Prevalence of hepatitis B, hepatitis C and human immunodeficiency viral infections in patients with inflammatory bowel disease in north India

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Background/Aims: Patients with inflammatory bowel disease (IBD) often require immunosuppressive therapy and blood transfusions and therefore are at a high risk of contracting infections due to hepatitis B (HBV) and hepatitis C (HCV) and human immunodeficiency virus (HIV). In the present study, we assessed the prevalence of these infections in patients with IBD. **Methods:** This retrospective study included 908 consecutive patients with IBD (ulcerative colitis [UC], n=581; Crohn's disease [CD], n=327) who were receiving care at a tertiary care center. Ninety-five patients with intestinal tuberculosis (ITB) were recruited as disease controls. Prospectively maintained patient databases were reviewed for the prevalence of HBV surface antigen, anti-HCV antibodies, and HIV (enzyme-linked immunosorbent assay method). HCV RNA was examined in patients who tested positive for anti-HCV antibodies. Prevalence data of the study were compared with that of the general Indian population (HBV, 3.7%; HCV, 1%; HIV, 0.3%). **Results:** The prevalence of HBV, HCV, and HIV was 2.4%, 1.4%, and 0.1%, respectively, in the 908 patients with IBD. Among the 581 patients with UC, 2.2% (12/541) had HBV, 1.7% (9/517) had HCV, and 0.2% (1/499) had HIV. Among the 327 patients with CD, 2.8% (8/288) had HBV, 0.7% (2/273) had HCV, and 0% (0/277) had HIV. One patient with CD had HBV and HCV coinfection. The prevalence of HBV, HCV, and HIV in patients with ITB was 5.9% (4/67), 1.8% (1/57), and 1.2% (1/84), respectively. **Conclusions:** The prevalence of HBV, HCV, and HIV in north Indian patients with IBD is similar to the prevalence of these viruses in the general community. Nonetheless, the high risk of flare after immunosuppressive therapy mandates routine screening of patients with IBD for viral markers. **(Intest Res 2017;15:97-102)**

Key Words: Inflammatory bowel disease; Colitis, ulcerative; Crohn disease; Hepatitis B; Hepatitis C

INTRODUCTION

The disease burden of IBD has increased significantly in India in the last few decades.[1] Patients with IBD are more likely to undergo surgery and receive blood transfusions and therefore are at a high risk of contracting blood-borne infections such as those caused by HBV and HCV and human immunodeficiency virus (HIV). Additionally, patients with IBD are likely to receive immunosuppressive therapy, which affects the course of these infections.[2] Although HBV and HCV do not affect the natural course of IBD, HIV is well recognized to do so.[3] Currently available data on the prevalence of these blood-borne infections are inadequate and inconsistent among different studies. Thus, the objective of the present study was to determine the prevalence of HBV, HCV, and HIV infection in patients with IBD (UC and CD) attending a tertiary referral hospital in north India.

METHODS

1. Patient Population

Patients with IBD who visited the Inflammatory Bowel Disease Clinic at All India Institute of Medical Sciences (AIIMS), New Delhi, from August 2004 to January 2016 were enrolled in this study. AIIMS is a tertiary care center serving as a referral hospital for patients from all over north India. Patients with intestinal tuberculosis (ITB) were enrolled as disease controls.

2. Study Design

This study involves a retrospective analysis of a referral IBD registry. Relevant clinical data were obtained from medical records pertaining to both the initial consultation and subsequent follow-up consultations throughout care within the practice. Prospectively maintained data included detailed information on the patient's disease and follow-up, including name, age, sex, address, diagnosis, medical history, results of clinical examination and laboratory investigations and ongoing treatment.

3. Diagnosis of Viral Infections

Data regarding the prevalence of viral infections (HBV, HCV, and HIV) were obtained from routinely performed ELISA-based serological tests for HBsAg, anti-HCV antibodies, and HIV for all patients at our center. However, all three viral markers were not available for all the patients in database. All patients who tested positive for anti-HCV antibodies underwent quantitative HCV RNA testing for confirmation. Patients with HBsAg positivity were diagnosed with HBV infection, and no confirmatory test was required. HIV serology was tested and reported as positive according to the guidelines of the National AIDS Control Organization (NACO).[4]

4. Prevalence of Viral Infections in the General Population

Data on the prevalence of HCV and HBV infection in the general population were obtained from the National Centre for Disease Control (NCDC) website.[5] NACO data were used to determine the prevalence of HIV in the general population.[4] In India, the hepatitis B vaccine has been covered under the Universal Immunization Programme since 2007, with a total of four doses administered at birth and then at 6, 10, and 14 weeks of age. However, the vaccination status of the patients in the current study could not be determined.

5. Data Analysis

The prevalence of the viral infections was recorded as percentages. Data were analyzed using Stata software (version 11.2; StataCorp LP, College Station, TX, USA). The prevalence of the three blood-borne infections was compared between patients with IBD and the general population by using the one-sample proportion test. The *P*-values less than 0.05 were considered statistically significant.

RESULTS

A total of 908 patients with IBD were enrolled at the IBD clinic of AIIMS between August 2004 and January 2016. Of these, 581 were diagnosed with UC (male, n=340; female, n=241; mean age, 36.9±11.7 years) and 327 were diagnosed with CD (male, n=201; female, n=126; mean age, 39.1±13.9 years).

1. Prevalence of HBV, HCV, and HIV Infection in Patients with IBD

According to NACO and NCDC data, the prevalence of HBV, HCV, and HIV in the general population in India is 3.7%, 1%, and 0.3%, respectively. In our study, we found that the prevalence of HBV, HCV, and HIV among the 908 patients with IBD (UC and CD) was 2.4% (20/829), 1.4% (11/790), and 0.1% (1/776), respectively. All three viral markers of all the patients were not available in the database. This led to different denominators while calculating prevalence of these infections in IBD patients.
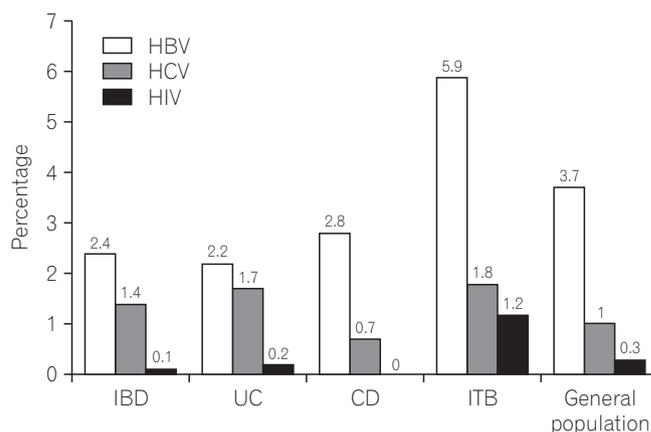

Fig. 1. Prevalence of HBV, HCV, and human immunodeficiency virus (HIV) in patients with IBD or intestinal tuberculosis (ITB).

When compared to prevalence of these infections in general population, the results were not statistically significant (P=0.05, P=0.26, and P=0.31, respectively) (Fig. 1).

2. Prevalence of HBV, HCV, and HIV in Patients with UC

Among the 581 patients with UC, 2.2% (12/541) had HBV, 1.7% (9/517) had HCV, and 0.2% (1/499) had HIV. Again, these rates did not differ significantly from the corresponding rates in the general population (P=0.07, P=0.09, and P=0.68, respectively).

Of the 21 patients with UC and concomitant HBV/HCV infection, 14 (66.7%) received steroids and eight (38%) received azathioprine (AZA) or 6-mercaptopurine (6-MP). Five developed cirrhosis (23.8%), and one patient with HCV infection died of acute on chronic liver failure (ACLF) (Table 1).

3. Prevalence of HBV, HCV, and HIV Infection in Patients with CD

Among the 327 patients with CD, 2.8% (8/288) had HBV and 0.7% (2/273) had HCV; no patient had HIV, while one patient had HBV and HCV coinfection. The prevalence of HBV and HCV in patients with CD was not significantly different compared to that in the general population (P=0.41 and P=0.65, respectively).

Three patients with CD (33.3%) diagnosed with HBV/HCV infection received steroids, while three (33.3%) received AZA or 6-MP. Of the nine patients with HBV/HCV infection, one developed cirrhosis (11.1%). Additionally, one patient with HBV died of ACLF (Table 2).

Table 1. Demographic and Clinical Characteristics of Patients with UC and Concomitant Viral Infections

Characteristic	HBV (n=12)	HCV (n=9)	HIV (n=1)
Median age (yr)	35 (24–65)	36 (28–52)	38
Sex			
Male	8 (66.7)	4 (44.4)	-
Female	4 (33.3)	5 (55.6)	1 (100)
Median duration of UC (yr)	7.0 (2.5–14.0)	4.5 (1.5–15.0)	5
Extent[a]			
E1	None	2 (22.2)	1 (100)
E2	7 (58.3)	4 (44.4)	-
E3	5 (41.7)	3 (33.3)	-
Disease course of UC			
Single episode	3 (25.0)	2 (22.2)	1 (100)
Chronic continuous	None	None	-
Intermittent relapses	8 (66.7)	6 (66.7)	-
Fulminant	1 (8.3)	1 (11.1)	-
Immunosuppression			None
Steroids	9 (75.0)	5 (55.6)	-
AZA/6-MP	5 (41.7)	3 (33.3)	-
Anti-TNF-α	None	1 (11.1)	-
Liver disease outcome			None
Cirrhosis	3 (25.0)	2 (22.2)	-
ACLF	None	1 (11.1)	-
Liver-related mortality	None	1 (11.1), ACLF	None

Values are present as number (%).

[a]The Montreal classification was used to classify the disease extent of UC.[6]

HIV, human immunodeficiency virus; AZA, azathioprine; 6-MP, 6-mercaptopurine; anti-TNF-α, anti-tumor necrosis factor-α; ACLF, acute on chronic liver failure.

Table 2. Demographic and Clinical Characteristics of Patients with CD and Concomitant Viral Infections

Characteristic	HBV (n=8)	HCV (n=2)
Median age (yr)	48 (21–69)	53 (37–69)
Sex		
Male	7 (87.5)	1 (50)
Female	1 (12.5)	1 (50)
Median duration of CD (yr)	4.5 (2.5–9.0)	7.0 (5.0-9.0)
Age at diagnosis[a]		
A1	1 (12.5)	None
A2	2 (25.0)	1 (50.0)
A3	5 (62.5)	1 (50.0)
Location		
L1	1 (12.5)	None
L2	5 (62.5)	1 (50.0)
L3	2 (25.0)	None
L4	None	1 (50.0)
Behavior		
B1	5 (62.5)	1 (50.0)
B2	3 (37.5)	1 (50.0)
B3	None	None
p	None	None
Immunosuppression		
Steroids	3 (37.5)	1 (50.0)
AZA/6-MP	3 (37.5)	1 (50.0)
Anti-TNF-α	None	None
Liver disease outcome		
Cirrhosis	1 (12.5)	None
ACLF	1 (12.5)	None
Liver-related mortality	1 (12.5), ACLF	None

Values are present as number (%).
[a]The Montreal classification was used to classify the clinical characteristics of CD.[6]
AZA, azathioprine; 6-MP, 6-mercaptopurine; anti-TNF-α, anti-tumor necrosis factor-α; ACLF, acute on chronic liver failure.

4. Prevalence of Viral Infections among Patients with IBD by Age Group

The prevalence of the viral infections in patients with IBD was also examined according to age. None of the patients (UC or CD) aged less than 20 years were found to have these viral infections. Further, no statistically significant differences in the prevalence of these infections were found among different age groups (Table 3).

Table 3. Prevalence of Viral Infections in Patients with IBD according to Age (Age-Stratified Analysis)

| Age (yr) | UC | | CD | |
	HBV (n=12)	HCV (n=9)	HBV (n=8)	HCV (n=2)
10–20	0/30 (0)	0/29 (0)	0/17 (0)	0/16 (0)
21–30	4/140 (2.9)	1/132 (0.8)	3/74 (4.1)	0/69 (0)
31–40	5/184 (2.7)	5/176 (2.8)	0/73 (0)	1/66 (1.5)
41–50	1/117 (0.9)	2/114 (1.8)	1/61 (1.6)	0/58 (0)
51–60	1/45 (2.2)	1/42 (2.4)	2/39 (5.1)	0/38 (0)
>60	1/25 (4.0)	0/24 (0)	2 /24 (8.3)	1/26 (3.8)
P-value	0.77	0.70	0.23	0.37

Values are present as number (%).

5. Disease Controls

Patients with ITB (n=95) were considered as disease controls. The prevalence of HBV, HCV, and HIV in this group was 5.9% (4/67), 1.8% (1/57), and 1.2% (1/84), respectively, and these rates for HCV and HIV were not significantly different from the corresponding rates in patients with IBD. In contrast, HBV was found to be more prevalent in patients with ITB than in those with IBD (P=0.04).

DISCUSSION

In current study, we found that the prevalence of HBV, HCV, and HIV infections did not differ between patients with IBD and the general population in India.

He et al.[7] determined that the prevalence of HBV infection (HBsAg positivity) in patients with CD and UC was 13.6% (61/449) and 16.8% (38/226), respectively, in a similar study, and they found no difference in prevalence compared to that of the general population in southern China, which is a highly endemic area for HBV and HCV. Studies have reported the prevalence of HBV infection in IBD patients to vary from 0.6% to 3.7%.[8-14] Some of these studies have also reported a higher prevalence of HBV infection in patients with IBD than in the general population, while some have reported no such difference. Our findings showed that the HBV prevalence in patients with IBD was 2.2% for those with UC and 2.8% for those with CD, which was lower than the prevalence in the general population but not significantly. A possible explanation for our findings could be that most patients at our center were from north India, which has a relatively lower prevalence of HBV than south or east India. The distribution of HBV in India is highly heterogeneous, with tribal popula-

tions from southern states showing a very high prevalence (>20%).[15]

Another finding of the current study was that HBV was significantly more prevalent in patients with ITB (5.9%) than in those with IBD (2.4%) (*P*=0.04). This finding is consistent with those of previous studies, which found HBV to be more prevalent in patients with tuberculosis with or without concomitant HIV infection. In a study from the United Kingdom, the prevalence of HBV was 2.6% in patients with tuberculosis, which was significantly higher than the national prevalence of 0.3%.[16] Another study from Brazil shown that the HBV seroprevalence in patients with tuberculosis without HIV was 14.6%.[17]

The prevalence of HCV infection in the patients with UC and CD in the current study was 1.7% and 0.7%, respectively, and it was not different from the prevalence in the general population. Biancone et al.[10] reported that the HCV prevalence in patients with CD in their study was 7.4%, and this was higher than that in the normal healthy controls in Italy. In a Chinese study, the prevalence of HCV infection was found to be 1.64% in patients in IBD, and this rate was higher than the reported prevalence in southern China.[18] Then, a study from France reported a higher prevalence of HCV infection (5.98%) in patients with IBD than in the general population,[19] and a Spanish study found that 1.59% of patients with UC and 0.79% of patients with CD tested positive for anti-HCV antibodies.[12]

Thus far, HIV in IBD has not been well described, and only case series and case reports are available on this subject. In our study as well, only one patient with UC had HIV infection, but no patient with CD did.

To our knowledge, this is the first study to describe the prevalence of HBV, HCV, and HIV infections in patients with IBD from India. The limitations of this study are that it is a retrospective study and all three viral markers of all the patients were not available for analysis. Additionally, the viral markers were examined only at baseline at the first presentation, and it is unclear what effect repeated testing would have had on the prevalence rates. However, the retrospective design should not affect the results as the data were prospectively maintained and data were collected from documented reports.

In conclusion, the prevalence of HBV, HCV, and HIV infection in patients with IBD (2.4%, 1.4%, and 0.1%, respectively) from north India was not found to differ from the corresponding prevalence in the general population. Nevertheless, management of such infections in IBD is very challenging given that these patients generally receive immunosuppressive therapy. The high risk of flare if these viral infections go undetected mandates routine screening of patients with IBD for HBV, HCV, and HIV.

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