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## Original Research Article

## Seroprevalence of Hepatitis B and C co-infection in HIV seropositive and HIV seronegative cases in a Tertiary care hospital in Southern Haryana

Shreya Behl<sup>1,\*</sup>, Aaditya Behl<sup>2</sup>, Pratibha Mane<sup>1</sup>, Jyoti Sangwan<sup>1</sup>, Prakriti Vohra<sup>1</sup><sup>1</sup>Dept. of Microbiology, SHKM Government Medical College, Gehbar, Haryana, India<sup>2</sup>Dept. of Community Medicine, Adesh Medical college and Hospital, Mohri, Haryana, India

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## ABSTRACT

**Introduction:** HBV (Hepatitis B virus) and HCV (Hepatitis C virus) are the causative agents of acute as well as chronic hepatitis. Nearly, two billion people are suffering with HBV and approximately 170 million people are infected with HCV infection around the world. While patients who are infected with HIV (Human Immunodeficiency Virus) 2-4 million are found to be having chronic HBV co-infection and 4-5 million are having HCV coinfection. Due to common mode of transmission of HIV, HBV and HCV like using shared needles, syringes, other injectable devices, sexual intercourse, or even mother to baby transmission, it is common to see HBV and HCV co-infection in HIV positive individuals.

**Materials and Methods:** This was a hospital based observational cross-sectional study. This study was conducted in Department of Microbiology, SHKM GMC, Nalhar, Nuh, Haryana. It was for one year. The sample size for HIV seropositive cases was 80 including 40 HIV positive and 40 HIV negative samples. Seroprevalence of HBV and HCV was identified on HIV positive and HIV negative samples.

**Results:** Seroprevalence of HBV and HCV was found to be higher in HIV positive individuals than HIV negative individuals. In HIV positive patients 10% individuals were HBsAg positive, 5% were HBeAg positive, 10% were positive by HBV RT-PCR. None of the HIV negative were coinfecting with HBV. Similarly HCV-HIV coinfection was seen in 12.5% of individuals with Rapid test, ELISA and RT-PCR. None of the HIV negative were coinfecting with HCV.

**Conclusion:** In HIV positive individuals HBV and HCV coinfection was seen and Co-infection of HBV and HCV was absent in HIV negative individuals. Regular screening is recommended for HBV and HCV in HIV positive individuals.

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## 1. Introduction

HBV (Hepatitis B virus) and HCV (Hepatitis C virus) are the causative agents of acute as well as chronic hepatitis. Nearly, two billion people are suffering with HBV and approximately 170 million people are infected with HCV infection around the world. While patients who are infected with HIV (Human Immunodeficiency Virus) 2-4 million

are found to be having chronic HBV co-infection and 4-5 million are having HCV coinfection. As per UNAIDS 2017, India has 2.1 million HIV patients which is second highest across the world. In HIV infected individuals around one third of the deaths due to the liver diseases are caused by HBV or HCV.<sup>1,2</sup> There were 940,000 deaths in HIV infected individuals due to AIDS related illnesses in the year 2017.<sup>3</sup> Severe morbidity is enhanced by HBV, HCV and HIV which can lead to major world health problems.<sup>4</sup> HIV prevalence in India is estimated approximately 2.1

\* Corresponding author.

E-mail address: [drshreya1993@gmail.com](mailto:drshreya1993@gmail.com) (S. Behl).

Million (21.40 Lakhs) individuals are infected with HIV as per National AIDS Control Organisation (NACO) 2017 report.<sup>1,5</sup>

Due to common mode of transmission of HIV, HBV and HCV like using shared needles, syringes, other injectable devices, sexual intercourse, or even mother to baby transmission, it is common to see HBV and HCV co-infection in HIV positive individuals. Reduced survival and increased progression to hepatic disease is seen with co-infections of HBV and HCV with HIV. The co-infection with HBV and HCV with HIV also leads to hepatotoxicity which is associated with antiretroviral therapy. Heterosexual route is the predominant route of transmission of HIV infection in India.<sup>1,6</sup>

Earlier HIV was poorly understood, fatal disease, now it is a treatable chronic disease with a chance of normal life expectancy. Due to this Comorbidities like cardiovascular diseases and non-AIDS malignancies are more commonly seen by health professionals. Similarly in HCV treatment, due to the establishment of direct-acting antiviral agents the cure rates have reached above 95% and associated drastic reduction in risk of hepatocellular carcinoma and reducing the liver transplantation due to cirrhosis in HCV infection. In HBV infection we can hope to get good drug development in future.<sup>7</sup> HIV positive individuals who are co-infected with HBV should be given HIV antiviral medication which have activity against HBV like tenofovir and entecavir.<sup>8</sup>

Due to coinfection of HIV, HBV and HCV leads to multiple health issues like liver related diseases, non-hepatic organ dysfunction which further leads to death. Due to morbidity and mortality caused by chronic viral hepatitis in HIV individuals there is increase in IPD admissions in healthcare system and evolving discussion on utilization of hepatic transplantation in these individuals.<sup>9</sup>

To the best of our knowledge, data on the seroprevalence of Hepatitis B and C in HIV positive individuals and its comparison with HIV negative individuals is not available in Haryana.

Hence, this study is undertaken to know the seroprevalence of Hepatitis B and C in HIV positive individuals and compare it with HIV seronegative individuals in the individuals attending ICTC individuals of SHKM GMC, Nalhar.<sup>10,11</sup>

## 2. Materials and Methods

### 2.1. Study design and setting

#### 2.1.1. Study type

This was a hospital based observational cross-sectional study. This study was conducted in Department of Microbiology, SHKM GMC, Nalhar, Nuh, Haryana.

#### 2.1.2. Study period

It was for one year from May 2021 to April 2022.

#### 2.1.3. Study subjects

The individuals who attended ICTC of SHKM GMC, Nalhar, Nuh, Haryana.

### 2.2. Inclusion criteria

1. HIV (Human Immunodeficiency Virus) seropositive individuals as per NACO guidelines from ICTC were taken as study group.

2. HIV seronegative individuals were taken as control.

### 2.3. Exclusion criteria

1. Individuals who were not willing to participate in the study.

2. Repeat sample of the same patient were excluded.

### 2.4. Sample size

The sample size for HIV seropositive cases was 40 for this study. The control group was also of the same number of individuals corresponding to age and sex.

### 2.5. Methods

The blood sample was collected by well trained laboratory technician of ICTC with universal precautions. About 5 ml of blood was collected aseptically by venepuncture after taking written and informed consent and HIV testing was done as per National AIDS control organisation (NACO) guidelines. Biomedical waste was disposed of as per biomedical waste management rules. This collected blood was allowed to clot and serum will be separated using centrifugation. The samples were stored at -20°C and these samples were tested by Rapid diagnostic test (RDT), Enzyme Linked Immunosorbent Assay (ELISA) and by RT PCR. All the demographic details of individuals were recorded.

## 3. Results

**Table 1:** Seroprevalence of Hepatitis B in both HIV seropositive and HIV seronegative individuals.

HBV	Frequency	Percent
HBsAg positive	4	5.0%
HBeAg positive	2	2.5%
Anti-HBs in HIV positive individuals	67	83.8%
Anti-HBe positive	2	2.5%
Anti-HBc positive	3	3.8%
RT PCR positive	4	5.0%
Total	80	100%

**Table 2:** - HCV Seroprevalence in both HIV positive and HIV negative individuals.

HCV	Frequency	Percent
Rapid	5	6.3%
ELISA	5	6.3%
RT PCR	5	6.3%
Total	80	100%

**Table 3:** Comparison of HBV results in HIV seropositive and HIV seronegative individuals

HBV	HIV		Total	p-value
	Negative	Positive		
HBsAg	0	4	4	0.040*
	0.0%	10.0%	5.0%	
HBcAg	0	2	2	0.152
	0.0%	5.0%	2.5%	
Anti-HBs	31	36	67	0.043*
	77.5%	90.0%	83.8%	
Anti-Hbe	0	2	2	0.152
	0.0%	5.0%	2.5%	
AntiHBc	0	3	3	0.047*
	0.0%	7.5%	3.8%	
RT-PCR	0	4	4	0.040*
	0.0%	10.0%	5.0%	
Total	40	40	80	

Rapid-HBsAg, Anti-HBs, AntiHBc and RT-PCR was significantly more among HIV positive subjects.

**Table 4:** Comparison of HCV results in HIV positive and negative individuals.

HCV	HIV		Total	p-value
	Negative	Positive		
Rapid	0	5	5	0.021*
	0.0%	12.5%	6.3%	
ELISA	0	5	5	0.021*
	0.0%	12.5%	6.3%	
RT-PCR	0	5	5	0.021*
	0.0%	12.5%	6.3%	
Total	40	40	80	

#### 4. Discussion

There are around 40 million chronic infections that are caused by HIV, while the Hepatitis C virus and the Hepatitis B virus are each responsible for 130 million and 370 million chronic infections, respectively.<sup>12</sup> It is estimated that liver disorders are directly or indirectly responsible for one third of the fatalities that occur among HIV patients. There have been reports of a rise in the incidence of HIV co-infection HBV/HCV across the world, which has become a new emergent public health problem on a global scale.<sup>13–15</sup> It is estimated that 10 percent of the 40 million people infected with HIV have chronic hepatitis B. This percentage is based

on global statistics.<sup>16</sup> The frequency of HIV and HCV co-infection fluctuates anywhere from 5 to 20 percent.<sup>17</sup>

The clinical course of HIV in patients who are infected with HIV is complicated by co-infection with HBV and/or HCV, which can also have a negative impact on the treatment of HIV infection. The prevalence of HBV and HCV co-infection in HIV has been variably reported in different studies.<sup>18–21</sup> The prevalence of HBV varies markedly among different HIV infected population and geographical location is one of the major determinants of prevalence. In regions with a low level of endemicity, the prevalence of HBV co-infection ranges from five to seven percent.<sup>19,22</sup> In moderate and high endemicity, it varies from 6-20 percent.<sup>20</sup> There is a wide range of possible HCV co-infection rates, ranging from 9 to 16 percent.<sup>21,23</sup> According to the findings of a study compiled by the TREAT Asia HIV Observational Database in Taiwan, the prevalence of HBV-HCV co-infection is approximately 10%.<sup>24</sup>

In present study, majority of the study population belonged to 21-30 years (27.5%), 31-40 years (23.8%), 11-20 years (15.0%), 41-50 years (12.5%), Above 60 years (11.3%) and 51-60 years (10.0%). Sharma et al.<sup>1</sup> found that the participants in the research had a mean age of 34.114 years old (range 2-70 years).

In contrast to the results of a research that was conducted by Choy et al.,<sup>25</sup> which found that a significant association existed between age 30–49 and more than 50 years of age and HIV-HBV co-infection, our discovery found no such association. This decreased prevalence of HIV-HBV co-infection among older HIV patients might be due to the low frequency of individuals in this category who are older than 35 years old. The precise explanation, however, has to be understood through the use of more prospective cohort studies.

The majority of HIV-positive patients were between the ages of 21 and 40, and they reported engaging in sexual activity. This finding was consistent with the one that had been published in the past.<sup>26,27</sup> It was revealed that a substantial association existed between HIV infection and a number of other demographic characteristics as well.

In our research work, it was found that there were 46.3% males and 53.8% females. Sharma et al.<sup>1</sup> found that 63% were males and 37% females. Shrestha et al.<sup>2</sup> stated that the majority of HIV patients who also had HBV infection were female (57.14 percent), making up more than half of these individuals. In the study by Chandra et al.,<sup>28</sup> there were 100 males out of 120 in group 1 and 104 were males out of 120 in group 2. Yang et al.<sup>29</sup> stated that 74.7 percent subjects were men and 25.3 percent were women. Males made up the majority of the infected population, which may be related to the fact that men are more likely to engage in high-risk behaviours and have a higher percentage of homosexuality and intravenous drug use than women do.

In current study, the predominant symptoms were fever, pain and loss of appetite. Chandra et al.,<sup>28</sup> observed that among group 1, the most prevalent symptoms that patients presented with were fever, lack of appetite, weight loss, and coughing.

In current investigation work, most of the study population was Housewife (40.0%). Majority of the study population was Married (77.5%). Sharma et al.<sup>1</sup> found that 77% were married.

We found in our study that there was Past h/o Diabetes Mellitus, Past h/o Diabetes Mellitus and Hypertension, Past history of hepatitis, Past history of Tuberculosis and Past history of tuberculosis and hepatitis among 1 (1.3%) each and Past history of hypertension and hepatitis among 4 (5.0%) subjects.

In present investigation, there were 4 (5.0%) only Smokers, 2 (2.5%) were only alcoholics and 1 (1.3%) each were Only Tobacco chewer and both Smoker & Alcoholic. Sharma et al.<sup>1</sup> found that majority of the patients were smokers (51 percent) and drank alcohol (27 percent) regularly in their daily lives.

#### 4.1. Hepatitis virus

It was found in the current study that for HBV, Rapid-HBsAg was positive among 5.0%, HBeAg was positive among 2.5%, Anti-HBs was positive among 83.8%, Anti-HBe was positive among 2.5%, AntiHbC was positive among 3.8% and RT-PCR was positive among 5.0%. Rapid-HBsAg, Anti-HBs, AntiHbC and RT-PCR was significantly more among HIV positive subjects. In current investigation, for HCV, Rapid, ELISA and RT-PCR was positive among 5 (6.3%) each. Rapid, ELISA and RT-PCR for HbC was significantly more among HIV positive subjects.

The rate of co-infection ranged from 30.4 percent in Nagpur<sup>30</sup> to 2.25 percent in Lucknow,<sup>31</sup> 7.7 percent in Chennai,<sup>32</sup> and 3.5 percent in Mumbai.<sup>33</sup> The researchers Chandra and colleagues,<sup>28</sup> observed that 15% of HIV-positive people also had HBV co-infection.

Sharma et al.<sup>1</sup> found that Patients who tested positive for HIV had a 14% chance of also being infected with hepatitis viruses. In HIV-positive patients, the prevalence of HBV infection was 11%, while it was only 2% in HIV-negative persons (P 0.01). The likelihood of having HBV co-infection in HIV-positive persons was eight times greater than in HIV-negative people. 13 percent of HIV-positive people were also infected with HCV, which is significantly higher than the three percent seen in HIV-negative people (P 0.001). In HIV-positive individuals, the rate of infection with either HBV or HCV was 21.4%, while it was only 3.3% in HIV-negative patients. When compared to HIV-negative persons, those living with HIV had a rate of co-infection that was six times greater.

Chandra and colleagues,<sup>28</sup> observed that among HIV patients, the presence of HBsAg was observed in 15% of

cases, while only 1.6% of cases were found in controls (P 0.001). 8.3 percent of patients in the HIV group tested positive for anti-HCV antibodies, but none of the controls tested positive for the antibodies. Three individuals out of a total of 28 who tested positive for HBsAg and HCV had a triple infection with HBV, HCV, and HIV. Antigen and antibody tests for the hepatitis B envelope (HBeAg and anti HBe) returned positive results in 33.3% and 55.5% of patients, respectively. HBV-DNA was found to be present in 55.6 percent (10/18) of samples (6 were HBeAg positive, 4 were anti-HBe positive). All patients with a positive anti-HCV test had detectable levels of HCV-RNA.

In our analysis, the prevalence of HCV co-infection (6.3%) was much greater than the reported rates of 1.6% in Lucknow,<sup>31</sup> and 2.3% in Chennai.<sup>32</sup> But was similar to 7.2% in Nagpur<sup>30</sup> and 8.0% in Mumbai.<sup>33</sup>

The findings are consistent with those of earlier research conducted in India.<sup>15,16</sup> According to Mittal et al.,<sup>34</sup> the prevalence of HBV and HCV in the Indian population is quite low. In HIV-seropositive women, we found an extremely high frequency of infections affecting the reproductive system.<sup>35</sup> Patients with reduced immune systems are more likely to become infected with HBV, whereas HCV is more effectively spread by percutaneous routes. Patients with weakened immune systems are more likely to become infected with HBV.<sup>36</sup>

Shrestha et al.<sup>2</sup> reported that approximately one-fifth of all people who were infected with HIV also had hepatitis B virus, hepatitis C virus, or both (23.63 percent). The rates of co-infection with HIV and HBV, HIV and HCV, and HIV-HBV-HCV, respectively, were 2.95 percent, 18.14 percent, and 2.53 percent, respectively, among these people.

Our findings on HBV co-infection in HIV-infected individuals were comparable to the study that was published by Mudawi et al.<sup>37</sup>, although they were somewhat lower than the findings that were reported by Abera et al.<sup>38</sup> from the Sudanese population and the Ethiopian population, respectively. It was discovered that HIV-seropositive participants who had heterosexual encounters had a greater frequency of HBV and HCV.<sup>39</sup>

Sharma et al.<sup>1</sup> stated that the only mothers who were found to transmit HCV and HBV from themselves to their children were HIV-positive. In addition, the rate of HCV infection transmission was higher among patients who had been exposed to contaminated needles and syringes, as well as among patients who had made multiple uses of single-use needles and syringes belonging to an infected person. This finding was in line with a report that had been made in India previously.<sup>40</sup> In HIV-positive male patients, the prevalence of HCV co-infection was significantly greater compared to that of HIV-positive female patients. This disparity may be attributed to a higher likelihood of sexual promiscuity.<sup>41</sup>

According to the findings of Lonita and colleagues,<sup>42</sup> the prevalence of HBV-HCV co-infection among PLWH

in Nepal was found to be 4.4 percent, whereas the prevalence of HCV infection was 19 percent. The pooled prevalence of co-infection with HBV, HCV, and combined HBV and HCV was 1.3 percent, 19.7 percent, and 4.6 percent, respectively, in a study that was conducted in Nepal between the years 1990 and 2020 and included a systematic review of previous research.<sup>43</sup> Nevertheless, epidemiological data on HIV-HBV, HIV-HCV, and HIV-HBV-HCV co-infections among HIV patients are scant and varied even within the country and internationally. This is true both domestically and internationally. In a study carried out by Bhattarai and colleagues,<sup>44</sup> the researchers found that the prevalence of HIV-HBV, HIV-HCV, and HIV-HBV-HCV co-infections was 3.62 percent, 2.93 percent, and 0.34 percent, respectively. It was shown that among PLWH in North India, the prevalence of HBV and HCV co-infection was 5.32 percent, whereas the prevalence of HCV infection alone was 2.43 percent.<sup>39</sup>

Similarly, the prevalence of HIV-HBV, HIV-HCV, and HIV-HBV-HCV co-infections among HIV patients was 9.27 percent, 9.98 percent, and 2.72 percent, respectively, in the province of Hunan in China.<sup>45</sup> In Ghana, the prevalence of HIV-HBV, HIV-HCV, and HIV-HBV-HCV co-infections among HIV patients was 12.5 percent, 5.5 percent, and 18.0 percent respectively in a study that was conducted by Boateng et al.,<sup>46</sup> and it was 6.1 percent, 0.5 percent, and 0.0 percent respectively in a study that was conducted by Pappoe et al.<sup>47</sup>

The liver damage that occurs in HIV patients may be directly related to the HIV infection, or it may be the result of other factors, such as a history of hepatitis, intravenous drug misuse or drinking in individuals who are already immunocompromised.<sup>48</sup> It is conceivable that the liver damage was caused by a combination of a few different circumstances, including starvation, infection, and the use of a potentially hepatotoxic antiretroviral medicine.<sup>49</sup>

In our study it was found that all the HBV positive individuals co-infected with HIV that is 4 individuals were having elevated liver enzymes. Similarly all the HCV positive individuals co-infected with HCV that is 5 individuals were having elevated liver enzymes.

People who get highly active antiretroviral medication are at a greater risk of contracting additional infections and having their HBV and HCV illnesses remain for longer. Both prenatal and sexual interaction are more likely to result in the transfer of hepatitis viruses when HIV is present. This is true regardless of the mode of transmission.<sup>50</sup> In addition, pregnant women have a higher risk of contracting an illness, which may be caused by lowered immunity or hormonal shifts.<sup>51</sup>

Our study is subject to a number of limitations. We did not conduct an investigation on the frequency with which other hepatitis viruses, such as hepatitis A, hepatitis D, and hepatitis E, are found in HIV-positive individuals. We

did not make any distinctions between heterosexual and homosexual activities with regard to the sexual method of transmission. We did not classify HIV-HBV patients, HIV-HCV patients, or HIV-HBV-HCV patients into distinct categories based on marital status, ethnicity, or educational level.

## 5. Conclusion

1. Majority of the study population belonged to 21-30 years (27.5%), 31-40 years (23.8%), 11-20 years (15.0%), 41-50 years (12.5%), Above 60 years (11.3%) and 51-60 years (10.0%).
2. There were 46.3% males and 53.8% females.
3. Most of the study population was Housewife (40.0%).
4. Majority of the study population was Married (77.5%).
5. There was Past history of Diabetes Mellitus, Past history of Diabetes Mellitus and Hypertension, Past history of hepatitis, Past history of Tuberculosis and Past history of tuberculosis and hepatitis among 1 (1.3%) each and Past history of hypertension and hepatitis among 4 (5.0%) subjects.
6. There were 4 (5.0%) only Smokers, 2 (2.5%) were only alcoholics and 1 (1.3%) each were Only Tobacco chewer and both Smoker & Alcoholic.
7. There were 40 serum samples (50.0%) positive for HIV and 40 serum samples (50%) negative for HIV.
8. For HBV in HIV positive cases, HBsAg was positive among 10%, HBeAg was positive among 5%, Anti-HBs was positive among 90%, Anti-HBe was positive among 5%, Anti-HBc was positive among 3% and RT-PCR was positive among 10% and For HBV in HIV negative individuals none was found positive.
9. For HCV in , Rapid, ELISA and RT-PCR was positive among 5 (12.5%) each. Similarly no sample was found positive for HCV in HIV negative individuals.
10. Rapid-HBsAg, HBeAg, Anti-HBs, Anti-HBe, Anti-HBc and RT-PCR was significantly more among HIV positive subjects as compared to HIV negative individuals.
11. Rapid test, ELISA and RT-PCR for HCV was significantly more among HIV positive subjects as compared to HIV negative individuals.

According to our research, HIV-positive people had increased chance of contracting HBV and HCV co-infections. In our research heterosexual was the most common route of transmission. As a result, it should be encouraged that HIV seropositive individuals to get tested for HBV and HCV. It is seen that co-infection of HBV and HCV in HIV positive individuals is more due to common routes of transmission.

As per this study screening of HIV positive individuals for HBV and HCV is highly recommended, this would help in prompt identification and treatment, leading to

improved outcomes for these individuals. This, in turn, would reduce the likelihood that these viral infections would prevent further transmission. Hepatitis B vaccine can help in reducing the hepatitis B infection. So, it should be encouraged. In case of HIV post exposure prophylaxis in needle stick injuries, anti-viral therapy in pregnant women, avoiding sharing of needles by i.v. drug abusers, avoiding multiple sexual partners, using proper protocol of injecting drugs by health care workers.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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## Author biography

**Shreya Behl**, Resident  <https://orcid.org/0009-0007-4552-8780>

**Aaditya Behl**, Intern  <https://orcid.org/0009-0007-5123-4666>

**Pratibha Mane**, Professor and HOD  <https://orcid.org/0000-0001-7518-0155>

**Jyoti Sangwan**, Professor  <https://orcid.org/0000-0001-8410-2212>

**Prakriti Vohra**, Professor  <https://orcid.org/0000-0002-7522-1700>

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