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## ORIGINAL ARTICLE

# Seroepidemiology Of Hepatitis B Virus Infection Diagnosed At A Teaching Hospital In Western Nepal: A Prospective Study

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### Background

Hepatitis B virus (HBV) infection is a major problem in developing countries and a major cause of jaundice in Nepal. Hepatitis B surface antigen (HBsAg) is the first serological hallmark of HBV infection. In a study of the Nepalese male population, inhabiting various districts, HBsAg was found to be positive in 4% of the population. The prevalence of HBV infection among patients attending the Manipal Teaching Hospital, a major healthcare provider in the western region of Nepal, has not been studied. Hence, the present study was carried out to determine the prevalence of HBV infection in patients attending the hospital and to assess the associated risk factors.

### Method

The study was carried out during the period from 15th March 2004 to 15th September 2005. Serum samples requisitioned for the investigation of HBsAg from the wards and the Out Patient Departments to the Department of Microbiology were included. The demographic and clinical details of the patients who tested positive for HBsAg, was obtained through a semi structured questionnaire, as well as from their medical records. The results were analyzed according to their demographic characteristics.

### Results

288 serum samples were included; 215 samples (74.6%) were from males. Inpatients accounted for 195 specimens (67.7%). Thirty-six (12.5%) samples were positive. The seroprevalence of HBsAg was higher among males, individuals from Kaski district where the hospital is located and ex-army and businessmen respondents. A majority of the positive individuals were males from Kaski district, students, ex-army men, agriculturists or housewives belonging to the 21 to 30, 41-50 or the 31-40 year age groups. High risk sexual behaviour was elicited in two individuals, intravenous drug abuse in two and a history of blood transfusion and dental manipulation in one each, while one person had shared razors with an infected person.

### Conclusion

The frequency of seropositivity among individuals who were referred for HBsAg testing was high. Various factors could have influenced the results. Further studies are required to assess the seroprevalence among all the patients attending the hospital OPD and admitted in the wards.

**Key Words:** Hepatitis B, Hepatitis B Surface Antigen, Nepal, Seroprevalence

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## Background

The burden of Hepatitis B virus (HBV) infection varies widely among different countries. In western countries, the disease is relatively rare and is acquired primarily in adulthood. In the South East Asian Region (SEAR), annually, approximately 14-16 million people are infected with HBV. It is estimated that there are 98 million HBV carriers which is almost 6% of the total population of this region [1],[2]. In Nepal, the total morbidity due to acute hepatitis HBV for the year 2004-2005 was 30,071 out of 9,699,858 hospital visits [3]. Hepatitis B consumes a substantial portion of health resources in developing countries [4].

HBV presently infects 2 billion people and is the ninth leading cause of death worldwide [5]. Approximately 350 million people are chronically infected with this virus [1],[2]. Hepatocellular carcinoma (HCC), which is caused by HBV infection, is one of the three leading causes of death due to cancer in most parts of Africa, Asia and the Pacific Basin, resulting in a million deaths annually [2]. 80 % of liver cancers are attributed to HBV, which is the most common cause of cancer mortality worldwide after smoking [6]. Among 35 million health care workers worldwide, 3 million are exposed to blood borne pathogens each year and 2 million of these are due to HBV. These injuries may result in 70,000 HBV infections [7].

Of the more than 350 million new cases of HBV infection, more than 100,000 occur in the United States (US) alone [5]. However, the prevalence is decreasing in developed nations. The prevalence of HBsAg chronic carriers is less than 2 % in Western Europe, North America and parts of South America and intermediate (2-7%) in Southern and Eastern Europe [8]. The Hepatitis B surface antigen (HBsAg) in serum is the first sero-marker to indicate active HBV infection, either in acute or chronic forms. HBsAg is the serological hallmark of HBV infection. In acute hepatitis B, HBsAg may be undetectable very rarely at the time of presentation, either because the levels of HBsAg never reach or have already declined below the

detectable threshold of the assay. The persistence of HBsAg for more than 6 months implies chronic infection [9].

The prevalence of chronic HBsAg carriers in developing nations of Asia and Africa is high (more than 8%) [8],[10]. In China, the prevalence of HBV is 20% (12). In Thailand, it was 10%; in Korea and Bangladesh, it was 9%; in Maldives, Indonesia and Bhutan, it was 6%; in India, it was 5% and in Sri Lanka, it was 1% for the year 2000 [1],[12].

HBV is a major cause of jaundice in Nepal [13]. A study among the Sherpa community revealed prevalence of HBsAg, anti HBs (antibody to HBsAg) and anti HBe (antibody to HBeAg), to be 1.9% 22.3%, and 24.3%, respectively [14]. HBsAg positivity was found to be 0.45% in a study among voluntary blood donors conducted in the Department of Microbiology, Universal College of Medical Sciences, Bhairahawa, Nepal [15]. In a study of the Nepalese male population inhabiting various districts, HBsAg was found to be positive in 4% of the individuals. The percent positivity of HBsAg was found to increase steadily from the Eastern (2%) to the Far Western (6.2%) development regions. The Kailali district showed a characteristically high prevalence, followed by Rukum and Kaski. Other districts having a high prevalence of HBsAg were Sankhuwasabha, Jhapa, Ramechhap, Sarlahi, Dhanusa, Baglung, Gulmi, Palpa and Dang [16].

Manipal Teaching Hospital is the teaching hospital of the Manipal College of Medical Sciences (MCOMS), a medical school in Pokhara city, western development region, Nepal. The hospital is a major healthcare provider for the region. The institution caters to the population of ten of the fifteen districts of the western development region of Nepal. The population of these ten districts was about 2 million according to the 2001 census [17]. We are not sure about the percentage of the population who use the services of the institution. The teaching hospital has a daily patient load of 500 outpatients and 150 inpatients, though it shows seasonal variations.

The prevalence of HBV infection among the patients attending the hospital has not been studied. Hence, the present study was carried out. The aims of the present study were to determine the prevalence of HBV infection among samples sent for investigation of HBsAg to the Department of Microbiology and to assess the associated risk factors.

### Method

The cross-sectional study was conducted during the period from 15th March 2004 to 15th September 2005. The study was approved by the Academic Committee of the institution. At the time when the study was carried out, the institution did not have an ethics committee.

All patients attending the hospital during the study period (both outpatients and inpatients), with a clinical request for HBsAg testing, were included in the study; however, previously known positives were excluded. Due to the ethical issues involved, no samples were collected from sources other than patients attending the hospital. Oral informed consent was obtained from all individuals undergoing HBsAg testing for inclusion in the study. Randomization was not done. Demographic and clinical details of the patients included in the study were obtained from their medical records. The parameters considered were gender, whether the patient was an inpatient/outpatient, the district from where the patient came, their occupation and age. There were no drop outs and all patients approached for inclusion in the study, consented to it. For testing for HBV, three ml blood was collected aseptically by venepuncture. The blood was allowed to clot, after which it was centrifuged and the serum extracted. The sera were analyzed for HBsAg by an immunoassay based on an immunochromatographic sandwich principle by using HBsAg Rapid Card Test, Hepacard (J Mitra and Co. Ltd.) as per the manufacturer's instructions.

The serum was stored at -20°C till adequate number of samples was collected to perform ELISA with a 3rd generation ELISA Kit, manufactured by Biokit, Spain. Repeatedly reactive results were considered as seropositive

for HBV infection. Patients found to be HBsAg positive were interviewed by one of the authors using a semi structured questionnaire, regarding risk factors and high risk behaviour for Hepatitis B. Relevant clinical details were retrieved from case records. Manipal hospital, being a teaching hospital, utmost importance was given to the maintenance of case sheets and regular audits conducted to assure compliance.

This study was done as a part of the requirement by Kathmandu University for the completion of M.Sc Medical Microbiology. Funds are allotted by the Medical School for such projects/thesis work by the students. Hence, the institution bore the involved expenses.

### Results

A total of 288 serum samples were included in the study. Two hundred and fifteen samples (74.6%) were from male patients. Inpatients accounted for 195 specimens (67.7%), while outpatients accounted for 89 specimens (30.9%). [Table/Fig 1] shows the distribution of tested patients according to gender, district, occupation and age group and the seroprevalence of HBsAg according to these characteristics. A large majority of patients [165 (57%)] were from Kaski district where the hospital is situated. One hundred and ninety-five samples (68%) were from patients admitted in various wards of the hospital. Thirty-six (12.5%) of the 288 patient samples were positive.

Characteristic (N=288)	Number tested n	Percentage of tested	HBsAg Positive	Percentage of seropositive (n)
<b>Gender</b>				
Male	215	74.6	30	13.9 (215)
Female	73	25.4	6	8.2 (73)
<b>Distribution of patients</b>				
Ward	195	67.7	na	na
Outpatient	89	30.9	na	na
Not available	4	1.4	na	na
<b>District</b>				
Kaski	165	57.3	18	10.9 (165)
Syangja	29	10.1	2	6.9 (29)
Tanahun	24	8.3	2	9.1 (24)
Baglung	19	6.6	4	21 (19)
Paabat	15	5.2	4	26.7 (15)
Others	36	12.5	6	16.7 (36)

A majority of the HBsAg positive individuals were males from Kaski district, students, ex-army men and agriculturists or housewives belonging to the age groups of 21-30, 41-50 or 31-40 years. Coinfection with HIV was seen in

two individuals (5.5%), while coinfection with HCV was not observed. High risk sexual behaviour was elicited in two individuals, intravenous drug abuse in two and a history of blood transfusion and dental manipulation in one each, while one person had shared razors with an infected person. The mode of transmission was not clear in a majority of the patients.

## Discussion

Of the 288 samples, 36 (12.5%) were found to be positive for HBsAg. Of the 36 positive samples, 30 (83.33%) were from males and 6 (16.66%) from females. The gender distribution was similar to that observed in a study done by Chander and co-workers [15]. A study done by Shrestha SM [18] showed the prevalence of HBsAg to be higher in males than in females, which was in agreement with this study. Zali and coworkers in Iran found the prevalence in males and females to be 1.9% and 1.5%, respectively [4].

Various studies done by different researchers have revealed different percentage prevalence of HBsAg in Nepal. A study done by Chander et al [15] in 2003, among blood donors at the Universal College of Medical Sciences, Bhairahawa, showed the prevalence of HBsAg to be 0.45%. Another study done in 2002 by Shrestha B [19] in a Nepali population which required medical check up for going abroad, detected the seroprevalence of HBsAg to be 0.93%. A study by Manandhar et al [16] on the seroprevalence of HBsAg in various districts of Nepal showed a prevalence of 4%. In 1996, Sawayama et al [20] studied the seroprevalence of HBsAg in two rural Nepali villages, where the prevalence was found to be 1.1%. The high prevalence found in this study may be because this was a hospital-based study. A majority of the samples were from people who presented with complaints of HBV infection and were clinically suspected of being infected and thus, it may not have revealed the disease status in the community.

In this study, 165 samples were from Kaski district in Pokhara city, where the hospital is located. The sample size from other districts was small. Among the samples from Kaski, 18

(10.9%) were HBsAg positive. The high seroprevalence of HBsAg in Kaski is supported by a study done by Manandhar et al [16] in 2000, according to which the percent positivity of HBsAg was found to increase steadily from the Eastern (2%) to the Far-Western (6.2%) development regions of Nepal. That study also noted a high prevalence of HBsAg in Kaski district. Ex-army men were seen to have the highest positivity rate (15.62%) among people from different occupations studied.

The age group of 21-30 years showed the highest rate of positivity. This observation was also supported by the study done by Chander et al [15], where they found most seropositive cases of HBsAg belonged to the age group of 15-45 years. A study done by Gyawali et al [13] also detected a higher prevalence of HBsAg in the age group of 21-30 years, which is similar to the results of our study. Also, this age group had the highest frequency (57 individuals) of testing for HBsAg. It may be because this age group has a higher frequency of going abroad for studies and employment and thus, more tests may have been done in this age group [21]. Of the 36 positive cases of HBsAg, the modes of acquisition of HBsAg by 29 individuals were not known. This might have been due to hesitation on the part of patients to reveal their behaviours such as extra marital sex, sharing of needles for intravenous (IV) drug use, etc. Two cases (5.55%) had a history of unprotected sex outside marriage. Since HBV is transmitted commonly via the sexual route, the mode of acquisition in these cases may have been sexual. In a study by Gyawali et al [13], at Tribhuvan University Teaching Hospital, Kathmandu, HBV infection was commonly found to be associated with heterosexual activity. Two (5.55%) of the positive cases had a history of IV drug abuse. One of these had a history of using injection buprenorphine. Since sharing of needles is common among IV drug users (IVDU), the contamination from needles used by an HBV infected person may have transmitted the infection to others. A study done by Shrestha et al [22] found the prevalence of HBsAg in IVDU in Nepal to be 5.5%. A study done by Gyawali et al [14] showed that 5% of the HBV infected

patients acquired the HBV infection from IV drug abuse.

Of the 36 samples showing the presence of HBsAg, 2 (5.55%) were also found to be infected with HIV, while none were positive for HCV. The co-infection between HBsAg and HIV could be due to the shared modes of transmission of the two diseases [23]. A study done by Devi et al found that 6.2% of hepatitis patients showed HIV seropositivity [23]. Of the 36 positive samples, 7 were detected during routine blood tests done as a requirement for going abroad. A recent study looked at the pattern of liver diseases among patients admitted to the liver unit of Bir hospital, the oldest hospital in Nepal over a six month period [24]. Alcohol consumption, followed by the presence of hepatitis B and C viruses were the major causes of chronic liver disease. A recent study looked at the seroprevalence of four transfusion transmissible infections among blood donors in Kathmandu, Nepal. The seroprevalence of HBV (HBsAg) was 0.47% [25]. A retrospective study among Nepalese blood donors over a six year period from 2001 to 2007 was conducted. The overall seroprevalence of HBV nationwide and at the Central Blood Transfusion Service in Kathmandu were found to be 0.82 and 0.92% [26].

Recently, there is an increasing trend among young people of going abroad for further studies and for employment. This may have resulted in the detection of HBsAg seropositivity in many patients who otherwise may have gone undetected until serious infection had set in. Thus, the routine testing of the HBsAg status may serve to improve the management of HBV infection and could be an option.

Preventing the transmission of blood borne pathogens requires a robust approach which includes having effective childhood immunization as a national policy which will reduce the burden of infection, vaccinating vulnerable groups, educating the public about high risk behaviours and committing healthcare workers to safe work practices.

The limitation of this study was that it was done in a tertiary care hospital which caters to patients

who are referred for complications of liver disease, which could cause a likely bias in sampling. Only patients who tested positive for HBsAg were interviewed and information about other respondents was obtained from case sheets. The data is also from an older time period. Patients visiting other hospitals or who did not have access to hospitals were not included.

## Conclusion

The frequency of seropositivity among individuals referred for HBsAg testing at the tertiary care hospital was high. Various factors could have influenced the results. Further studies are required to assess the seroprevalence among all patients attending the hospital OPD and wards.

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## Conflicts of interest

The authors declare that they have no competing interests.

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