed for those patients who were HIV positive as well as HBsAg positive. The control group included persons who were HIV negative but HBsAg positive. Liver function test of this control group was also performed during the same study period. Values obtained from both the test and control group were compared.

The serum samples of suspected HIV positives were tested according to NACO testing strategy III, which stipulates the use of three test kits. If found negative the samples were excluded and samples that were positive for HIV, were tested for hepatitis B surface antigen (HBsAg) using ELISA.

Serum alkaline phosphatase (ALP), serum amino alanine transaminase (ALT) and total Bilirubin of the patients co-infected with HIV-HBV and HBV alone were measured at one week intervals starting from the day the patient tested positive for HBsAg. Three such data were obtained for each patient.

Normal Range: Total Bilirubin: up to 1.2 mg/dl; Serum ALT: 0 – 38 IU/L; Serum ALP: 25- 148 IU/L

RESULTS

In the present study, serum of 200 patients positive for anti HIV 1& 2 antibodies was tested for hepatitis B surface antigen (HBsAg). A total of 15 patients were found to be positive for HBsAg i.e. the prevalence rate was found to be 7.5 %. Out of these 15 patients, 7 were male and 8 were female. Of these 15 patients 9 (60%) were in age group of 21-40yrs.

The extents of liver damage in these 15 patients were measured by performing liver function test (LFT). Three parameters viz. total bilirubin, alkaline phosphatase (ALP) and alanine amino transaminase (ALT) were incorporated in the liver function test. Liver function test was performed in the first week, second week and third week starting from the day the patient tested positive for HBsAg and showed symptoms of hepatitis. The values so obtained were compared with the liver function test (consisting the same three parameters) of persons who were anti HIV negative but HBsAg positive i.e. the control group.

Table1: Comparison of mean and SD of total bilirubin, ALP and ALT in HIV-HBV co infected and HBV alone infected individuals in 1st, 2nd and 3rd week

Week	Mean total bilirubin (mg/dl)		Mean serum ALT (IU)		Mean serum ALP (IU)	
	Control group (Mean ± SD)	Test group (Mean ± SD)	Control group (Mean ± SD)	Test group (Mean ± SD)	Control group (Mean ± SD)	Test group (Mean ± SD)
1st	3.59 ± 1.03	1.6 ± 0.36	260.6 ± 73.4	184.2 ± 14.3	158.3 ± 50.0	91.9 ± 10.22
2nd	2.51 ± 0.68	0.96 ± 0.18	210.8 ± 60.9	154.2 ± 15.5	98.8 ± 37.6	64.5 ± 9.7
3rd	1.35 ± 0.48	0.89 ± 0.09	148.2 ± 22.4	128.5 ± 13.18	55.4 ± 15.94	42.4 ± 7.06

Total bilirubin concentration in serum of control and test groups were compared, the difference for the first, second and third week was found to be highly significant ($P<0.0001$). The differences in alkaline phosphatase values for the test and control group for the first, second week and third week was found to be highly significant ($P<0.0001$ for first and second week, $P<0.05$ for the third week). Serum alanine amino transaminase levels difference in the test and control group for the first and second week was found to be highly significant ($P<0.0001$) Difference for the third week was also significant enough ($P<0.05$). The

difference in mean of LFTs in control group and test group are statistically significant, which suggest that LFT levels may not accurately reflect the level of liver disease in HIV- HBV co-infection. The best indicator of grade and stage of liver disease is liver biopsy.[3]

DISCUSSION

Various studies have been done across the world to determine the rate of co-infection of HIV and HBV. Difference in prevalence of HBsAg in HIV positive in the present study and the studies done by Saravannan et al[9] and Shire et al[10] was statistically insignificant (P>0.05), while with that of Swati Gupta et al[1], Takhiwale et al[8] and Ejele et al[11] was found to be significant (P<0.05). The difference can be explained by the fact that there was a variation in the sample size. Swati Gupta et al studied a total of 451 patients and Ejele et al a total of 1500 patients. Both the studies were done in 2003-04, in the last three years incidence of HIV and HBV has increased worldwide. This may also contribute to the variation. Most important distinguishing factor is the geographical difference.

Age related distribution of HIV-HBV co-infection in present study on comparison with that of Swati gupta et al[1] and Risbud et al[12] was found to be statistically insignificant (P>0.05). It was also observed that co-infection was most prevalent in the age group of 21 to 40 years. Prevalence of HIV infection is highest in the same age group. It's very much likely that presence of HIV infection makes the transmission of hepatitis B virus more efficient both through sexual as well as perinatal contact. About two thirds of patients with AIDS develop hepatomegaly and abnormalities in serum biochemical parameters of liver function[3].

The present study compared total bilirubin, alkaline phosphatase (ALP), and alanine amino transaminase (ALT) levels in HIV-HBV co-infected patients with patients infected with HBV only. The difference was highly significant in case of Bilirubin (P<0.0001) and ALT and significant in case of ALP (P<0.05).

No significant difference was observed in mean total bilirubin and ALT when the values were compared with that obtained by Gilson et al[7] and Soriano et al[13] (P>0.05). But when alkaline phosphatase values were compared, significant difference was observed with those obtained by Gilson et al (P<0.05). Their findings in fact indicate that serum ALP levels increase in patients with HBV-HIV co-infection as compared to HBV infected patients only. They also could not justify this increase in level but speculated that it may be due to sub-clinical cholangitis in HIV infected patients or side effect of drug such as co-trimoxazole[7]. No statistically significant difference was observed with the findings of Soriano et al (P>0.05).

HBV is not directly cytopathic to liver cells on the contrary hepatic necrosis is mediated by Th1 lymphocyte induced cytotoxic T lymphocytes (CTL). Therefore any process that affects quantity and quality of immune response will have a bearing on the outcome of liver damage in HBV infection [8].

The observations in the present study i.e. increase in total bilirubin, serum ALT and serum ALP levels are consistent with evidence of an immunological pathogenesis of liver damage in chronic HBV infection, and HIV associated immunosuppression giving rise to less active liver disease [2, 7].

CONCLUSION

In present study, prevalence of hepatitis B surface antigen (HBsAg) was found to be 7.5% amongst these HIV positive patients; co-infection was highest in the age group of 21-40 years 60%. In HIV-HBV co-infected patients the amount of total Bilirubin, ALP and ALT was found to be considerably lower as compared to HBV infected persons only.

HIV positive patients have an impaired cellular immune function. When hepatitis B virus infects such a patient, the host is unable to mount an effective immune response against the hepatocytes infected with HBV. So, hepatic cell damage is less as compared to person whose cellular immune function is normal. But normal viral replication goes on without any hindrance sans any clinical manifestation of the hepatitis. Moreover when the immune function of the patient is restored to some extent there occurs a full blown disease of hepatitis with all the signs and symptoms.

From the present study it is fairly clear that the co-infection of HIV and HBV is an emerging problem that should be addressed immediately. Such co-infected individuals also face increased risk of hepatotoxicity from anti-retroviral therapy. Individuals with HIV-HBV co-infection should have both the infections completely assessed in order to decide on the best therapeutic option for both viruses.

Hepatic damage in case of co-infected patients should not be assessed only on the basis of serum liver enzyme estimation as their rise is not significant enough in these cases. Liver biopsy accompanied by liver function test provides a clearer picture of nacroinflammation.

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