Trends of Hepatitis Virus Infections in a Tertiary Care Hospital in Nepal, 2012-2023

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ABSTRACT

Objectives: To monitor the trends of incidence of different hepatitis virus infections during 2012–2023 in a tertiary care hospital in Nepal.

Methods: A descriptive study was conducted using demographic and serological data from 2012 to 2023 at Tribhuvan University Teaching Hospital. The serological tests were performed by enzyme-linked immunosorbent assays from the patient's serum.

Results: The incidence of HAV infections showed a downward trend from 2012–2016 (37.6%- 17.7%), increased in 2017–2019 (33.9%-27.8%), and then gradually decreased to 10.2% in 2023. In case of HEV infection, the incidence did not show any trend over the ten years period (from 2012-2018: 5.4%-13.3%; 2020: 7.1%; 2021:14.7%; 2023: 4.2%). The incidence of HBV infection was nearly unchanged between 2.5-3.1% from 2012-2023, the incidence of HCV infection was between 0.7-1.8% during the same period. The proportion of male cases was higher for all hepatitis infections and adult cases (15-47 years old) were in higher proportions except hepatitis A.

Conclusion: While the incidence trends of hepatitis B infections have been nearly the same over the past ten years, the trends of hepatitis A, E, and C infections are declining. Extensive preventive efforts are essential for reducing the infection rates to a low level.

Keywords: Hepatitis viruses, trends, incidence, ELISA, tertiary care hospital, Nepal

INTRODUCTION

Hepatitis infection is a major public health problem throughout the world, and viral hepatitis caused 1.3 million deaths in 2022, attributing 83% to hepatitis B and 17% to hepatitis C {World Health Organization (WHO, 2024). Various clinical manifestations among patients have been reported, from more frequent subclinical forms to fulminant hepatitis (Patrick et al., 2013).

Among water-borne hepatitis, hepatitis A virus (HAV) infections are predominant, and hepatitis E outbreaks occur mostly in East and South Asia (WHO, 2023). Hepatitis A infections are more frequent in children, but they remain asymptomatic (Migueres et al., 2021). Therefore, it is difficult to get accurate epidemiological or microbiological data. Studies from some developing countries reveal that up to 43.5% of children have serological markers of past hepatitis A infection by the age of five (Gupta et al., 2019). There is a safe and effective vaccine available to prevent HAV transmission, but it has not been included in the national immunization program.

Hepatitis E virus (HEV) infections are endemic in many tropical and subtropical countries, including East and

Date of Submission: October 2, 2024
Date of Acceptance: November 27, 2024
Published Online: December 31, 2024
DOI: https://doi.org/10.3126/tujm.v11i1.81310

South Asia. The updated global data on HEV infections is not available. The WHO (2023) reported that approximately 20 million people around the world are infected each year with HEV, and an estimated 44000 deaths occurred in 2015. Nepal is also an endemic country for HEV infections. Many outbreaks and three great epidemics had occurred in the past, including in Kathmandu Valley, and another epidemic of HEV occurred in Biratnagar in 2014, affecting many people, including 1,861 hospital patients with acute illnesses (Shrestha, 2006; Shrestha et al., 2015). A study carried out in Kathmandu Valley has reported 4.8% seroprevalence of HEV infection among the 923 volunteered participants (Katuwal et al., 2023. HEV is a concern since 25% of HEV-infected pregnant women in their third trimester may develop fulminant hepatic failure leading to death (Ranger-Rogez et al., 2002). Although there are safe and effective vaccines produced to stop the spread of HEV, however, its availability is limited in Nepal.

Approximately one-third of the world's population has serological evidence of past or present infection with the hepatitis B virus (HBV), and 254 million people are chronically infected. Among them, approximately 1.1 million people died mainly from liver cirrhosis and hepatocellular carcinoma in 2022 (WHO, 2024). In Nepal, although the prevalence of hepatitis B and C among the general population is as low as 0.9% and 0.4%, respectively, this percentage is higher among injecting intravenous drug users, sex workers, and HIV-positives (Ministry of Health and Population (MoHP), 2023). Globally, safe and effective vaccines against HBV are accessible. Immunization against hepatitis B is a crucial intervention for the prevention of virus transmission, thus reducing the burden of the disease. The national immunization program focusing children under 15 months of age has contributed to the decrease in newborn and child deaths in Nepal attributable to Hepatitis B (MoHP, 2023).

According to recent estimates, approximately 50 million people around the world have been chronically infected with HCV, of whom an estimated 242,000 died in 2022, mostly from cirrhosis and hepatocellular carcinoma (WHO, 2024). A study in Nepal has also shown that 5% to 10% of patients with hepatocellular carcinoma were seropositive for HCV (Shrestha, 2018). The seroprevalence of anti-HCV among the Nepalese population has been reported around1% (Shrestha et al., 1998; Karki et al., 2008; Sawayama et al., 1999; Shrestha, 2003; Shrestha, 2006). Among intravenous drug users (IDU), Shrestha et al. (1998) reported an HCV infection rate of 94%, whereas another study has shown a seropositivity rate of 85.5% in 2003 in Kathmandu valley (Shrestha, 2003). There is no vaccine developed for HCV yet; however, effective treatment with antiviral drugs is available to cure the disease.

The burden of viral hepatitis disease and mortality in Nepal, with the great diversity and distribution of different viral strains, shows the importance of understanding the incidence trends of acute and chronic hepatitis. In Nepal, there are limited number of studies showing the trends of all hepatitis infections. In this study, we collected retrospective data of 6 years from 2012 to 2019, and prospectively collected data of 4 years from 2020 to 2023. We analyzed these data to observe the incidence trends of hepatitis infections. These data are from Tribhuvan University Teaching Hospital Kathmandu, Nepal, where people throughout the country seek treatment for many diseases. The clinicians from other hospitals and health care facilities also refer patients to this hospital. Therefore, we collected sero-epidemiological data from the last 10 years of hepatitis positive patients. The objective of this study was to monitor the incidence of different hepatitis virus infections during 2012–2023 in a tertiary care hospital in Nepal.

METHODS

Study design

This was a sero-surveillance study based on data from a referral level Tribhuvan University Teaching Hospital in Kathmandu, where we collected and analyzed all tested and positive cases of hepatitis virus infections during a 10-year period from 2012 to 2023.

Data collection period

The collection period of data was from 2012 to 2023 excluding 2013 and 2014. We collected data of all examined and positive cases of HAV, HEV, HBV, and HCV infections in the Department of Microbiology at Tribhuvan University Teaching Hospital (TUTH).

Data collection procedures

Descriptive data on recently diagnosed HAV, HEV, HBV, and HCV infections, along with sociodemographic details including age and gender, were extracted from the records of the hospital. We collected retrospective data from 2012 to 2019. We tested the specimens as referred by clinicians from 2020 to 2023 and recorded the test results and demographic data. During the study period, 11237 were tested for hepatitis A, 10512 for hepatitis E, 94376 for hepatitis B and 61393 for hepatitis C.

Detection methods for hepatitis viruses

The serological tests were performed by enzyme-linked immunosorbent assays (ELISA) to detect IgM antibodies for hepatitis A virus (HAV) (Dia. Pro Diagnostic Bioprobes, Milano-Italy) and hepatitis E virus (HEV) (Dia. Pro Diagnostic Bioprobes, Milano-Italy), surface antigens for hepatitis B virus (HBV) (Autobio Diagnostics Co., Ltd., Zhengzhou, China), and total antibodies for hepatitis C virus (HCV) (Autobio Diagnostics Co., Ltd., Zhengzhou, China), from the patient's blood serum. The test procedure was performed as per manufacturer instructions supplied as package inserts and kit literature along with the ELISA kits.

Data management and analysis

Statistical analysis by Excel spreadsheet in Windows 10. SPSS version 25.0 was used for all data analysis presented in text, table and figures. The hospital-based incidence of newly diagnosed hepatitis cases was calculated as the number of new cases of each hepatitis among the total tested for each hepatitis in percent in each calendar year. We also calculated distribution of hepatitis virus infections according to gender and age group. The inferential statistics were calculated by the chi-square test to compare disease incidence of hepatitis over the years. All tests were considered to be statistically significant at $p < 0.05$.

Ethical consideration

The epidemiological analysis was based on anonymous data from the hospital. Ethical approval was obtained from the Ethics Review Board of Nepal Health Research Council (Ref. 775/2019 amendment 12/2024). In case of prospective tests of samples from 2020, we obtained written informed consent from the patients. In case of retrospective data collection before 2020 from the hospital record, anonymous data was collected.

RESULTS

Hospital based incidence of water borne viral hepatitis infections

The incidence of HAV infections showed a downward trend from 2012–2016, from 37.6% (239/636) in 2012 to 17.7% (251/1418) in 2016 ($p<0.0001$). It increased significantly in 2017 –2019 compared to 2016; (33.9%, 535/1580 in 2017 ($p<0.0001$) and 27.8% (341/1228) in 2019 ($p<0.0001$). It gradually decreased from 2020–2023 up to 10.2% (168/1653) in 2023 but not statistically significant ($p=0.075$). In the case of HEV, the incidence was 5.4% (30/555) in 2012, then gradually increased significantly to 13.8% (126/915) in 2016 ($p<0.0001$) and remained at almost the same level until 2018. Again, the incidence started to decrease significantly to 7.1% (41/578) in 2020 ($p=0.0001$), rose significantly to 14.7% (145/984) in 2021($p<0.0001$), and decreased significantly to 4.2% (72/1724) in 2023 ($p<0.0001$) (Figure 1).

Hospital based incidence of blood borne viral hepatitis infections

The incidence of HBV infection was 2.8% (278/9867) in 2012, and it remained nearly unchanged in the following year until 2023. In the case of HCV infection, the incidence was 1.7% (84/5045) in 2012, then gradually decreased significantly to 0.7% (54/8100) in 2018 ($p<0.0001$). Again, the incidence started to increase significantly to 1.8% (71/3866) in 2020 ($p<0.0001$), then started to decrease significantly to 1.1% (89/7987) in 2023 ($p=0.0018$) (Figure 2). As compared to 2023 with 2012, the HCV incidence has decreased significantly ($p=0.0036$).

Among the total hepatitis cases (2200 hepatitis A cases, 1087 hepatitis E cases, 2603 hepatitis B cases, and 735 hepatitis C cases), the percentage of male cases was found to be higher in all hepatitis infections. Similarly, a percentage of adult cases aged between 15 and 47 (median age for hepatitis E is 41, B is 32, and C is 38) years were found high in all hepatitis B, C, and E, whereas a percentage of child cases (median age is 7 years) were found high in hepatitis A (Table 1).

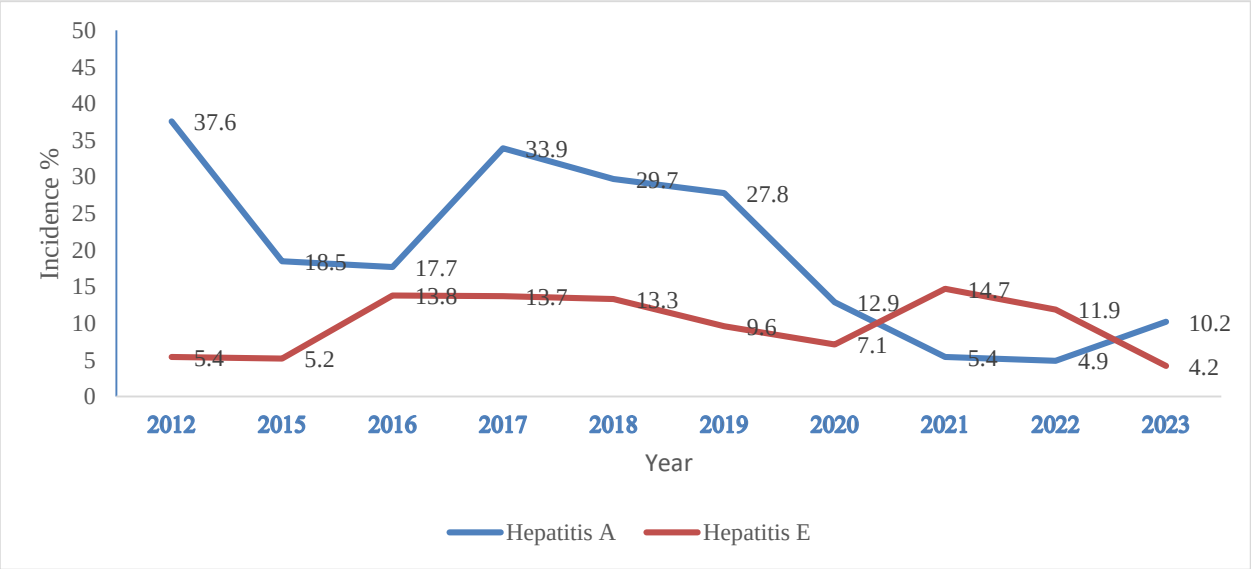

Figure 1: Year wise hospital-based incidence of water borne hepatitis infections, 2012-2023

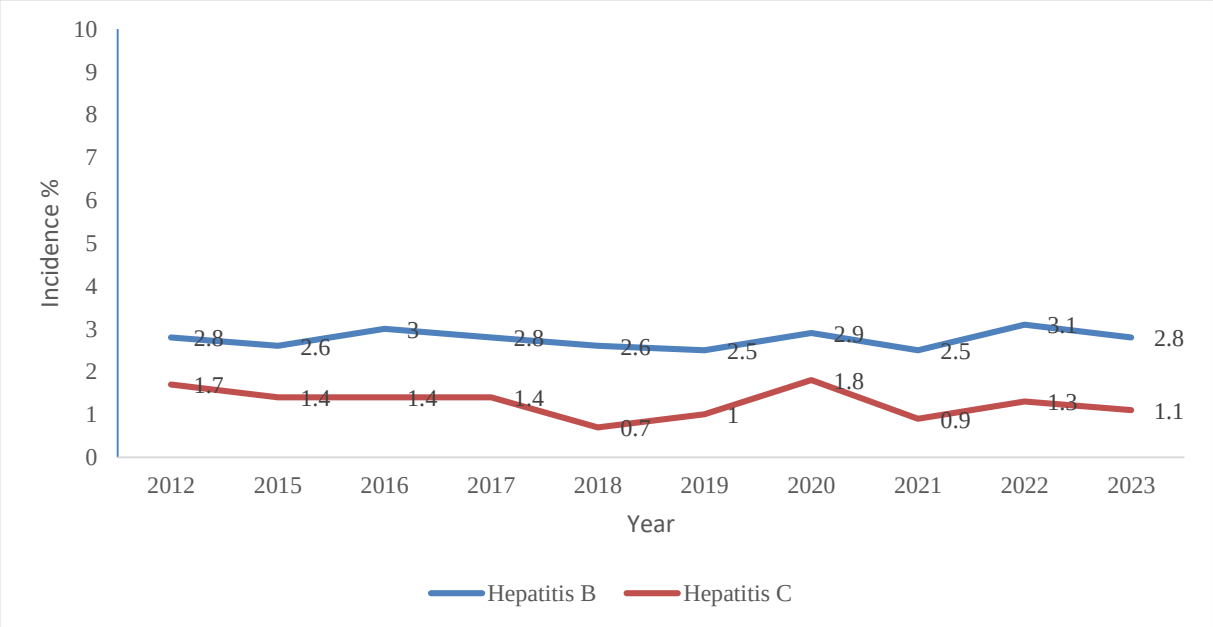

Figure 2: Year wise hospital-based incidence of bloodborne hepatitis infections

Table 1: Demographic distribution of hepatitis cases

Demographic characters	Hepatitis A (N=2200)	Hepatitis E (N=1087)	Hepatitis B (N=2603)	Hepatitis C (N=735)
Gender	%	%	%	%
Male	**58.7**	**67.0**	**66.6**	**81.5**
Female	41.2	33.0	33.3	18.5
Age (years)				
<15	**78.7**	8.3	2.2	1.2
15-47	15.1	**53.4**	**61.4**	**67.1**

48-63	1.5	25.2	19.3	20.1
>63	0.7	9.0	11.9	6.5
Median age of infection in different years (IQ range)				
2015	7 (9.5)	23 (19)	32 (27)	37 (17)
2016	8 (7)	37 (24.3)	30 (22)	35.5 (16)
2017	7 (6)	36 (24)	34 (29)	40 (16)
2018	7 (7)	35 (27)	32 (22)	42.5 (16)
2019	7 (6)	36 (28)	38 (30)	35 (18)
2020	8.5 (7)	36 (22)	36.5 (31)	40 (20)
2021	8 (10.25)	47 (17)	42 (30)	40 (17)
2022	13 (35.75)	47 (17.5)	42 (33)	36 (18)
2023	8 (8)	45.5 (15.8)	42 (31)	42 (23)
Median age of all years	7(7)	41(23)	32(25)	38(19)

DISCUSSION

Viral hepatitis is a significant public health issue in underdeveloped nations. This study offers new perspectives on the epidemiological state of HAV, HEV, HBV, and HCV infections in Nepal, which are essential for policy making toward prevention and focusing on certain populations.

In Nepal, waterborne outbreaks with hepatitis A and hepatitis E infections are frequent. The decadal trends of viral hepatitis showed that the hospital-based incidence of hepatitis A has decreased by more than one third, but it is still above 10%. A study conducted in our neighboring country, India, revealed a 12.6% prevalence of hepatitis A, which is consistent with our findings (Murhekar et al., 2018). Another study on systemic review conducted in India also showed similar statistics, as the prevalence of hepatitis A was shown to vary between 2.1% and 52.5% (Kumar et al., 2023). Our findings are supported by a study conducted over a period of 8 years at the teaching hospital of northern India where 16.9% were shown to be reactive to anti-HAV IgM antibodies (Bansal et al., 2022).

The results indicate that hepatitis A infections decreased during the COVID-19 pandemic and again increased slightly after 2022. This could be due to less movement of people during the COVID-19 pandemic due to lockdowns and less exposure to contaminated food and water since hepatitis A infections are often associated with the level of access to safe drinking water, socioeconomic status, and hygiene (WHO, 2010).

The hospital-based incidence of hepatitis E virus infection remained around 5% in most of the years, except in outbreak situations. A study conducted in our neighbor country, India, revealed a 16.1% prevalence of hepatitis E, and another study conducted at a teaching hospital of northern India over a period of 8 years where 14.9% were reactive for anti-HEV IgM antibodies, which is higher than our findings (Murhekar et al., 2018; Bansal et al., 2022).

The hepatitis E infections were increased during the COVID-19 period. This temporary spike in hepatitis E could be due to novel circumstances, such as the mega earthquake in 2015 in Nepal and the COVID-19 pandemic (Basnyat et al., 2015; Katuwal et al., 2023). During these events, large number of people got foods in shelter donated from different volunteers and organizations which might have compromised the quality of food and potability of drinking water. These findings highlight the need for continuous monitoring of water-borne viral hepatitis in Nepal.

In this study, hepatitis A cases were found in more males than females and in children less than 15 years of age. However, a hospital-based study in 2014 in Kathmandu revealed more female cases than males for hepatitis A infections (Gupta et al., 2018). According to studies done in India, there were high number of pediatric cases (Murhekar et al., 2018; Kumar et al., 2023; Bansal et al., 2022). The European Surveillance System notifications of hepatitis A from 2010 to 2019 revealed more male cases and a young population (Severi et al., 2023). The sero-prevalence study from Hungary also showed a higher prevalence of hepatitis A among the young population (Reuter et al., 2022). In endemic countries like Nepal, many children in their childhood are already exposed to the infection and are natu-

rally immunized. Among them, only a few cases might develop symptoms at a young age. With natural immunity developed in childhood, adults could be less infected (WHO, 2022). However, hepatitis A infection in children in Nepal needs further investigation.

In this study, hepatitis E infection was found more among males and young people aged 15–47 years, indicating that the hepatitis E virus is continuously circulating in the Nepalese population. The higher number of adult cases were found in a study carried out in India (Murhekar et al., 2018; Bansal et al., 2022). The sero-prevalence studies revealed a higher prevalence of hepatitis E among males than females (Van Gageldonk-Lafeber et al., 2017; Niederhauser et al., 2024). This could be due to the increased exposure of this population to contaminated water, eating more frequently, and more exposure opportunities to viruses (Nicolini et al., 2020).

The incidence of hepatitis B has stayed relatively constant over the course of a decade, despite increases in public health awareness, the introduction of hepatitis B vaccination, and preventive steps to stop the spread of viruses in Nepal, whereas the incidence of HCV has been seen in decreasing trends over the years. This might be due to the preventive measures applied to stop the transmission of viruses, along with direct-acting antiviral drugs available with a success rate of over 95% for treating patients with HCV (WHO, 2024). A higher proportion of both hepatitis B and C patients were males among those aged 15–47 years during the period 2012–2023. Nepal is among the low-prevalence countries for hepatitis B and C (<1%) among the general population, but the prevalence is higher among specific risk populations such as people living with HIV (PLHIV), people who inject drugs, and sex workers ((MoHP, 2023). A systematic review of Nepal studies on hepatitis B and C summarized that a higher seroprevalence of hepatitis B was detected in people who inject drugs, patients with jaundice, sexual and household contacts of people chronically infected by HBV, survivors of sex trafficking, and the Tibetan population living in Kathmandu valley. There was higher seroprevalence of hepatitis C among people who inject drugs, PLHIV, and people with hepatocellular carcinoma (Naveira et al., 2018). A study on systemic review conducted in India also showed similar statistics on hepatitis, as the rate of hepatitis B varied from 0.8% to 21.4% of the population, and rate of hepatitis C varied from 0.5% to 53.7% (Kumar et al., 2023).

In all cases of hepatitis, we found that male cases dominated female cases. It could be due to the nature of our society's built-up work division. In our society, the male population is more active towards outdoor work, and they are more likely to get infected with hepatitis viruses.

The limitation of this study is that we presented data with limited variables. There were very few variables recorded on the manual register since clinicians fill out the requisition form with the minimum patients' information. We could not get records of 2013 and 2014 and data of these two years has not been presented. Since this is a study with limited variables and without follow up with the patients, we were unable to present the results according to the socioeconomic status of the patients, different geography, and different risk groups such as pregnant women for hepatitis E, sex workers, IDUs, etc. for hepatitis B and C.

Conclusion

In conclusion, while the trends of incidence of blood borne hepatitis B virus infections have been nearly the same over the past ten years, the trends for water-borne hepatitis A, E and blood-borne hepatitis C infections are declining. Apart from hepatitis A, adult males account for a higher proportion of viral hepatitis cases. Preventive efforts should break the chain of transmission since hepatitis A and E infections spread through the faecal-oral route, while hepatitis B and C infections spread through any means of body fluid inoculation. This work can be used as a benchmark for future research, as it represents the most recent epidemiological trends of HAV, HEV, HBV, and HCV from the serological data of a tertiary care hospital in Nepal.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to Diwash Shrestha, in charge of the serology lab, former Heads of Department Professor Dr. Jeevan Bahadur Sherchand, Professor Dr. Basistha Prasad Rijal, Prof Dr. Keshav Parajuli, Tribhuvan University Teaching Hospital, Kathmandu, Nepal, for their support in conducting this study.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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