

Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Co-infection among HIV infected individuals at tertiary care hospital in western Nepal

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Abstract:

Background: The HIV, HBV and HCV viruses are the major public health concern all over the world including Nepal. The aim of the study is to determine the rate of HBV and HCV co-infections in patients with HIV infection.

Methods: The study cohort included 218 consecutive HIV infected patients who were examined for co-infection with HBV or HCV or both at Manipal teaching hospital, Western Nepal. The demographic data of the subjects was collected retrospectively. The data was analyzed with SPSS software and EPI Info to measure the correlation of variables and infection rates.

Results: In the course of six years study period, a total of 25,708 samples were collected for HIV screening test. The 218 (0.8%) screen test positive for HIV were confirmed as per WHO guidelines. The overall rate of co-infection with HBV and or HCV was 7.3% (16 of 218 patients). Only 7 (3.2% [CI 1.3, 6.5]) were positive for both HIV and HBV infection markers and 9 (4.1% [CI 1.9, 7.7]) were positive for HIV and HCV infection markers. None were positive of all three virus markers.

Conclusion: It is advisable to implement regular screening for Hepatitis B Virus and Hepatitis C Virus among all HIV infected individuals and their sexual partners.

Key words: HIV; HBV; HCV; Co-infection.

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Introduction

Human immunodeficiency virus (HIV), Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are the three most common chronic viral infections documented worldwide [1,2]. It is estimated that more than 33 million people are infected with HIV worldwide [3]. Patients of HIV infection may also be co-infected with HBV or HCV or both since these viruses share routes of transmission. Approximately 20% of HIV-positive patients who acquire acute HBV infection develop chronic HBV infection compared to only 5% of HIV-negative persons [4]. Hepatic diseases are one of the leading causes of morbidity and mortality in co-infected patients [5]. Hematological disorders associated with these viruses, have shown to decrease the life expectancy in HIV-infected patients. The increased life expectancy due to highly active antiretroviral therapy (HAART), focus has now shifted to management of chronic HBV and HCV infections. The rate of co-infection in HIV patients may be different in different geographical areas as this is affected by the mode of transmission and load of infection in the population [6,7,8]. It is observed that, those HIV-infected individuals who are co-infected with hepatitis viruses display rapid progression to severe liver disease and have an increased risk of hepatotoxicity associated with anti-retroviral therapy [9]. The HIV-HBV or HIV-HCV co-infection has been reported worldwide, and some studies provide evidence that the rate of HBV is higher than that of HCV in HIV-infected patients [8,10,11]. Conflicting results are reported in some studies [12]. The marked influence of HIV on the natural history of hepatitis viruses in the form of increasing viral load and frequent re-activations makes it imperative to determine the occurrence of co-infections.

The literature regarding the rate of co-infection of HBV and HCV in HIV-infected patients in Nepal is scanty. The study was conducted to probe the seroprevalence of HBV or HCV co-infection in HIV amongst patients attending a tertiary care hospital in western Nepal.

Materials and Methods:

Study design and the participants:

The present retrospective study was conducted for a period of six years from 2008 to 2013 in Manipal Teaching Hospital, a tertiary care centre in western Nepal. Patients attending hospital were screened for HIV based on clinical grounds and/or as a routine investigation for patients undergoing surgery were included in the study. A demographic data like age, gender, marital status of the subjects were collected retrospectively from medical records.

Virological assays:

Diagnosis of HIV infection was established as per the guidelines laid down by WHO for HIV testing. Serum samples collected from HIV-positive patients were tested for hepatitis B surface antigen (HBsAg) and antibodies to HCV. All these patients were screened by rapid spot test and positive cases were confirmed by ELISA. The tests were conducted using a commercial kit obtained from J Mitra and Co Pvt Ltd (New Delhi, India). Manufacturer's instructions were followed while performing the tests.

Inclusion criteria:

1. Only confirmed HIV-positive patients anonymously tested for hepatitis B and C virus markers were included in the study.

Exclusion criteria:

1. Person who has not tested for HIV infection.
2. Persons who fail to meet above inclusion criteria.

Outcome Variable: The outcome variables included in this study were total HBV and HCV co-infected HIV patients.

Explanatory variable: The explanatory variable was age, gender, marital status and year-wise distribution of HBV and HCV in HIV-infected patients.

Sample size calculation: In a pilot study done prior to this study with 100 patients showed a proportion of 0.07 HbsAg and HCV co-infection among HIV patients, with precision 4% and 95% CI required sample size was 156. We included all the data available from 2008 to 2013 in this study.

Statistical analysis: The data gathered was analyzed using SPSS software and EPI Info to measure the correlation of variables as well as infection rates.

Ethical committee approval: Ethical committee approval was taken from the institutional ethical committee, Manipal Teaching Hospital, Pokhara, Nepal. The research was conducted in compliance with the latest version of the Declaration of Helsinki.

Results:

Epidemiological characteristics

A total of 25,708 samples were tested for HIV antibodies during the study period, of which 218 (0.8%) tested positive for HIV and confirmed as per the guidelines laid down by WHO for HIV serology. Out of these 61% (133/218) were males and 39% (85/218) were females between the age group of 20 to 65 years. The overall rate of co-infection was 7.3% (16/218), among which 7 (3.2% [CI 1.3, 6.5]) were positive for both HIV and HBV infection while 9 (4.1% [CI 1.9, 7.7]) were positive for HIV and HCV. No specimen was positive for all three (HIV, HBV, HCV) markers. Out of 218 HIV-positive

cases 6 (2.8 %) were in the 0-10 years age group, 4 (1.8%) in the 11-20, 57 (26.1%) from 21-30, 83 (38.1%) from 31-40, 43 (19.7%) from 41-50 and 25 (11.5%) from greater than 51 age group (Table 1).

Table 1: Cross tabulation of age group, gender, marital status with HBsAg and HCV.

Variable	N (%)	Hbs Ag % (CI)	HCV % (CI)
Age group			
0-10	6 (2.8)	00	00
11-20	4 (1.8)	00	00
21-30	57 (26.1)	3, 5.3 (1.1, 14.6)	3, 5.3 (1.1, 14.6)
31-40	83 (38.1)	2, 2.4 (0.3, 8.4)	6, 7.2 (2.7, 15.1)
41-50	43 (19.7)	2, 4.7 (0.6,15.8)	00
51 - above	25 (11.5)	00	00
Gender			
Female	85 (39.0)	6,7.1 (2.6, 14.7)	00
Male	133 (61.0)	1,0.8 (0, 4.1)	9,6.8 (3.1, 12.5)
Marital status			
Unmarried	54 (24.8)	00	4, 7.4 (2.1, 17.9)
Married	164 (75.2)	7, 4.3 (1.7, 8.6)	5, 3.0 (1.0 , 7.0)

HBV and HCV co-infection

Age: The age specific seroprevalences was not significantly different among HBV and HCV co-infection in HIV positive patients, although it was marginally higher in the age group of 21-40 years (figure 1).

Gender: Co-infection of HBV with HIV were more amongst female than the men [p=0.009]. Interestingly all HCV-HIV co-infected patients were male [p=0.014].

Marital status: It was found that marital status as a significant factor. The co-infection with HCV among unmarried HIV

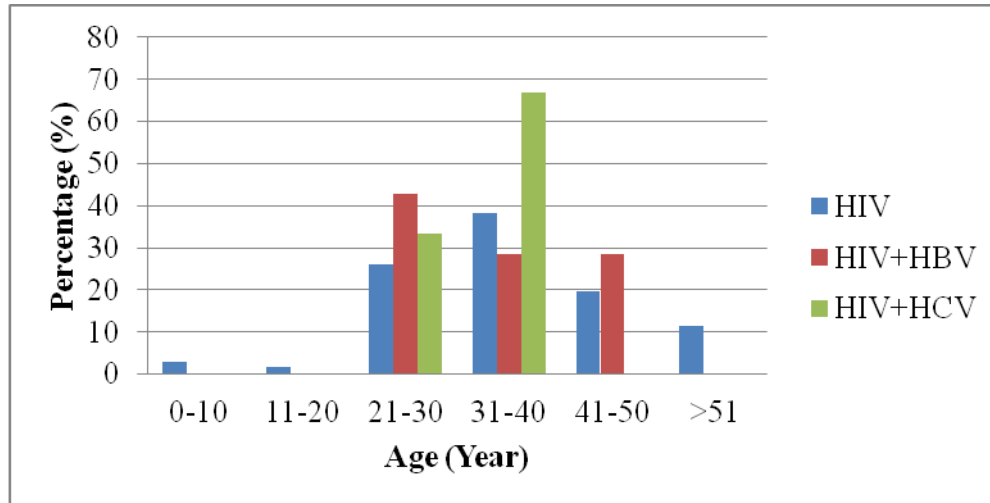
positive patients was more vis-à-vis married patients [p=0.16]. All patients co-infected with HBV - HIV were married [p=0.12].

Year: On analyzing year wise distribution of HBV and HCV in HIV infected patients in our study population, it was noted that HBV co-infection rate varied between 0-10% and HCV co-infection rate between 2.1-7.4 %. However, no year wise trend could be observed in the co-infection rates [Table 2].

Table 2: Year wise distribution of HBV and HCV in HIV infected Patients

Year	HIV cases n	HBsAg, % (CI 95 %)	HCV, % (CI 95%)
2008	59	1, 1.7 (0, 9.2)	2, 3.4 (0.4, 11.9)
2009	28	3, 10 (2.1 , 26.5)	1, 3.3 (0.1 , 17.2)
2010	35	2, 5.6 (0.7 ,18.7)	2, 5.6 (0.7 , 18.7)
2011	40	0	2, 7.4 (0.9 , 24 .3)
2012	26	1, 2.1 (0.1 ,11.1)	1, 2.1 (0.1, 11.1)
2013	30	0	1, 5.3 (0.1, 26.0)
Total	218	7	9

Figure 1: Age-related distribution of HBV and HCV in HIV infected Patients



Discussion:

HIV infection:

HIV is responsible for about 40 million chronic infections while Hepatitis C and Hepatitis B cause 130 million and 370 million chronic infections respectively [1]. Prevalence of HIV in Nepal is approximately 0.3 %. It is estimated that one third of deaths in HIV patients are directly or indirectly related to liver diseases [1]. Compared to HIV-mono-infected patients, HIV-hepatitis co-infection are at increased risk of developing liver enzyme elevations on antiretroviral therapy [13]. Failure to diagnose and treat co-infection at an early stage results in serious complications and sequelae.

HBV and HCV co-infection:

The prevalence of co-infections in the different geographical area around the world displays great variation. However, in most parts of the world including Nepal, very few studies about the occurrence of co-infections with these viruses has been done. In US and Europe, HIV and HBV co-infection was reported to be 6 to 14 % while reports for HIV and HCV varied in the range of 25 to 50 % (9, 10). In India the overall rate of infection with HBV and HCV varies from 1– 6% [14,15,16]. The rate of HBV and HCV co-infection in HIV patients has been reported in few studies in Nepal [2,17]. In study conducted among volunteer blood donors in Nepal, P Ghimire *et al.*, found the co-prevalence of HBV/HIV to be 0.033% [2]. Surendra Karki *et al* reported the co-infection rate of 10.8% (7/65, 95% CI= 4.4- 20.9) for HCV and HIV in the blood donors. All co-infected donors were male; 86% (6/7) of them were volunteer blood donors of age 21-30 years old [17].

No study pertaining to incidence of co-infections with these viruses has been done in western Nepal till date. The HIV-HCV co-infection was commoner than HIV- HBV co-infection in our study. Lack of available vaccines for HCV vis-à-vis existing vaccines for HBV is one of the crucial factors among the several

other diverse factors responsible for higher rate of HCV co-infection. Besides, in comparison to HCV, sexual transmission of HBV is higher and more often it is transmitted via injection in drug addicts. The high rate of drug addiction reported in Nepal is also a matter of grave concern.

Co-infection with the three viruses increase the risk of acute and chronic liver insufficiency, cirrhosis, hepatic failure and mortalities in comparison to when a person is infected with only one of these viruses. Therefore, diagnosing HBV and HCV in HIV- infected patients is essential for proper management and early intervention.

Some studies have shown that male patients were significantly at a higher risk to develop HBV co-infection, but in our study HBV co-infections in female patients were more prevalent than in their male counterpart.

People with unsafe sexual relationships and addiction to drugs injection should always be careful as the chances of virus getting transmitted are high among them. The implications of screening tests for HBV or HCV co-infection in HIV patients are of great of importance in Nepal too, as the number of patients getting infected with HIV is on an increasing trend. The knowledge of co-infection in patients of HIV is vital since these patients, as they live longer on antiretroviral treatment will also need to be managed for their co-infection with HBV

or HCV. The replication of HBV and HCV in HIV patients should be actively monitored while receiving antiviral therapy and this monitoring system should be made a part of clinical care [18]. The derangement of liver functions as a result of ART or opportunistic infections may also complicate the situation. Compared to HIV-mono-infected patients, those with HIV-hepatitis co-infection are at increased hazard of developing liver enzyme elevations on antiretroviral [13]. Hepatitis viruses in HIV may lead to faster progression to liver cirrhosis and a higher risk of antiretroviral therapy induced hepatotoxicity.

Conclusion:

It is advisable to implement routine screening for HBV and HCV among all HIV infected individuals and their sexual partners, before these viruses ride over the present HIV epidemic to cause liver related morbidity and mortality in these patients.

Limitation of study:

Data lacks the risk factors associated with the co-infection of HBV or HCV. It is a single hospital based study with limited sample size and sampling frame.

Future scope of the study:

Hepatic diseases are one of the leading causes of morbidity and mortality in co-infected patients. Clinical trials are needed to further our knowledge on Treatment option and management of co-infected patients.

What is already known on this topic:

The HIV-HBV or HIV-HCV co-infection is already known and has been reported worldwide.

What this study adds:

The study adds the information on seroprevalence of HBV or HCV co infection in HIV amongst patients attending a tertiary care hospital in western Nepal.

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Conflict of interest:

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Author's Contribution:

HS Supram participated in study design, data collection & analysis and wrote the manuscript. S Gokhale contributed

towards providing clinical relevance, distilling the material and manuscript preparation. B Sathian assisted with the overall study design and the statistical analysis. DR Bhatta contributed towards distilling the material and manuscript preparation.

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