Indian J Med Res 147, June 2018, pp 588-593
DOI: 10.4103/ijmr.IJMR_1151_16

Quick Response Code:

Hepatitis B & C virus infection in HIV seropositive individuals & their association with risk factors: A hospital-based study

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Received July 15, 2016

***Background & objectives*: Hepatitis B and hepatitis C virus (HBV and HCV) cause acute and chronic hepatitis, and infections with HBV and HCV are common in HIV-infected patients. The present study was conducted to determine the co-infection of hepatitis B and C virus in stored serum samples of HIV-positive/negative individuals attending an Integrated Counselling and Testing Centre (ICTC) in north India and their association with certain risk factors.**

***Methods*: This study included a total of 840 serum samples, of which 440 were from HIV seropositive individuals and 400 were from control individuals seeking voluntary check-up of HIV status at ICTC. Serum samples were used for the detection of HBV and HCV infection.**

***Results*: HBV infection (11%) was found to be less in contrast to HCV (13%) amongst the HIV seropositive. In controls, HBV and HCV infection was two and three per cent, respectively. Co-infection of HBV and HCV was found in 15 of 109, and in controls, it was 2 of 15. Age group between 21 and 40 was significantly associated with HBV and HCV infection. Heterosexual contact was the leading mode of acquiring HBV and HCV infection.**

***Interpretation & conclusions*: HBV and HCV co-infection was found to be significantly higher in HIV-positive individuals in comparison to normal population. Hepatitis virus infection leads to rapid progression of liver cirrhosis in HIV-infected patients. Routine check-up of HIV seropositive patients for hepatitis virus may be required to monitor clinical outcome.**

Key words Co-infection - hepatitis B - hepatitis C - HIV

Hepatitis B virus (HBV) and hepatitis C virus (HCV) cause acute and chronic hepatitis. Around two billion population are infected with HBV, and approximately 170 million people suffer from HCV infection worldwide[1]. Amongst the human immunodeficiency virus (HIV)-infected patients, about 2-4 million have been reported to have chronic HBV co-infection, while 4-5 million are co-infected with HCV[2]. The severity of HBV and HCV infection depends on multiple factors including age, mode of transmission and immune status at the time of infection.

Globally, around 38.6 million of HIV infections are estimated to have occurred at the end of 2005[3], while chronic HBV and chronic HCV were reported

in about 370 and 130 million, respectively. According to UNAIDS 2017, India, with approximately 2.1 million cases of HIV infection, harbours the second highest number of these patients in the world[4]. HIV-HBV co-infections have been documented in India; six per cent of HIV-HBV co-infection have been reported in clients from Chennai, southern India[5], while the figures for Chandigarh, (Northwest India)[6] and Mumbai (Western India)[7] are 7.5 and 16 per cent, respectively. About one-third of deaths due to liver diseases in HIV-infected patients are attributable to co-infection with either HBV or HCV[8]. During early childhood, modes of transmission play a leading role on the fate of infection. Both hepatitis viruses and HIV can be transmitted through the use of intravenous drug in adults or unprotected sexual intercourse[9]. The major routes for HIV transmission are similar to that of hepatotropic viruses; as a result, infections with HBV and HCV are common in HIV-infected patients. Co-infections of HBV and HCV with HIV have been found to be associated with reduced survival and increased risk of progression to liver disease and also hepatotoxicity associated with antiretroviral therapy[10].

In India, HIV infection is predominantly acquired through heterosexual route; information is available on differential transmission rate and role of demographic factors affecting HBV or HCV prevalence in HIV-positive persons[11]. This study was aimed to determine the co-infection of hepatitis B and C virus in HIV-positive patients, their transmission through heterosexual contact and any association with demographic factors of these patients attending an Integrated Counselling and Testing Centre (ICTC) located in north India.

Material & Methods

This study was carried out during January to December 2011, in the ICTC attached to the University College of Medical Sciences, Delhi, India. The study protocol was approved by the ethics committee of the Institution. Anonymized serum samples that have outlived their purpose and held in storage a −20°C were used in the study.

Sample collection: A total of 840 consecutive serum samples were utilized for the study. A total of 440 samples were from HIV seropositive patients who were registered at the antiretroviral treatment (ART) Clinic of the Guru Teg Bahadur (GTB) Hospital, Delhi. Four hundred samples were from direct walk-in clients requesting for voluntary check up of HIV status at ICTC. The profile of study participants is given in Table I. Socio-economic status was assessed using revised Kuppuswamy's socio-economic status scale[12].

Viral diagnosis

Detection of HIV infection: About 5 ml of whole blood was collected aseptically by venepuncture. The collected blood was allowed to clot; serum was separated by centrifugation at room temperature. Antibody to HIV infection was tested by three rapid diagnostic tests, each of different antigen or test principle. Testing algorithm adhered to National Guidelines on HIV testing specified by the National AIDS Control Organisation (NACO), Ministry of Health & Family Welfare, and Government of India. Detection of the HIV infection was done using approved test kits, namely, (*i*) Combaids (Arkray Healthcare Private Limited, Japan), (*ii*) Retroscreen (Tulip Diagnostics Private Limited, Goa), (*iii*) Instachk (Transasia Bio- Medicals Limited, Mumbai).

The HIV seropositive serum samples were labelled, coded and stored at −20°C. The coded samples were tested for HCV and HBV using ELISA kits.

Detection of HCV infection in HIV positive patients: Detection of the HCV infection was done using (Monolisa® HCV Ag-Ab ULTRA and Monolisa® Biorad, Gurugram, India), in serum samples of HIV-positive patients. Test was performed according to the manufacturer's instructions. After the reaction was terminated, the optical density (OD) was measured at 450/620 nm using a 'sunrise' ELISA reader (Mumbai). The presence of antibodies to HCV and / or HCV capsid antigen was determined by comparing the absorbance for each sample with the cut-off value, which was calculated by dividing the mean of the OD readings for the three positive controls by four. Readings below the cut-off value were considered non-reactive; samples below the cut-off value by 10 per cent were retested. Samples above the cut-off values were considered initially reactive and retested in duplicate before a final interpretation was made. Results were compared with those of AxSYM HCV version 3.0 (Abbott GmbH, Wiesbaden, Germany), a microparticle enzyme immunoassay (MEIA) for the qualitative detection of antibodies to hepatitis C virus in human serum or plasma for the same samples.

Detection of HBV co-infection in HIV-positive patients: HbsAg was detected by ELISA using the Monolisa® Hbs Ag ULTRA kits, Bio-Rad as per manufacturer's instructions. All samples were tested in duplicate.

Table I. Socio-demographic characteristics of study population

Characteristics	Cases HIV +ve (n=440)	Control HIV-ve (n=400)	*P*	OR (95% CI)
Age (yr)				
<30	278 (63)	365 (91)	<0.001	0.16 (0.1106-0.2448)
>30	162 (37)	35 (9)		
Gender				
Male	275 (63)	104 (26)	<0.001	4.744 (3.531-6.373)
Female	165 (37)	296 (74)		
Educational status				
Uneducated	372 (84)	127 (32)	<0.001	11.760 (8.425-16.414)
Educated	68 (15)	273 (68)		
Marital status				
Unmarried	100 (23)	30 (8)	<0.001	3.627 (2.351-5.598)
Married	340 (77)	370 (92)		
Employment status				
Unemployed	172 (39)	372 (93)	<0.001	0.048 (0.0314-0.0742)
Employed	268 (61)	28 (7)		
Partner status				
Positive	182 (41)	16 (4)	<0.001	16.930 (9.915-28.908)
Negative	258 (59)	384 (96)		
Socio-economic status				
Low	375 (85)	361 (90)	0.03	0.62 (0.4085-0.9509)
High	65 (15)	39 (10)		
Alcohol intake				
Yes	120 (27)	165 (41)	<0.001	0.534 (0.3999-0.7133)
No	320 (73)	235 (59)		
Abstainer	18 (15)	67 (40)		
Light drinker	20 (17)	53 (32)		
Moderate drinker	35 (29)	25 (15)		
Heavier drinker	47 (39)	20 (12)		
Smoking/tobacco chewing				
Light smokers/tobacco users (1-5 cigarettes per day)	85 (38)	34 (68)	<0.001	7.25 (5.1137-10.305)
Heavy smokers/tobacco users (>5 cigarettes per day)	139 (62)	16 (32)		
Yes	224 (51)	50 (13)		
Non-smoker/tobacco users (1 or 2 cigarettes on a couple of occasions in the previous 30 days)				
No	216 (49)	350 (87)		

Values in parentheses are percentages. OR, odds ratio

Statistical analysis: All statistical analyses were performed using the software GraphPad InStat version 3.0 (GraphPad Software La Jolla, CA, USA). Chi-square test/Fisher's exact test (SPSS Inc., Chicago, IL, USA) was used to compare the presence of HBV and HCV between HIV seropositive women/healthy controls.

The odds ratio and 95 per cent confidence intervals and multivariate analysis were done as a measure of the association between demographic details and different infections and their risk.

Results

The socio-demographic characteristics of the study population are given in Table I. Of the 440 HIV-positive individuals, 275 (63%) were males and 165 (37%) females. The mean age of the study group was 34±11.4 yr (range 2-70 yr); 340 (77%) were married, and partners of 182 (41%) were also seropositive. Most of the patients had the habit of smoking (51%) and alcohol (27%) intake. Data were also included for the 400 individuals attending the hospital for voluntary check-up of HIV status, who were found to be HIV negative and tested during the same period for HCV and HBV infection. There were 104 (26%) males and 296 (74%) females in this category.

Presence of viral co-infections in HIV positive and negative individuals: The co-infection with hepatitis viruses in HIV-positive patients was 14 per cent. The frequency of HBV infection in HIV-positive patients was 11 per cent, while it was two per cent in HIV-negative individuals (P<0.01) [95% CI 8.41 (3.5-19.8)]; HBV co-infection in HIV seropositives was 8-fold higher than in HIV-negative individuals (Table II). HCV co-infection amongst HIV seropositives was 13 per cent as compared to three per cent in HIV-negatives (P<0.001).

The infection with either HBV or HCV was seen in 21.4 per cent (94/440) in HIV-infected patients, it was 3.3 per cent in HIV-negatives (P<0.01), [95% CI 6.77 (3.7-12.2)]. Rate of co-infection was 6-fold higher in HIV patients compared to HIV-negative individuals.

Association of age with presence of HBV and HCV infection in HIV seropositives: The majority of the HIV-infected individuals were in the age group of 21-40 yr (34%). Mean age of HIV-positive patients was 34 yr. HBV and HCV co-infection with HIV was predominant in the age group 31-40 yr. The rate of infection was low in the age group of 1-10 yr (Fig. 1).

Mode of transmission and rate of infection: In the present study, heterosexual contact was the leading mode of acquiring HBV and HCV infection, at 42 and 44 per cent, respectively, followed by blood transfusion (4%) and homosexual contact (2-3%). Mother-to-child transmission accounted for approximately (1%), while the rate of transmission of infection was higher for HBV (4%) and HCV (8%) in patients inadvertently exposed to contaminated needle/syringe (NS) of infected person (Fig. 2).

Discussion

The present study highlighted the presence of HBV-HCV co-infection amongst the HIV-infected patients and comparing it with apparently healthy north Indian population. In our study, majority of HIV

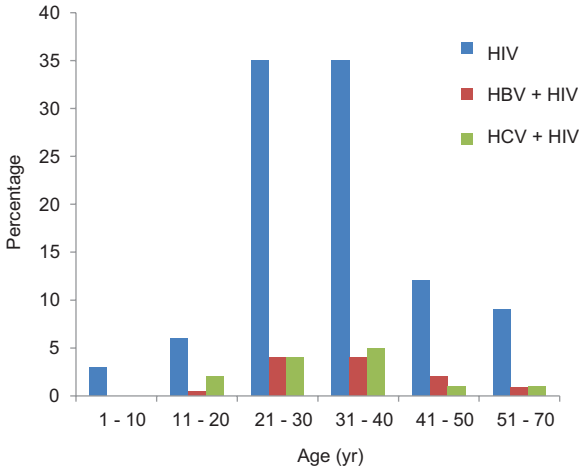

Fig. 1. Age-related distribution of hepatitis B and C virus in HIV-positive patients.

Table II. Presence of hepatitis B virus and hepatitis C virus in cases and controls

Infection	HIV+ve (n=440)	HIV-ve (n=400)	*P*	OR (95% CI)
Hepatitis B^+	50 (11)	6 (2)	<0.001	8.419 (3.56-19.86)
Hepatitis B^-	390 (89)	394 (98)		
Hepatitis C^+	59 (13)	9 (3)	<0.001	7.569 (3.56-16.05)
Hepatitis C^-	381 (87)	391 (97)		
Hep B^+ + Hep C^+	15 (14)	2 (13)	0.96	1.037 (0.212-5.064)
Hep B^+/Hep C^+	94 (86)	13 (87)		

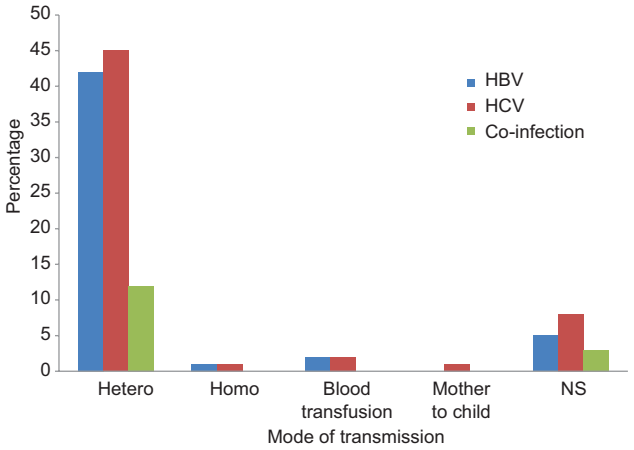

Fig. 2. Prevalence of hepatitis B virus, hepatitis C virus and co-infection in association with the mode of infection transmission. NS, needle/syringe; Homo, homosexual; Hetero, heterosexual.

seropositive patient's age was 21-40 yr and they were sexually active. This finding was in concordance to that reported previously[13,14]. Some other demographic factors were also found to be significantly associated with HIV infection.

HBV (11%) and HCV (13%) co-infection in HIV seropositive was higher than in control population, which is in good agreement with previous studies from India[15,16] . Mittal *et al*[17] reported low prevalence of HBV and HCV in Indian population. We observed a high prevalence of reproductive tract infections in HIV-seropositive women[18]. The immunosuppressed patients fall into the high-risk group of acquiring HBV infection, while the transmission of HCV occurs more efficiently through percutaneous routes[19].

In HIV patients, the liver damage may be directly associated with HIV infection or it may be due to events such as prior hepatitis/intravenous drug abuse and alcoholism in already immunosuppressed patients[7]. Probably, other factors such as malnutrition, sepsis or administration of possible hepatotoxic antiretroviral medication may also be responsible for liver damage[20]. Highly active antiretroviral therapy recipients are more vulnerable to other infections and persistence of HBV and HCV infections. The presence of HIV infection makes the transmission of hepatitis viruses easier, through prenatal as well as sexual contact[21]. Moreover, pregnant women are prone to infection, perhaps owing to low immunity and hormonal changes[22].

Our findings on HBV co-infection in HIV-infected patients were similar with the study reported by Mudawi *et al*[23] but slightly lower than those reported by Abera *et al*[24] from Sudanese and Ethiopian population, respectively.

The heterosexual contacts were found with higher prevalence of HBV and HCV in HIV-seropositive participants[25]. In the present study, transmission of HCV and HBV from mother-to-child was found in one per cent HIV-positive women only. Besides, transmission of HCV infection was also higher amongst the patients exposed to contaminated needles and syringes as well as multiple use of single-use needles and syringes of infected person, which was in accordance with previous report from India[26]. HCV co-infection was higher in HIV-positive male patients in comparison to female group, perhaps attributable to higher rate of sexual promiscuity[15,27].

In conclusion, our findings showed that the HIV seropositive individuals had a high risk of acquiring HBV and HCV co-infections predominantly through heterosexual contact. Therefore, it would be beneficial if the HIV seropositive individuals screened routinely for parallel HBV/HCV infection.

Acknowledgment

Authors acknowledge the National AIDS Control Organization, ART clinic and ICTC of GTB Hospital, Delhi, India, for providing HIV-1 infected blood samples.

***Financial support & sponsorship*:** Authors acknowledge the Indian Council of Medical Research, New Delhi, India for providing financial support for the study.

***Conflicts of Interest*:** None.

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