



## ASSESSMENT OF LIVER FUNCTION TEST IN HIV-HBV CO-INFECTED PATIENTS AT ART PRAYAGRAJ, NORTHERN INDIA

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**ABSTRACT** **OBJECTIVES:** 1. To detect the prevalence of hepatitis B virus in HIV positive individuals  
2. Impact of HBV- HIV on liver function tests.

**MATERIAL AND METHODS:** A total of 2163 confirmed HIV positive (WHO strategy III) treatment naïve patients enrolled for first time at the ART center were screened for HBsAg by ELISA. LFTs were performed in HIV- HBV coinfecting (n=113) and from HIV monoinfected patients (n=100; control group).

**RESULTS:** In HIV-HBV co-infected patients the amount of ALT is increased in (62.8% vs 26%), AST in (25.6% vs 19%), ALP in (34.5% vs 17%), serum Bilirubin in (53% vs 8%) was found to be considerably higher as compared to HIV infected persons only and the difference was statistically significant. Hypoalbuminaemia was seen in 46.9% of HIV- HBV coinfection and only in 16% of HIV patients.

**CONCLUSION:** HIV/HBV Coinfected patients had significantly higher serum bilirubin, ALT alkaline phosphatase and lower albumin. HIV infected individuals face increased risk of hepatotoxicity from anti-retroviral therapy. So prior to the initiation of antiretroviral treatment (ART) monitoring individuals with HIV-HBV coinfection should have both the infections completely assessed, in order to decide on the best therapeutic option for both viruses.

**KEYWORDS :** HIV/HBV Coinfection, LFT, HBV, HIV

### INTRODUCTION

Liver disease caused by chronic hepatitis B virus (HBV) is emerging as a significant cause of morbidity and mortality among human immunodeficiency virus (HIV)-infected individuals.<sup>[1]</sup> HBV and HIV have common routes of transmission and endemic areas, but HBV is about 100 times more infectious.<sup>[2]</sup> The worldwide epidemic of hepatitis B and HIV have led to new understanding of the complicated interactions between these two viruses. HBV co-infections in HIV positive individuals is of utmost importance due to the underlying consequences such as the hepatological problems associated with these viruses, which have been shown to decrease the life expectancy in the HIV-infected patients. It is characterized by more rapid progression of liver disease including accelerated fibrosis, cirrhosis and hepatocellular carcinoma and higher liver-related mortality and morbidity. In addition, there are reports of complex interactions with antiretroviral therapy (ART) including hepatotoxicity, reactivation of "silent" HBV infection and immune reconstitution syndromes (IRIS).<sup>[3]</sup> There is lack of data regarding correlation of liver enzymes and CD4 cell count among HBV-HIV coinfecting patients. Hence the present study was performed to see effect on liver function test of HBV-HIV coinfecting patients.

### MATERIALS AND METHODS:

#### STUDY SAMPLES:

The present study was carried out in the Department of Microbiology, Moti Lal Nehru Medical College, Allahabad from December 2013 to November 2016. HIV positive cases diagnosed as per National AIDS Control Organization (NACO) guidelines were included.<sup>[4]</sup> A total of 2163 consecutive confirmed HIV positive (WHO strategy III) treatment naïve patients (age: 18–60 years) who were first time attendees at the ART centre were screened for the study and anonymously tested for hepatitis B surface antigen (HBsAg). None of these patients gave a history of vaccination against HBV. None of the patients received antiviral therapy against HBV. Patients with age < 2 years, >60 years and pregnant women were excluded from the study. All patients were subjected to CD4 count and liver function tests (LFT). This research protocol was approved by the Institutional Ethics Committee of Moti Lal Nehru Medical College, Allahabad.

#### serology:

All 2163 HIV patients samples were screened for HBsAg by ELISA test (Hepalisa J. Mitra and Co. Private Limited India). One hundred and thirteen consecutive HBsAg reactive patients were enrolled in this study after obtaining written, informed consent.

### Biochemistry:

Liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST) serum bilirubin, serum alkaline phosphatase (ALP) and serum albumin were carried out for all patients using a fully automatic autoanalyzer (Olympus AU 400 Clinical Chemical Analyzer, Japan) on the same day of blood collection. Normal range: Serum ALT: 10–40 U/L; serum AST: 20–40 U/L; serum bilirubin: 0.2–1.1 mg/dL; serum ALP: 25–120 IU/L; serum albumin: 3.5–5 g/dL. CD4 T-cell count estimation was done by FACS Calibur™ flow cytometer (Becton Dickinson, California, USA).

### Statistical Analysis:

Comparison of liver function tests of HIV mono-infected and HIV/HBV co-infected patients was done by software SPSS 17.0 (USA)

### RESULTS

A total of 2163 consecutively confirmed HIV positive treatment naïve patients were screened for HBV at ART centre. HBV Coinfection was seen in 113 (5.2%) HIV positive patients. Of these HBV/HIV Co-infected patients 76 (67%) were males and 37 (33%) were females with 5 (4.4%) patients in the age group of 2-20, 73 (64%) patients in the age group of 21-40 years and 36 (32%) patients in the age group of 41-60 years. 76 (67%) patients were illiterate. Most common risk factor observed was sexual contact (82%) followed by spouse positivity in 21 (18.5%) patients and history of blood transfusion in 8 (7%) patients. Only 56 (49.5%) patients were alcoholic. Majority of the infected population (73%) were from rural area.

A subject was divided into two groups: Those with HIV alone and those co-infected with HBV. The mean age of HIV infected was 34 years. Majority (59%) of HIV patients were of age 21-40 years as in HIV-HBV Coinfected patients as shown in (table 1).

**Table 1: Comparison of sociodemographic characteristics between HIV monoinfected and HIV/HBV Co-infected individual**

Variable	HIV Monoinfected (n=100)	HIV-HBV Coinfected (n=113)
Male gender, number(%)	71(71%)	75(66%)
Risk factors for HIV/HBV Co-infection, number(%)		
(i) Heterosexual	76(76%)	82%
(ii) Men who have sex with Men	1(1%)	None

(iii) Injecting drug use	9(9%)	6(5%)
(iv) Blood transfusion	5(5%)	8(7%)
(v) Mother to child	3(3%)	None
(vi) Unknown	6(6%)	8%
Age		
2-20yrs	2(2%)	5(4.4%)
21-40yrs	59(59%)	73(64%)
41-80yrs	39(39%)	36(32%)
Educational status		
Illiterate	34(34%)	76(76%)
Literate	66(66%)	(37)37%
Alcohol use,number(%)		
(i) Habitual	11(11%)	37(32.7%)
(ii) Social	31(31%)	19(16.8%)
(iii) Never	47(47%)	57(50%)

**Clinical Details:**

Fever was the most common clinical symptom among HBV-HIV and HIV monoinfected (70% vs 92%) followed by weight loss ( 56% vs 63%), Cough & dyspnoea (43% vs 32%). Some of the symptoms such as ulcers in oral cavity, skin lesions were significantly higher in the HIV mono infected patients as compared to HIV-HBV Co- infected patients(Table 2).

**Table 2: Clinical Details of HIV/HBV Coinfected Patients and HIV Monoinfected Patients**

S.No	Symptoms	HIV/HBV Coinfected n=113(%)	HIV Monoinfected n=100(%)
1	Fever	92(81%)	70%
2	Weight loss	76(63%)	56%
3	Cough & Dyspnoea	32(28.3%)	43%
4	Diarrhoea	47(41.5%)	23%
5	Ulcers in oral cavity	46(40.7%)	22%
6	Fatigue and malaise	81(71.6%)	26%
7	Skin lesions	11(9.7%)	21%
8	Smoking	29(25%)	22.5%
9	Hypertension	13(11.5%)	24.5%

**Effect of Hepatitis B virus co-infection on liver function test and other Biochemical Parameters**

On the analysis of biochemical parameters it was found that the median serum bilirubin(0.61 vs. 0.3 mg/dl; P<0.05), ALT (44 vs. 28 U/l; P<0.05) ,AST (41 vs 32 U/l; P<0.01), alkaline phosphatase(210 vs. 136 U/l; P<0.001) were significantly higher among HIV/HBV co- infected patients than HIV mono-infected ones (Table 3). Hypoalbuminaemia was seen among 46.9% of HIV/HBV Co-infected individuals.

**Table 3: Comparison of LFT in HIV/HBV Coinfected and HIV monoinfected patients**

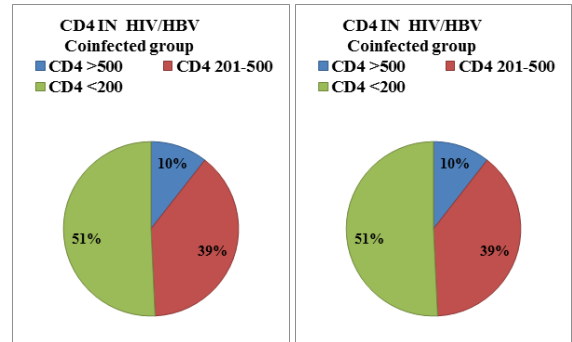
Liver Enzymes	HIV/HBV Coinfected n=113(%)		HIV Monoinfected n=100(%)	
	Normal	Elevated	Normal	Elevated
ALT U/L	42(37.1%)	71(62.8%)	73(73%)	26(26%)
AST U/L	84(74%)	29(25.6%)	69(69%)	19(19%)
ALP IU/L	74(65.4%)	39(34.5%)	83(83%)	17(17%)
Serum Bilirubin (mg/dl)	53(47%)	61(53%)	92(92%)	8(8%)

AST,asparatate transferase;ALT,alanine aminotransferase

**Association of CD4 T-Cell count with HIV infection and HIV/HBV Co-infection**

The difference in median baseline CD4 T cell count was not significant between HIV monoinfected and HIV/HBV coinfectd. The mean CD4 T-cell count in the HIV-infected group was 340 cells/μL while in the HIV/HBV co-infected group it was 195 cells/μL. Although proportionately more of the HIV/HBV coinfectd patients had CD4 count <200 cells/μl (58/113; 51.3%) as compared to HIV monoinfected patients (19%) which is statistically significant(Fig.

1).Among HIV/HBV Co-infected individuals with CD4 count <200cells/μl median serum albumin level was lower as compared to those with CD4>200 cells/μl.



**Figure 1: Comparison of CD4 Cells in HIV/HBV Coinfected and HIV monoinfected patients**

**DISCUSSION**

The prevalence of HIV in India is quite high and it has the second highest number of people living with HIV.<sup>[5]</sup> Among HIV infected patients, 2-4 million are estimated to have chronic HBV infection while 4-5 million are co-infected with HCV.<sup>[6,7]</sup> Various studies have been done across the world to determine the rate of infection of HIV and HBV. Co-infection of HBV with HIV complicates the clinical course, management and may also adversely affect therapy for HIV infection.

Our study shows prevalence of 5.26% co-infection which is comparable to those of D. W. Taura et al, Abdel-kader and Saillour et al, who have reported prevalence of HIV-HBV co-infection of 6%, 6.3% and 6.9% respectively.<sup>[8,9,10]</sup> We found higher rate of Co-infection in HIV patients as compared to 2.25% from lucknow<sup>[11]</sup>, 1.7% from Agra<sup>[12]</sup>, 3.5% from Mumbai<sup>[13]</sup>, 2.61% in New Delhi<sup>[14]</sup>. In our study the commonest risk factor is sexual contact in HIV (76%) and HIV-HBV(82%) Coinfectd patients which is lower than 100% sexual transmission in study done by Goyal et al<sup>[2]</sup>. Our study showed male predominance (66%) amongst HIV infected patients which correlated with studies of Sanjiv Ahuja et al. (62%)<sup>[15]</sup> and other studies (73% and 86%) which are higher than in our study.<sup>[16,17]</sup> The most common age found in our study was 21-40 years which is the normal age for HIV positivity in India and correlates with Naval Chandra et al.<sup>[8]</sup>, Sanjiv Ahuja et al.<sup>[9]</sup> and Oslanisun Olofemi Adewole et al.<sup>[20]</sup> In HIV/HBV co-infected patients seropositivity is high in illiterate. The poor educational status of these patients in the present study contributes to limited knowledge and awareness of HIV transmission and thus higher seropositivity rates. The CD4+ count less than 200 cells/μl was seen in significantly more number of patients in HBV co-infection than in HIV alone. This reflects that immune status in HIV-HBV co-infection was more compromised than in HIV alone. This study has shown that the level of serum ALT, ALP, Serum Bilirubin is higher in HIV and HBV co-infected patients compared to HIV mono-infected patients. This is consistent with a study done in Kolkata<sup>[21]</sup> and South India<sup>[22]</sup>. However This study has also shown that CD4 count of the HIV mono-infected patients was significantly higher than that of the patients co-infected with HBV. Furthermore, mean serum level of ALT,AST and ALP of some HBV factors on HIV transcription favour enhanced HIV replication leading to faster CD4 T-cell decline in HIV/HBV co-infected individuals.<sup>[23]</sup>

A recent WHO report<sup>[24]</sup> recommends, screening for HBV before initiation of ART and using ART containing tenofovir and either lamivudine or emtricitabine in HIV and HBV co-infected patients.

**CONCLUSION**

In conclusion, it is evident from the present study that there is increasing trend in prevalence of HIV/HBV Coinfection. We recommend correct choice of drug at ART centre of HIV/HBV Coinfectd to prevent from Hepatotoxicity. Also there should be a regular monitoring of liver enzymes and CD4 T-cell counts. This would help in reducing morbidity and mortality from antiretroviral drug associated hepatotoxicity among these patients.

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