



## Prevalence of Hepatitis B and Hepatitis C Infections in HIV Infected Patients Attending a Tertiary Care Hospital in North-East India

Sanjib Gogoi<sup>1\*</sup>, N. K. Hazarika<sup>1</sup>, Syed Tanwir Alam<sup>1</sup>, Jashbeer S. Roy<sup>1</sup>  
and Dina Raja<sup>1</sup>

<sup>1</sup>Department of Microbiology, Guwahati Medical College, Guwahati: 32, Assam, India.

### Authors' contributions

This work was carried out in collaboration between all authors. Author SG designed the study, collected data, wrote the protocol and wrote the first draft of the manuscript. Author NKH designed the study and corrected the final manuscript. Author STA did the literature search. Author JSR performed the statistical analysis. Author DR interpreted ELISA results. All authors have read and approved the final manuscript.

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### ABSTRACT

**Aims:** To study the co infection of Hepatitis B (HBV) and/or Hepatitis C virus (HCV) in Human Immunodeficiency Virus (HIV) infected patients attending tertiary care teaching hospital in North East India.

**Study Design:** This study was a cross sectional study.

**Place and Duration of the Study:** Department of Microbiology, Guwahati Medical College & Hospital, Guwahati, Assam, India for a period of one year (August 2010- July 2011).

**Methodology:** Serum samples of 180 HIV positive patients were collected randomly who gave consent to participate in the study and were tested for hepatitis B surface antigen (HBsAg) and anti-HCV antibodies by enzyme linked immunosorbent assay (ELISA) method. The retrospective demographic data of the subjects were collected.

\*Corresponding author: Email: [drgogoisanjib24@gmail.com](mailto:drgogoisanjib24@gmail.com);

**Results:** Out of 180 HIV positive patients (126 males and 54 females), 22 (12.2%) cases were HBsAg positive and 8 (4.4%) were anti-HCV positive. Triple infection with HBV, HCV and HIV was not found in any patient. The commonest mode of transmission for HIV alone (113/180; 75.3%) and HIV-HBV co infection (18/22; 81.8%) was sexual route, and for HIV-HCV co infected patients, Intravenous Drug Use (IDU) was the commonest route of transmission (4/8; 50%). Concomitant infection of HIV and HBV was found to be significantly more in the symptomatic group (59.1%) compared to asymptomatic group (4.5%) ( $P$  value < 0.001). CD4+ T-lymphocyte count less than 200/ $\mu$ l was seen in 11 of 30 co-infected cases (36.7%).

**Conclusion:** Co infection with HBV and HCV is a common problem in HIV infected patients in India. Hence, all HIV patients need to be routinely screened for markers such as HbsAg for hepatitis B and Anti HCV for HCV infection so as to take early treatment initiative to prevent the morbidities.

*Keywords: HIV; HBV; HCV; co infection.*

## 1. INTRODUCTION

Human immunodeficiency virus (HIV), Hepatitis B virus (HBV), and Hepatitis C virus (HCV) has evolved as a matter of major public health concern throughout the world because of the morbidity and mortality due to liver diseases associated with the co infection of these viruses [1,2]. HBV and HCV co-infections are more prevalent among HIV infected individual due to shared or overlapping routes of transmission [2]. The HIV infected individuals, co-infected with HBV and/or HCV not only carry an increased risk of progression to severe liver disease which decreases their life expectancy but also have a high susceptibility towards anti retroviral therapy induced hepatotoxicity [3]. The prevalence rates of co infection with HBV and HCV in HIV infected patients vary worldwide depending on the geographic regions, risk groups and the type of exposure involved which may differ significantly from country to country and also in different geographical areas of the same country [1].

Although studies were done regarding prevalence of HBV/HCV co infection in HIV infected individuals in different parts of India [1,2], study done for the same from North East India is very rare. This study was therefore carried out in the Department of Microbiology of a premier tertiary care Government Medical College & Hospital of North East India to determine the prevalence of coinfection of HBV and HCV in HIV infected patients along with the mode of transmission of HIV, Hepatitis B and Hepatitis C.

## 2. MATERIALS AND METHODS

### 2.1 Study Area and Population

The present study was conducted in Guwahati Medical College & Hospital, which is a tertiary

care teaching hospital serving mainly the patients of North eastern region of India. Therefore, this study aims to cover a wide range of patient groups from entire North East India in terms of education and socioeconomic conditions.

### 2.2 Ethical Clearance

Institutional Ethical Committee clearance (ethical committee of Guwahati Medical College & Hospital, Guwahati, Assam) was obtained before starting this study.

### 2.3 Study Duration

The study was conducted over a period of one year (August 2010 - July 2011).

### 2.4 Subject Selection

A total of 180 HIV positive patients above 15 years of age were selected randomly who were willing to participate in the study.

Written informed consent was taken from every patient before including them in the study.

The patients were among all the subjects who were tested positive for HIV in the Integrated Testing and Counselling Centre (ICTC) of the Institution where the study was performed. Every patient included in the study was asked about his or her sociodemographic profile and other relevant history such as sexual behavior, substance abuse, other co morbid conditions and all these data were recorded in a predesigned proforma maintaining strict confidentiality. Determination of route of transmission was done by taking history of the patients, where the patients were told about different possible of route of transmission of HIV and Hepatitis viruses (HBV and HCV) and the patients had to

recall his or her exposure to any such route/ routes at any point of their life and then patient's response was noted down in the proforma. Educated patients (who can read and write) were given the proforma (in local language as well as in English) to be filled up by them. All the patients were given privacy so that they respond to the questions in an independent and unbiased way without any undue pressure, maintaining the confidentiality of their identity.

## 2.5 Method of Sample Processing and Analysis

From each subject under study, 5 ml of blood was collected after proper explanation of the intention of sample collection and serum was separated. The serum samples were stored at -70°C till the tests were performed.

The HIV status of the clients were determined at the ICTC centre as per testing guidelines, protocols and strategy prescribed by the National AIDS Control Organization (NACO) [4].

The serum sample of 180 confirmed HIV positive patients were screened for HBV and HCV infection using Third generation ELISA kits; Hepatitis B surface antigen (HBsAg) for HBV and antibodies to Hepatitis C virus (Anti HCVs) for HCV, both manufactured by J. Mitra & Pvt. Ltd, New Delhi, India. The results of all the tests were interpreted as per manufacture's guidelines.

## 2.6 Statistical Analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean  $\pm$  SD, and categorical variables are presented as absolute numbers and percentage. Data were checked for normality before statistical analysis using Shaipro Wilk test. Continuous variables were compared using ANOVA and further multiple comparison test was used. Categorical variables were analyzed using the chi square test.

For all statistical tests, a *P* value less than 0.05 was taken to indicate a significant difference.

## 3. RESULTS AND OBSERVATIONS

Out of 180 HIV positive patients, 124(68.89%) were males and 56(31.11%) were females. The

number of males and females infected only with HIV was 102 (68%) and 48 (32%) respectively. Majority (66.7%) of HIV infected patients belonged to the age group of 31-40 yrs.

Total of 30 (16.67%) patients were infected with Hepatitis viruses i.e. 22 (12.2%) HBV and 8 (4.4%) HCV positive and no patient was found to be infected with all these three viruses (HIV+HBV+HCV). Majority 12 (54.5%) of HBV co infected patients were in the age group of 31-40 yrs, whereas in case of HCV majority 6 (75.0%) of patients belonged to the age group of 41-50 years (*P* value <0.001). Male gender predominance was observed (19 HIV+ HBV and 5 HIV+ HCV). But this gender difference between Hepatitis virus co infected patients (HIV+HBV and HIV+HCV) and patients infected only with HIV, is not statistically significant (*P* value 0.192).

The major route of transmission of HIV infection was sexual route (75.3%) followed by blood transfusion (5.3%) and Intravenous Drug Use (3.3%). The major route of transmission (81.1%) in case of HIV/HBV co infected patient is also through sexual route. But in case of HIV/HCV co infected patients the main route of transmission was through Intravenous Drug Use (50%) and the difference is significant (*P* value <0.001)

It was found that majority (59.1%) of HIV positive patients co infected with HBV were in the symptomatic stage of HIV infection (WHO Stage 3) compared to those infected with only HIV (11.3% in WHO Stage 3) (*P* value <0.001). In case of HIV/HCV co infected patients majority (62.5%) belongs to WHO Stage 2 of HIV infection.

The CD4 count less than 200 cells/mm<sup>3</sup> was seen in 42/150 (28%) patients who were only infected with HIV, 9/22 (40.9%) in HIV/HBV co infected patients and 2/8 (25%) in HIV/HCV co infection. (*P* value 0.445). The mean CD4 count of the patients infected only with HIV was 251.53 $\pm$ 91.53 cells/mm<sup>3</sup> whereas the mean CD4 count of the HIV/HBV and HIV/HCV co infected patients was 210.41 $\pm$ 71.15 cell/mm<sup>3</sup> and 236.25 $\pm$ 68.45 cell/mm<sup>3</sup> respectively. This difference of mean CD4 count among these three groups (only HIV infected, HIV/HBV and HIV/HCV co infected) was not statistically significant (*P* value 0.123). The results are summarized in the Table 1.

**Table 1. Summarized results of present study**

Variables	Total (180)	HIV alone (n=150)	HIV+HBV (n=22)	HIV+HCV (n=8)	P value
<b>Sex</b>					
Male	126	102 (68%)	19 (86.4%)	5 (62.5%)	0.192
Female	54	48 (32%)	3 (13.6%)	3 (37.5%)	
<b>Age</b>					
15-20	6	6 (4%)	0 (0%)	0 (0%)	< 0.001
21-30	22	22 (100%)	0 (0%)	0 (0%)	
31-40	114	100 (66.7%)	12 (54.5%)	2 (25%)	
41-50	30	16 (10.7%)	8 (36.4%)	6 (75%)	
51-60	8	6 (4%)	2 (9.1%)	0 (0%)	
<b>Mode of transmission</b>					
Blood transfusion	8	8 (5.3%)	0 (0%)	0 (0%)	0.433
Sexual IDUs	132	113 (75.3%)	18 (81.8%)	1 (12.5%)	<0.001
Response not available	9	5 (3.3%)	0 (0%)	4 (50%)	<0.001
	31	24 (16.0%)	4 (18.2%)	3 (37.5%)	0.290
<b>WHO staging</b>					
1	52	50 (33.3%)	1 (4.5%)	1 (12.5%)	< 0.001
2	96	83 (55.3%)	8 (36.4%)	5 (62.5%)	
3	32	17 (11.3%)	13 (59.1%)	2 (25%)	
4	0	0 (0%)	0 (0%)	0 (0%)	
<b>CD4 count</b>					
<200 / $\mu$ l	53	42 (28.0%)	9 (40.9%)	2 (25%)	0.445
>200/ $\mu$ l	127	108 (72%)	13 (59.1%)	6 (75%)	
<b>Mean CD4 count</b>					
	180	251.53 $\pm$ 91.53	210.41 $\pm$ 71.15	236.25 $\pm$ 68.45	0.123

#### 4. DISCUSSION

The primary aim of the present study was to determine the prevalence of co infection of hepatitis viruses (HBV and HCV) in HIV infected patients attending a tertiary care government teaching hospital of North East India. The importance of estimation of load of these hepatitis viruses lies in the fact that with the introduction of effective and safe antiretroviral therapy, HIV positive individuals tend to live a longer life, but the co infection of these hepatitis viruses may in turn increase the morbidity as well as mortality of this group of patients [5].

The present study estimated the prevalence of HBV and HCV coinfection in HIV infected patients to be 12.2% and 4.4% respectively. The studies done on the similar topic in various parts of India as well as in rest of the world found that the prevalence of co infection of HIV and HBV varies from as low as 1.7% (Ankur G, et al. [6]) to as high as 17.5% (Nyirenda, et al. [7]). Studies done in North India such as Tripathi, et al. [8] and

Ahuja et al. [3] reported the prevalence of HIV/HBV co infection to be 2.25% and 4.9% respectively. Whereas Saravanan, et al. [9] and Chandra et al. [2] in their studies done in South India found the coinfection of HIV and HBV to be 9% and 15% respectively. Sarkar, et al. [10] reported the prevalence of HIB and HBV co infection in Eastern India to be 8.3%. Studies done in other developing nations such as Iran, Zambia and Kenya reported the prevalence of coinfection of HBV and HIV to be 14.5%, 9.9% and 6% respectively [1,11,5].

The prevalence of co infection of HCV and HIV in various studies varies from 1.1% to 72%. [1,3,5,6-9,11]. Triple infection (HIV with HBV and HCV) was rare in these studies except the study done by Mohammadi, et al. [1] where the prevalence of coinfection of HIV with both HBV and HCV was 7.9%.

The results were found to be variable in these studies which justify the fact that prevalence of co infection with HBV and HCV in HIV infected

patients vary worldwide depending on the geographic regions, risk groups and the type of exposure involved. Most of the studies did not find any patient infected with all these three viruses (HIV, HBV and HCV), so as the finding in the present study as well.

In our study group, the heterosexual route (75.3%) was the predominant route of acquiring HIV infections than other modes of transmission. The HIV infection rate was higher in males in comparison to females i.e. 68% and 32% respectively ( $P$  value 0.192). In case of HIV/HBV co infection the same result was noted i.e. major route of transmission was heterosexual route (81.8%) and the male gender predominance (86.4%). Studies done in various regions of India also reported that males were significantly at a higher risk of acquiring HBV co infection in HIV infected patients [12,13,14]. Present study shows that most (54.5%) of HIV/HBV co infected patients belonged to the age group of 31-40 yrs, which is the normal age group where the HIV positivity is reportedly higher as per Indian studies [14,15]. This also suggests that sexual route could also be the common mode of transmission for both HBV and HIV.

The route of transmission of HCV in HIV positive patients showed a striking difference from the major route of transmission in case of HIV/HBV co infected patients i.e. unlike HIV/HBV co infected patients, main route of transmission was not sexual but through IDU (50%) and the difference is significant ( $P$  value <0.001). Alinaghi, et al. also found high rate of HIV/HCV co infection among IDUs (57%) [16]. Our finding can be explained by the fact that in North East India IDU is a predominant mode of transmission of HIV/AIDS and the prevalence of HIV/HCV co infection in intravenous drug abuser was reported as high as 50-90% by Saha, et al. in their study done in Manipur [17]. In the present study, sexual route of transmission was suspected only in one patient with HIV/HCV co infection as she denied having exposure to any other possible routes of transmission of HCV such as IDU and she was in a monogamous relationship with her husband with an active sex life who was also HIV positive. Therefore, this particular case was considered only as a suspected case of transmission of HCV through sexual route because studies have shown that sexual route of transmission of HCV is still a doubtful fact [18]. Transmission of HCV in this particular case may be due to sharing of contaminated personal items with her husband

who might be the index of HCV infection, though we did not able to rule out husband's HCV status. Various authors from India such as Gupta et al. [15] and Saravanan, et al. [9] reported a similar finding that sexual route may not be the major route of transmission of HCV in HIV infected patients, taking into consideration about the fact that most of the HIV/HCV co infected patients in their study group did not fall in the sexually active group and are mainly above the age of 51 yrs. In our present study also the HIV/HCV co infection was found to be highest (75.0%) in the age group of 41-50 years.

Our study shows that the co infection of HBV and HCV is more in patients who are at the symptomatic stage of HIV infection i.e. 59.1% HIV/HBV co infected patients were in stage 3 and 62.5% HIV/HCV co infected patients were in stage 2 of WHO clinical staging of HIV. This finding of our study correlates with the study of Tankhiwale, et al. [19] who reported that concomitant infection of HIV and HBV is more in symptomatic group (40.68%) compared to asymptomatic group (19.6%) [19]. Similar finding was noted by Tripathi et al. [8] where out of 14 HIV/HBV co infected patients 8 (57.1%) patients were in symptomatic stage of HIV infection by WHO criteria and out of 10 HIV/HCV co infected patients 9(90%) patients were in symptomatic stage of HIV infection by WHO criteria and 1 patient was in primary stage of HIV infection.

In our study it was found that there was no statistically significant difference in the mean CD4 count of only HIV infected patients and patient with co infection of either HBV or HCV ( $P$  value 0.123). This finding is in contrast to the other studies such as Olanisum, et al. [20] and Sungkanuparph, et al. [21], where they have reported that the mean CD4 count of co infected (either HBV or HCV) patients were less than the patients infected only with HIV. This difference of this finding may be because of the fact that high or low CD4 counts depends at what stage of immune status the CD4 count was tested.

The present study has certain limitations. Firstly, as this is a cross sectional study, we were unable to adequately establish a casual relationship between the time of exposure and subsequent infection. Secondly, molecular techniques such as HBV DNA, HCV RNA and viral load were not done due to lack of resources and financial constraints. Thirdly, Immunosuppression from HIV infection may impair antibody formation, and false negative HCV antibody tests have been

reported in individuals co-infected with HIV [22,23]. It is unlikely that the low seroprevalence of HIV/HCV co-infection was due to selection bias because the patients that were included in the study were from a wide range of socio economic strata of North East India attending this tertiary care centre.

## 5. CONCLUSION

To conclude, routine evaluation and monitoring of HIV infected patients for concurrent infections of HBV and HCV is necessary, since the present study shows 12.2% and 4.4% of HIV infected individuals to be co infected with HBV and HCV respectively. Since the institution where the study was carried out is a tertiary care centre, serving patients from the entire North East region of India, our study may reflect the burden of these conditions in this part of the country. The implication of HBV and/or HCV co-infection in HIV patients is of serious concern to the Indian socioeconomic condition as there is a significant increase in the number of patients diagnosed with HIV disease in recent years. The knowledge of co-infection in a HIV positive patient is vital since these patients, as they live longer on antiretroviral treatment will also need to be managed for their co-infection with HBV and HCV. Proper protocol for screening of the high-risk population for these infections would definitely aid in prompt diagnosis and early treatment with improved outcomes which in turn may decrease the further spread of these chronic viral infections in HIV infected patients.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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