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To Observe the Seroprevalence of Hepatitis B and Hepatitis C Co-Infection in HIV Seropositive Patients in North India

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ABSTRACT

Background: Human immunodeficiency virus (HIV) and Hepatitis B and C viruses (HBV and HCV) are the most common chronic viral infections worldwide. These viruses have similar modes of transmission, mainly through blood and blood products, sharing of needles to inject drugs and sexual intercourse, making co-infection with these viruses a usual event. HBV and HCV co-infection in HIV positive individuals is of paramount importance because of the underlying consequences such as hepato-biliary problems associated with these viruses.
Aim: To observe the seroprevalence of Hepatitis B and Hepatitis C co-infection in HIV seropositive patients.
Materials and methods: This study has been conducted at LLR and Associated Hospitals, GSVM Medical College, and ART plus centre Kanpur (UP) India from April 2017 to September 2018. This is a hospital-based cross-sectional study in which a total of 300 adult male and female HIV seropositive patients of 18 years and above were included in the study. The already diagnosed HIV seropositive patients by HIV testing as per NACO guidelines were investigated by ELISA for HBsAg and ELISA for HCV antibodies.
Results: The rate of HBsAg co-infection was 11% (33/300) and that of HCV co-infection was 7 % (21/300) in HIV seropositive patients. In the present study, the seroprevalence of Hepatitis B was 11% which is similar to the prevalence reported by Saravanan S et al (9%) and Gupta et al (7.28%) but higher than that reported by Tripathi et al (2.25%) and Gupta et al (5.3%). HCV prevalence in our study group was 7 % which is closer to the prevalence reported by Kumarasamy et al (4.8%) but lower than that reported by Lincoln D et al (13.1%).
Conclusion: The main routes of transmission of HIV, HBV, and HCV are similar, therefore, infections with HBV and HCV are likely in HIV infected patients. Therefore, it would be better to screen for these viruses in all the HIV infected individuals and their sexual partners as soon as possible.

Keywords: Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human Immunodeficiency Virus (HIV), Co-infection.

INTRODUCTION

Human immunodeficiency virus (HIV) and Hepatitis B and C viruses (HBV and HCV) are the most common chronic viral infections worldwide. These viruses have similar modes of transmission, mainly through blood and blood products, sharing of needles to inject drugs and sexual intercourse, making co-infection with these viruses a usual event. The degree of immunodeficiency is an important factor in the progression of hepatitis among individuals co-infected with HBV and/or HCV. HBV and HCV co-infection in HIV positive individuals is of paramount importance because of the underlying consequences such as hepato-biliary problems associated with these viruses, which have been shown to decrease the survival rates and life expectancy in the HIV-infected patients.

Approximately 36.9 million people are living with HIV worldwide at the end of 2017 (WHO). It is

estimated that HCV affects 2–15% of people living with HIV worldwide (and up to 90% of those are people who inject drugs) and that chronic HBV infection affects an estimated 5–20% of people living with HIV. In India, there was an estimated adult (15-49 years) HIV prevalence of 0.22% (0.16 to 0.30%) in 2017. Around 21.4 lacs PLHIV (persons living with HIV) were living in the country. Almost 97% of the total PLHIV belonged to the 15+ years age group[1].

HIV and HBV have similar modes of transmission, hence co-infection is common which causes an increased risk for life-threatening complications for people living with both infections. When both HIV and HBV co-infect a patient, the mortality rate from chronic hepatitis B is increased above that of either infection alone with a more speedy progression of liver fibrosis and an increased rate of cirrhosis decompensation[2].

HCV infection is more common in intravenous drug users or recipients of blood and blood products. HIV and HCV both are transmitted through blood and body fluids and hence co-infection of these two viruses is also common. Both can infect patients for even years before symptoms are apparent. HIV co-infection has a great influence on the life cycle of HCV and the natural history of HCV infection. Studies have shown an increased rate of HCV replication in patients co-infected with HIV. Some studies in hemophilic patients have found HCV viremia to be higher in HIV infected than in HIV negative patients. It has been reported that HIV-HCV co-infected patients have symptomatic liver disease more frequently than those with HCV infection alone. Hepatitis C virus produces a chronic infection in ~80 % of infected individuals. Like HBV, this virus is also an important cause of liver fibrosis, cirrhosis, and HCC. Ye Shaodong et al[3] (2014) reported HIV-HCV co-infection as 1.2 % to 98.5 % in the countries of South and South-East Asia.

The prevalence of hepatitis B and C in HIV infected individuals has been reported to be higher than that in the general population. With a more rapid progression of liver disease in HIV patients with hepatitis B and C, HBV and HCV have become major causes of liver-related morbidity and mortality in these patients. As a result, great emphasis has been given on the diagnosis of HBV and HCV in the management of HIV infected patients.

Hepatitis B is a major public health problem in Indian subcontinent where the average carrier rates in the general population are estimated to be about 4%. Moreover, data on the prevalence of HCV infection in the Indian subcontinent are scarce.

Padampriyadarshini et al[4] from South India reported that out of the 951 HIV-infected patients, 61 patients (6.4%) were HBsAg positive and 20 (2.1%) had anti HCV antibodies in their blood. In addition, the rate of HBV and/or HCV co-infection in HIV patients have been variably reported depending on the risk group , type of exposure involved and the geographic region.

The literature regarding the prevalence of HIV co-infection with HBV and/or HCV in India is scarce. Hence, this study was done to investigate the co-infection pattern of HBV and HCV among HIV infected subjects.

Materials and methods:

This is a hospital-based cross-sectional study was conducted at LLR and Associated Hospitals, GSVM Medical College, and ART plus centre Kanpur (UP) India from April 2017 to September 2018. In which a total of 300 adult male and female HIV seropositive patients of 18 years and above were included in the study.

Study period: From April 2017 to September 2018.

Place of study: LLR and Associated Hospitals, GSVM Medical College and ART plus centre Kanpur (UP), India.

Design of the study: Hospital-based cross-sectional study conducted on adult HIV seropositive patients.

Inclusion criteria:

All adult male and female HIV seropositive patients of 18 years and above.

Exclusion criteria:

- HIV negative patients
- Patients not giving consent for the study

Eligible patients were included in the study after they were counselled about the study, its nature, and relevance. All the patients were interviewed and

Volume 1, Issue 4; November-December 2018; Page No. 143-148

clinically examined along with the recording of demographic variables. Informed consent was obtained from all subjects and patient's confidentiality was maintained. Ethical clearance was obtained from the ethics committee, GSVM Medical College, Kanpur (UP) India.

Investigations:

1. HIV testing as per NACO guidelines
2. ELISA for HBsAg
3. ELISA for HCV antibodies.

Statistical analysis: The data was analyzed using SPSS version 13. The data was presented by the mean and standard deviation (SD) for continuous variables and by the frequency with their respective percentages for categorical variables. Chi-square test was used to test the association between categorical variables. A p value of < 0.05 was considered as statistically significant.

Results:

Serum samples from a total of 300 HIV-positive patients were tested in this study. The demographic data of these patients were recorded. Out of 300 patients, 195 (65 %) were males and 105 (35 %) females. The majority of the HIV-infected patients were in the 21-50 years age group. Mean age of the HIV positive patients was 36.49+/- 8.69 years (95% CI) (Table 1)

TABLE 1: AGE WISE DISTRIBUTION OF CASES

AGE (YEARS)	No. of Cases	Percentage (%)
<21	00	0
21-30	99	33
31-40	102	34
41-50	99	33
>50	00	00
TOTAL CASES	300	100

TABLE 2: AGE WISE DISTRIBUTION OF HBV/ HCV CO-INFECTED PATIENTS

AGE GROUP (Years)	**ELISA for HBsAg**		**TOTAL CASES**	**ELISA for HCV Ab**		**TOTAL CASES**	**Co infection with both Hep.B and Hep.C**
	Reactive	**Non Reactive**		**Reactive**	**Non Reactive**		
<21	00	00	00	00	00	00	00
21-30	33	66	99	00	99	99	00
31-40	00	102	102	00	102	102	00
41-50	00	99	99	21	78	99	00
>50	00	00	00	00	00	00	00
TOTAL CASES	**33**	**267**	**300**	**21**	**279**	**300**	**00**

Volume 1, Issue 4; November-December 2018; Page No. 143-148

Mean age of the HIV-HBV co-infected patients was 28.36+/- 1.51 years (95% CI) while that of HIV-HCV co-infected group was 47.14 +/- 2.53 years (95% CI) (Table 2).

All HIV-HBV co-infected patients were seen in the 21-30 year age group (100%) while HIV-HCV co-infection was found only in the 41-50 years of age (100 %) (Table 2).

Overall, the prevalence of co-infection in HIV-positive patients with both hepatitis B and C viruses was 18 % (54/300). Among all the co-infected patients, there were 39 males and 15 females. Co-infection of HIV with both HBsAg & HCV (Triple infection) was not seen in any HIV patient (Table 2,3).

TABLE 3: GENDER WISE DISTRIBUTION OF HBV/HCV CO-INFECTED PATIENTS

SEX	ELISA for HBsAg		TOTAL CASES	ELISA for HCV Ab		TOTAL CASES	Coinfection with both Hep.B and Hep.C
	Reactive	Non-reactive		Reactive	Non-reactive		
MALES	18	177	195	21	174	195	00
FEMALES	15	90	105	00	105	105	00
TOTAL CASES	**33**	**267**	**300**	**21**	**279**	**300**	**00**

The rate of HBsAg co-infection was 11% (33/300) in HIV positive patients. Among males, HIV/HBV co-infection was seen in 18 out of 195 (9.2 %) patients. Among the females, HIV/HBV co-infection was seen in 15 out of 105 (14.2 %) patients (Table 3).

The overall rate of HCV co-infection was 7 % (21/300) in HIV positive patients. Among males, HIV/HCV co-infection was seen in 21 out of 195 (10.8 %) patients. Among females, HIV/HCV co-infection was not found in any of 105 (0 %) female patients. A statistically significant difference (p-value 0.002) was seen in HCV co-infection rates between HIV positive men and women.

Discussion

Among the HIV infected patients worldwide, 2 to 4 millions are estimated to have chronic HBV co-infection while 4 to 5 million are co-infected with HCV[5]. A large number of people are living with HIV in India too. Co-infection of HBV and/or HCV with HIV may complicate the clinical course, management and may also negatively affect the therapy for HIV infection.

Approximately two-thirds of patients with AIDS develop abnormalities in liver function tests[6]. Liver dysfunction may be directly related to HIV infection or may result from conditions such as intravenous drug abuse, alcoholism or prior viral hepatitis, which are highly prevalent in patients with HIV infection. In addition, sepsis, malnutrition or the administration of possibly hepatotoxic antiretroviral medications may also lead to liver dysfunction[7,8].

The life expectancy of patients with HIV has increased due to reduced frequency of opportunistic infections as a consequence of highly active antiretroviral therapy (HAART). As a result, the attention has shifted to the management of concurrent illnesses like chronic HBV and HCV infections having a potential to increase long-term morbidity and mortality. Due to the common risk factors and the transmission routes, HIV patients have an increased risk of both HBV and HCV infection as compared to those uninfected with HIV.

The reported co-infection rates of HBV and HCV in HIV patients have been variable worldwide depending on the risk group, type of exposure involved and geographic region. In India, HBV and HCV co-infection among HIV infected patients have been reported infrequently from region to region.

Gupta et al[9] analyzed serum samples from 451 HIV positive patients for HBsAg and HCV antibodies

Volume 1, Issue 4; November-December 2018; Page No. 143-148

during a period of three years (Jan 2003 to Dec 2005) at a tertiary care hospital in New Delhi, India. The prevalence rate of HBsAg in this population was 5.3% as compared to 1.4% in apparently healthy donors ($p < 0.001$). Though the prevalence of HCV co-infection (2.43%) was lower than HBV in this group of HIV positive patients, the prevalence was significantly higher ($p < 0.05$) than controls (0.7%). Co-infection of HIV with both HBsAg & HCV (Triple infection) was not seen in any HIV patient.

Another study was done at a referral hospital in North India. A total of 620 HIV positive patients were studied. HBV co-infection was detected in 2.25% and HCV co-infection in 1.61% patients (Tripathi et al[10]).

Saravanan S et al[11] from South India studied a total of 500 HIV positive patients and reported that HBV co-infection was detected in 45/500 (9%) patients and HCV co-infection in 11/500 (2.2%) patients.

A study was done at AIIMS, New Delhi India for a period of 6 years between January 2002 to December 2007. A total of 837 HIV positive patients (631 males and 206 females, M:F:: 3:1) were enrolled in the study. Amongst them, 7.28 % of HIV positive patients showed the presence of HBsAg as compared to 1.4 % in HIV negative control group.

Our study findings indicate that HIV-infected men and women are at a higher risk of viral co-infections as illustrated by the high prevalence of HBsAg (11%) and HCV Antibody (7%). Overall, males (13%) are found to be co-infected more than females (5%). This is similar to previous reports that males are associated with higher risk of co-infections with HBV[5].

Our findings show that the prevalence of co-infection for HBV/HIV was highest in the 21-30 years age group, which is the normal age group where the HIV infection is reportedly higher as per Indian literature. This also suggests that sexual route could also be the common route of transmission for both HBV and HIV. In contrast to the HIV/HBV co-infection observed among the sexually active age group viz. (21-30 years), the HIV/HCV co-infection was higher among the 41-50 years age group, which indicates that HCV transmission could have been non-sexual and/or parenteral.

In our study, HIV-HBV co-infection was comparable in both males and females (18 vs 15). In contrast, HIV-HCV co-infection was seen in males only and no HIV positive female was found to be co-infected with HCV. Among all the co-infected patients, there were 39 males and 15 females.

In the present study, the seroprevalence of Hepatitis B was 11% which is similar to the prevalence reported by Saravanan S et al[11] (9%) and Gupta et al (7.28%) but higher than that reported by Tripathi et al[10] (2.25%) and Gupta et al[9] (5.3%).

HCV prevalence in our study group was 7 % which is closer to the prevalence reported by Kumarasamy et al[7] (4.8%). Lincoln D et al[12] also reported that the prevalence of HCV antibody in HIV infected patients was 13.1%.

High prevalence rates of HIV-HCV co-infection were also reported by Saha et al[13] who found an HCV co-infection rate of 92% in intravenous drug-users from Northeast India (Manipur) but in those patients, 25% had a history of blood transfusion and 50% were injection drug users (IDU).

The prevalence of HIV-HCV co-infection in our study is higher than reported from other parts of India [Gupta et al[9] (2.43%) and Tripathi et al[10] (1.61%)]. Further, the chronic HCV co-infection rate in our study is higher than that observed by Padmapriyadarsini et al[4] from South India in which 6.4% were HBsAg positive and 2.1% had demonstrable anti HCV antibodies.

None of the female cases in our study was HIV-HCV co-infected. HIV co-infection appears to increase the rate of HCV transmission by sexual contact. Mostly, the women in India are in a monogamous relationship with their husbands and usually acquire HIV infection from their spouse. Therefore, while the risk for HCV acquisition in steady monogamous relationship is quite low[9], we need to consider other factors responsible for the transmission of Hepatitis C virus infection.

Conclusion:

In our study, the prevalence of Hepatitis B and Hepatitis C co-infection in HIV positive patients is found to be 11 % and 7 % patients respectively. This is significantly higher as compared to the prevalence of these two hepatitis virus infections in the general population of this region.

Volume 1, Issue 4; November-December 2018; Page No. 143-148

The presence of HBV and/or HCV co-infection in HIV patients is challenging to the growing Indian economy as currently there is an increase in the number of patients diagnosed with HIV disease. The knowledge of co-infection in an HIV positive patient is of utmost importance since these patients, as they have a longer life-expectancy on antiretroviral treatment, will also require management for their co-infection with HBV and/or HCV. Therefore, routine screening for hepatitis B and C virus infections in all HIV positive patients should be made mandatory in all developing countries including India.

Limitation of study: The present study has certain limitations. Firstly, this is a cross-sectional study unable to adequately establish a causal relationship between the time of exposure and subsequent infection. Secondly, the study was conducted with patients limited to a tertiary hospital setting and not community setting. However, the results can be considered to approximate for clinical care of our HIV-infected patients. Moreover, during this study, HIV negative group was not enrolled. Immuno-suppression from HIV infection may impair antibody formation and false-negative HCV antibody tests have been reported in individuals co-infected with HIV.

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Volume 1, Issue 4; November-December 2018; Page No. 143-148