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# Human Immunodeficiency Virus and Hepatitis B Virus Dual Infection in Nepal

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## Abstract

**Background:** Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) infections are emerging public health problems, particularly in developing counties like Nepal. The study aims at finding prevalence and pattern of CD4 cell count among HBV co-infected HIV positive individuals in Nepal.

**Methods:** This is a descriptive cross-sectional study carried out in three Volunteer Counseling and Testing (VCT) clinics, one from Dharan and two from Kathmandu Nepal.

**Results:** 5.75% of HIV infected individuals had HBV dual infection. 33.4% of patients who harbored dual HIV and HBV infection had multiple sex partners. No significant association was observed between HBV co-infection and Injecting Drug Users (IDU). The mean CD4 cell count was found to be significantly more among HBV uninfected cases compared to HBV infected ones at six months' duration (P=0.006) and one years' duration (P=0.027) after taking anti-retroviral therapy (ART).

**Conclusion:** HBV co-infection was more among those having multiple sex partners. ART helped increase CD4 cell count among HBV co-infected and uninfected HIV positive patients, but the results were better among HIV mono-infected individuals.

**Keywords:** HIV; HBV co-infection; CD4 cell count

## Introduction

Globally, two billion people have been infected with Hepatitis B Virus (HBV) [1]. Among Human Immunodeficiency Virus (HIV) infected individuals, HBV infection prevalence is approximately ten times higher than in general population [2]. National estimates indicate that approximately 63,528 adults and children are infected with the HIV virus in Nepal, with an estimated prevalence of about 0.39% in the adult population [3]. Yet, there has not been adequate study of HIV and HBV dual infection in Nepal.

Injection drug use (IDU) has become increasingly common in Central and South Asia [4]. IDU contributes significantly to the introduction, maintenance, and spread of HIV [5]. Co-infection of HIV significantly modifies the natural history of HBV infection [6]. Evidences indicate that HIV-positive individuals are more likely to be infected with HBV than HIV-negative individuals [7]. Persistent HBV infection can result in cirrhosis, liver failure, and hepatocellular carcinoma [8].

The study aimed at finding the prevalence of HBV co-infection among HIV positive individuals and tracing the pattern of response of anti-retro viral therapy (ART) on mean CD4 cell count.

## Materials and Methods

### Setting

The study was carried out in three different places viz. B. P. Koirala Institute of Health Sciences (BPKIHS), Dharan; Society for Positive Atmosphere and Related Support to HIV and AIDS (SPARSHA) Nepal, Kathmandu; and Sukhra Raj Tropical and Infectious Disease Hospital, Teku, Kathmandu (TEKU Hospital). It was done with due privacy in their respective Volunteer Counseling and Testing (VCT) Clinic by face to face interview with the HIV infected individuals based on pretested semi-structured questionnaire. Also, an address was given to the past medical documents, for better authenticity of the information, which most of them had themselves.

### Sampling technique

Purposive sampling

### Study subjects

The target population of the study was the HIV infected persons visiting the VCT Clinic either for taking medications or for follow-up of regular checkup. Among those who gave supportive consent, an approach was made to include all individuals whether they were already taking medications or about to start. A total of 313 HIV infected individuals were interviewed. The diagnosis of HBV dual infection was made on the basis of HBsAg positivity status of the patients. The patients were followed for one year.

## Study design

This is a cross sectional, descriptive study which includes primary and secondary data.

## Inclusion criteria

Those who gave supportive consent and who could report CD4 cell count were included in the study. Patients with other diseases like Tuberculosis and Hepatitis C virus infection were also a part of the study.

## Exclusion criteria

Those who didn't give consent and who couldn't report CD4 cell count were excluded.

## Statistical analysis

The data was entered into Microsoft Excel 2007 and analyzed in SPSS 17.0. Mean, median and standard deviation were calculated. Mann-Whitney Test and Chi square test were applied to find out statistical significance in numeric (CD4 cell count) and categorical (Gender, Marital Status) data respectively. Probability of significance was set at 5% level of significance. Odds Ratio (OR) and its 95% confidence interval (CI) were also calculated to examine strength of association between the categorical variables and its' limit.

## Ethical consideration

Ethical consent was taken from institutional review board BPKIHS, Dharan; SPARSA NEPAL, Kathmandu and Sukhra Raj Tropical and Infectious Disease Hospital (Teku, Kathmandu). Verbal consent was also taken with the individuals who were diagnosed to be HIV infected. Privacy of participants was maintained during interview with due consideration of the emotional aspect.

## Results

As shown in Table 1, the mean age of the individuals was 33.7 years. Nearly 25% were females. 72.8% were married, 8% were unmarried, 14.1% were single, and 5.1% was widow/wider. 65.5% were IDU. HBV and HIV co-infection was found in 5.75% of the HIV infected individuals. About 94% were receiving ART. Nearly two third of HIV infected individuals had a history of IV drug use, more than a quarter admitted to multiple sexual partners, 18.5% had no history of extramarital sexual relationships and 0.6% acquired HIV infection from each blood transfusion and vertical transmission. 33.4% of patients who harbored HBV had multiple sex partners. No significant association was observed between HBV co-infection and IDU. Also tuberculosis co-infection (36.1%) and HCV co-infection (41.53%) was common among HIV cases. HCV co-infection was significantly more among IDU than among non-IDU (OR=56.99, CI=17.48-185.79, P<0.001).

Table 2 shows that the average CD4 cell count was not significantly high among those who had HIV mono-infection compared to those who had HBV co-infection until six months of ART. However, at six months' duration (P=0.006) and one years' duration (P=0.027) the mean CD4 cell count was found to be significantly more among HBV uninfected cases. But then after, there was no significant association on average CD4 cell count among the two groups.

| Variables | | Frequency | Percentage |
|---|---|---|---|
| Gender | Male | 234 | 74.8 |
| | Female | 79 | 25.2 |
| Marital Status | Married | 228 | 72.8 |
| | Unmarried | 25 | 8 |
| | Single | 44 | 14.1 |
| | Widow | 6 | 1.9 |
| | Widower | 10 | 3.2 |
| Hepatitis Dual infection | HBV | 18 | 5.75 |
| | HCV | 130 | 41.53 |
| TB Dual infection | Yes | 113 | 36.1 |
| | No | 200 | 63.9 |
| IDU | Yes | 205 | 65.5 |
| | No | 108 | 34.5 |
| ART | Being Taken | 295 | 94.2 |
| | Not Being Taken | 18 | 5.8 |

**Table 1:** Socio-demographic profile of HIV infected individuals who volunteered for the study (n=313).

| CD4 Count | HBV Co-infection | | Total | P value |
|---|---|---|---|---|
| (Six Monthly) | Present (n=18) | Absent (n=295) | (n=313) | |
| Just Before Starting ART | (173.61 ± 108.68), 189.00, 18 | (196.88 ± 121.69), 171.00, 295 | (195.55 ± 120.94), 172.00, 313 | 0.617 |
| (Mean ± SD), Median, No. | | | | |
| At 6 Months' Duration | (204.00 ± 56.71), 210.00, 18 | (275.21 ± 123.15), 259.00, 272 | (270.79 ± 121.27), 255.00, 290 | 0.006* |
| (Mean ± SD), Median, No. | | | | |
| At 1 Year's Duration | (229.69 ± 74.02), 220.00, 13 | (307.44 ± 146.33), 300.00, 216 | (303.03 ± 144.24), 293.00, 229 | 0.027* |
| (Mean ± SD), Median, No. | | | | |
| At 1.5 Years' Duration | (283.75 ± 97.63), 246.50, 8 | (330.73 ± 148.10), 324.00, 166 | (328.57 ± 146.30), 317.00, 174 | 0.345 |

| | | | | |
|---|---|---|---|---|
| (Mean ± SD), Median, No. | | | | |
| At 2 Years' Duration (Mean ± SD), Median, No. | (311.67 ± 110.84), 285.50, 6 | (343.66 ± 155.93), 333.00, 115 | (342.07 ± 153.81), 330.00, 121 | 0.455 |
| At 2.5 Years' Duration (Mean ± SD), Median, No. | (296.50 ± 28.99), 296.50, 2 | (395.52 ± 199.27), 349.00, 54 | (391.98 ± 196.53), 347.00, 56 | 0.354 |
| At 3 Years' Duration (Mean ± SD), Median, No. | (284.00 ± -), 284.00, 1 | (382.11 ± 148.93), 391.00, 35 | #(379.39 ± 147.69), 376.00, 36 | NA+ |
| At 3.5 Years' Duration (Mean ± SD), Median, No. | (271.00 ± -), 271.00, 1 | (416.08 ± 169.52), 414.00, 24 | (410.28 ± 168.47), 387.00, 25 | NA+ |

**Table 2:** Change and comparison of CD4 cell count in HIV infected persons six monthly, among those who had HBV co-infection and those who hadn't, during the course of ART for three and half years. (n=313).

*Significant value +NA- Not Applicable.

P value was calculated by Mann-Whitney Test (Non-parametric test).

## Discussion

The study showed that 5.75 % had HBV co-infection. Low HBV co-infection could be due to resolution of HBV infection after the acute phase that occurs in 90%–95% [4]. 33.4% of HBV co-infected individuals revealed history of having had multiple sex partners. This result is in accordance to other study by Neaigus A which states those with greater sexual risk exposure are at greater risk of ever being HBV infected [9].

The association between Hepatitis viral co-infection and CD4 T lymphocytes count is currently a subject of debate, with some studies showing no existence of a relationship and others showing the association [10]. The picture in our study also pointed to the latter. Until six months of ART, the average CD4 cell count among those individuals who had HBV co-infection was less than those who didn't. Then after having taken ART, the HBV uninfected persons improved significantly. At six months' duration (P=0.006) and one years' duration (P=0.027) the mean CD4 cell count was found to be significantly more among HBV uninfected cases. But then after, there was no significant association on average CD4 cell count among the two groups. The degree of immunodeficiency represents an important factor in the progression of hepatitis among individuals co-infected with HBV [11]. Co-infection with HIV and HBV has been associated with more rapid progression of liver disease and higher rates of mortality [12]. As shown in Figure 1, the CD4 cell count was always to the higher margin among HIV mono-infected individuals compared to those having the dual infection. When both HBV and HIV co-infect a patient, the mortality rate from chronic hepatitis B is increased above that of either infection alone with a faster rate of progression to liver cirrhosis and hepatocellular carcinoma [11]. Further, hepatotoxicity is a common side effect associated with the use of many therapeutic agents. Drug-related hepatotoxicity of antiretroviral therapy for HIV infection is more frequent among patients who are co-infected with Hepatitis viruses [13]. Co-infection of HBV has been associated with increased risk of antiretroviral-therapy related hepatotoxicity and increased risk of progression to liver disease, which is a major cause of morbidity and mortality in HIV-infected patients [14].

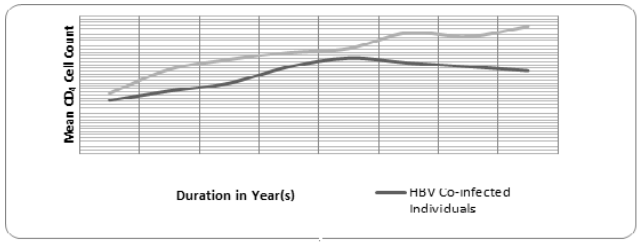


**Figure 1:** Comparison of Mean CD4 cell count, six monthly, among those who had HBV co-infection and those who hadn't, during the course of ART for three and half years. (n=313)

In general, viral hepatitis can be prevented through vaccination, risk reduction education and transmission diminution [15]. Reductions in community incidence rates of HIV infection and Hepatitis B among IDUs have also been noted in association with syringe exchange programs [16]. Yet syringe exchange approach has controversially mixed results. Vaccination is a widely accepted strategy for lowering the incidence of HBV infection in HIV-infected individuals [2].

HBV and HIV co-infection is an emerging health issue in Nepal. HBV co-infection was found more among those having multiple sex partners. Mean CD4 cell count was found to be higher among HBV uninfected individuals than HBV co-infected ones after ART. Hence, ART plays an important role in increasing CD4 cell count and this increment is more among HBV uninfected HIV positive individuals.

## Limitations

The limitations of the study, due to resource constraints, were along the following lines:

HBeAg, anti-HBe and HBV DNA could not be included.

Patients taking medication for HBV infection could not be incorporated.

Relationship between helper T cell and suppresser T cell could not be ascertained.

## Acknowledgement

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