



OCCURRENCE OF HEPATITIS B AND HEPATITIS C AND THEIR DUAL INFECTIONS: A GREAT PUBLIC HEALTH CONCERN

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ABSTRACT

Introduction-Viral hepatitis is one of the major public health concern worldwide. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are of great concern due to their association with cirrhosis and hepatocellular carcinoma.

Aims & Objectives-i)To determine the frequency of Hepatitis B surface antigen and anti-HCV antibodies in patients coming to a tertiary care teaching hospital ii)To estimate the occurrence of co-infection with hepatitis B virus and hepatitis C virus iii) To analyse the risk factors associated with hepatitis B, hepatitis C and their co-infections.

Method- This prospective study included serum samples which were subjected to detection of HBs antigen and anti-HCV antibodies using rapid immunochromatographic card tests, which were further confirmed by Enzyme Linked Immunosorbent Assay (ELISA).

Results- Out of total of 12,502 cases, the seropositivity of HBs antigen and anti-HCV antibodies was found to be 3.6% (452/12,502) and 6.1% (758/12,502) respectively. The frequency of co-infection (HBs antigen and anti-HCV antibodies) was found to be 0.8% (99/12,502). Male to female ratio for hepatitis B, hepatitis C and co-infection was 2.1:1, 1.6:1 and 2.3:1, respectively. The commonest risk factor associated with seropositivity of HBV was intravenous drug use, followed by blood / blood components transfusion. Hepatitis C infection was most commonly seen with blood / blood components transfusion, followed by intravenous drug use.

Conclusions: Counseling and health education regarding the safe injection practices, safe sexual practices, screening of blood / blood products and vaccination against HBV are the essential steps to combat viral hepatitis.

KEYWORDS : Anti-HCV antibodies, Co-infection, HBV, HCV, Hepatitis B surface antigen

INTRODUCTION:

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are of public health importance worldwide, due to their burden of liver-related morbidity and mortality.^{1,2} HBV and HCV are endemic in India and are culprit for causing acute hepatitis. About 50%-70% cases of acute hepatitis lead to chronic liver disease (CLD), particularly cirrhosis and hepatocellular carcinoma.³⁻⁵ In India, there are estimated 43-45 million hepatitis B surface antigen carriers and 3%-4% of the population is infected with hepatitis B virus.⁶ Hepatitis C virus is one of the major cause of post-transfusion hepatitis and results in CLD.⁵ It has been analyzed that approximately 1.8%-2.5% population is presently infected with HCV in India.⁷ The unscreened blood / blood products transfusion, unsafe injection practices, PWID (People who inject drugs) and multiple sexual partners, play a significant role in transmission of HBV and HCV, thereby increasing their prevalence.^{8,9} Coinfection with HBV and HCV results in severe liver disease and poses an increased risk of progression to HCC.^{8,10} Coinfections of HBV and HCV are more common with HIV-infected patients, as they share the major routes of their transmission.¹¹

The present study was undertaken to determine the frequency of seropositivity of HBs Ag and anti-HCV antibodies in a tertiary care hospital in western Uttar Pradesh, to analyze their co-infections and identify the risk factors associated with their transmission.

MATERIALS AND METHOD:

The prospective study was carried out in the Department of Microbiology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, over a period of one year, from June 2019 to May 2020 after obtaining approval from the institutional ethics committee.

The study included all blood samples received, in the Microbiology Laboratory, for detection of HBs Ag test (Hepatitis B surface antigen) and anti-HCV antibodies, from patients attending various out - patient departments and patients admitted in different wards and intensive care units of our tertiary care hospital.

Sample Collection:

5 ml of venous blood sample was collected from the patients by a trained phlebotomist in red top vacutainer.

Serum Separation:

Whole blood sample was allowed to clot for 60 minutes at room temperature. Once the clot had formed, sample was centrifuged for serum separation.

Serum Storage:

Serum samples were stored at 2-8°C for upto 1 week or at -20°C for upto 1 month.

Sample Processing:

a. Detection of HBsAg

Screening of HBV infection was done by detection of HBs Ag using rapid immunochromatographic card test (Hepacard, J. Mitra and Co. Private Limited, India) as per the manufacturer's instructions. Samples reactive by card test were further confirmed by ELISA for HBsAg (Hepalisa, J. Mitra and Co. Private Limited) according to kit's instructions.

b. Detection Of Anti-HCV Antibodies

Screening of HCV infection was done by detection of of Anti-HCV antibodies using rapid immunochromatographic card test (Tridot, J. Mitra and Co. Private Limited) as per the manufacturer's instructions. Samples reactive by card test were further confirmed by third generation ELISA (HCV Microlisa, J. Mitra and Co. Private Limited) according to kit's instructions.

Statistical Analysis:

Study was done using retrospective data collected over two years of duration. All data are expressed as absolute numbers and percentage to serve the purpose of descriptive analysis in current study. Categorical data were presented in tabular form along with frequency and percentage.

RESULTS:

Blood samples were received in the laboratory from a total of 12,502 patients, for the detection of both HBs Ag and anti-HCV antibodies. Out of total of 12,502 cases, the serum samples reactive for only HBs Ag by immunochromatographic card test were 452 (3.6%), the results of which were found to be concordant with hepatitis B ELISA. The serum samples reactive for only anti-HCV antibodies by card test were 758 (6.1%), all of which were also reactive by hepatitis C ELISA. Thus, the seropositivity of HBV infection and HCV infection was found to be 3.6% (452/12,502) and 6.1% (758/12,502), respectively. Out of total of 12,502 cases, 99 were reactive for both HBs Ag and anti-HCV antibodies by immunochromatographic card tests and were further confirmed by ELISA for HBV and ELISA for HCV. The frequency of co-infection (HBs Ag + anti-HCV antibodies) was found to be 0.8% (99/12,502).

Patients with hepatitis B, hepatitis C and co-infection, most commonly, belonged to the age group of 20-40 years. Hepatitis B

(67.9%) and hepatitis C (62.1%) were more common in males as compared to females. Cases of dual infection with HBV and HCV also showed male preponderance (69.7%).

Male to female ratio for hepatitis B, hepatitis C and co-infection was 2.1:1, 1.6:1 and 2.3:1, respectively.

The commonest risk factor associated with seropositivity of HBV was intravenous drug use (39.8%), followed by blood / blood components transfusion (26.3%), multiple sexual partners (23.2%), needle stick injuries (5.5%), hemodialysis (4.6%) and organ transplantation (0.4%) (Table 1).

Hepatitis C infection was most commonly seen with blood / blood components transfusion (39.3%), followed by intravenous drug use (26.5%), multiple sexual partners (15.7%), hemodialysis (8.4%) needle stick injuries (6.9%), organ transplantation (2.2 %) and tattooing (0.9%) (Table 2).

Co-infection with hepatitis B virus and hepatitis C virus was predominantly associated with needle stick injuries (34.3%), followed by blood / blood components transfusion (23.2%), intravenous drug use (18.2%), multiple sexual partners (14.1%), hemodialysis (8.1%) and organ transplantation (2%) (Table 3).

Table 1: Risk Factors Associated With Seropositivity Of HBV (n=452)

Risk factor	Positive cases (n=452)	Percentage (%)
Blood / blood components transfusion	119	26.3
Intravenous drug use	180	39.8
Multiple sexual partners	105	23.2
Needle stick injuries	25	5.5
Hemodialysis	21	4.6
Tattooing	0	0
Organ transplantation	2	0.4

Table 2: Risk Factors Associated With Seropositivity Of HCV (n=758)

Risk factor	Positive cases (n=758)	Percentage (%)
Blood / blood components transfusion	298	39.3
Intravenous drug use	201	26.5
Multiple sexual partners	119	15.7
Needle stick injuries	52	6.9
Hemodialysis	64	8.4
Tattooing	7	0.9
Organ transplantation	17	2.2

Table 3: Risk Factors Associated With The Cases Of Co-infection With HBV and HCV (n=99)

Risk factor	Positive cases (n=99)	Percentage (%)
Blood / blood components transfusion	23	23.2
Intravenous drug use	18	18.2
Multiple sexual partners	14	14.1
Needle stick injuries	34	34.3
Hemodialysis	8	8.1
Tattooing	0	0
Organ transplantation	2	2.0

DISCUSSION:

Viral hepatitis is primarily associated with life threatening complications such as liver cirrhosis, primary hepatocellular carcinoma, hepatic fibrosis and steatosis.¹⁵ Hepatitis B virus and hepatitis C virus are the blood-borne pathogens, propagating around the globe, including in India. Due to the shared mode of parenteral transmission, co-infections with HBV and HCV are common in highly endemic areas and in high risk population.^{1,12,13}

India holds for the significant proportion of the global hepatitis B burden, accounting for 10-15% of HBV carrier state. India has been recognized as an intermediate endemic country, with a 3.7% point-prevalence of HBV.^{14,15} It has been estimated that annually, one million Indians are at risk of getting hepatitis B, and about 100,000 deaths occur due to HBV infection.^{15,16}

In the present study, the seropositivity of HBV infection was found to be 3.6%.

In 2018, a study done by Agarwal L et al.¹⁷ reported the seroprevalence of HBs Ag in hospital-based population to be 3.9% in Uttar Pradesh. In northeast India, Roy A et al.¹² had documented 17.4% seroprevalence of HBV in 2017.

A systematic review and pooled analysis by Schweitzer et al., covering 161 countries, reported HBsAg prevalence in India to be 1.46%.¹⁸ Studies carried out in Rajasthan,¹⁹ Andhra Pradesh,²⁰ and Karnataka,²¹ observed the seroprevalence of HBs Ag to be 0.87%, 1.06%, and 1.63%, respectively.

In our study, the seropositivity of HCV infection was found to be 6.1%. Agarwal L et al.¹⁷ had reported the seroprevalence of anti-HCV antibodies in hospital-based population to be 1.76% in Uttar Pradesh in 2018. In 2010, a study conducted in Rajasthan, by Sood S et al.,¹⁹ found the HCV prevalence of 0.28%. In 2012, Kaur R et al.²² observed the HCV prevalence of 1.4% in Punjab.

India accounts for a large share of the global hepatitis C burden, with 1-1.5% prevalence. About 15 to 18 million population live with acute or chronic hepatitis C infection in India.^{23,24}

The variation in the prevalence of hepatitis B virus and hepatitis C virus depends on the behavioral, environmental, socio-economic status and host factors, that influence their transmission.^{18,25}

In our set up, the frequency of co-infection with HBV and HCV was found to be 0.8%.

In 2017, a study done by Desikan et al.²⁶ reported the prevalence of co-infection in India to be 1.89%. Agarwal L et al.¹⁷ showed dual infection in 0.16% cases in Uttar Pradesh in 2018. A study conducted by Saravanan et al.²⁷ reported co-infection in 5.9% patients of chronic liver disease. Grewal US et al.² reported co-infection in 4% cases of CLD in Punjab. Patients with co-infections are prone to develop chronic liver disease and progression to hepatocellular carcinoma and show poor response to treatment.^{2,28,29}

In our study, HBV infection, HCV infection and their co-infections were most commonly seen in the age group of 20-40 years. Male predominance was found for hepatitis B (2.1:1), hepatitis C (1.6:1) and co-infection (2.3:1).

These findings are similar to the study done by Grewal US et al.² who reported that majority of the HBs Ag positive patients (61.54%) belonged to the age group of 21-40 years and showed male predominance. A study done in Manipur, by Devi KS et al.³⁰ found HBs Ag positivity to be higher in the age group of 22-32 years. Agarwal L et al.¹⁷ observed that seroprevalence of hepatitis B among males and females was 5.5% and 2.4%, respectively. Sood S et al.¹⁹ reported higher prevalence of HBV in males and stated that the possible reason could be that females clear the HBV infection more efficiently as compared to males.

Grewal US et al.,² Agarwal L et al.¹⁷ and Sood S et al.¹⁹ found HCV infections more common in males as compared to females.

In our study the commonest risk factor associated with seropositivity of HBV was intravenous drug use, followed by blood / blood components transfusion, multiple sexual partners, needle stick injuries and hemodialysis. Hepatitis C infection was most commonly seen with blood / blood components transfusion, followed by intravenous drug use, multiple sexual partners and hemodialysis. Co-infections with HBV and HCV were predominantly associated with needle stick injuries followed by blood / blood components transfusion, intravenous drug use, multiple sexual partners, hemodialysis and organ transplantation. In a study done by Agarwal L et al.¹⁷ blood / blood products transfusion was found to be a significant risk factor for both HBV and HCV infection.

In India, usage of unsterilized needles and syringes / unsafe injection practices have been associated with outbreaks of HBV infection in different regions. In our country, median population attributable fraction for chronic hepatitis B linked to injections was estimated to be 46% while that for hepatitis C and HIV was 38% and 12%, respectively.^{31,32}

Reddy et al.³³ found dual infection with HBV and HCV in 3.7% patients undergoing hemodialysis.

Saravanan S et al.²⁷ observed that the rate of HBV and HCV co-infection among the PWID (people who inject drugs) was 13.7%. Javadi A et al.³⁴ and Roy A et al.¹² reported a co-infection rate of 12.1% and 9.7 %, respectively, among PWID.

Co-infections should be a matter of concern, emphasizing the importance of education of masses regarding various modes of transmission of HBV and HCV. An essential step is encouraging and motivating health care providers to adopt infection prevention and control practices, so as to combat viral hepatitis.³⁵

CONCLUSIONS:

In India, viral hepatitis contributes to a significant health related burden, resulting in ensuing outcomes such as liver cirrhosis and hepatocellular carcinoma. Therefore, screening of high risk population becomes the most important approach for the prevention and control of HBV and HCV. The study highlights the need of awareness by counseling and health education, regarding the safe injection practices, safe sexual practices and screening of blood and blood products. Early detection of the infection and timely treatment results in better prognosis, thereby limiting the liver - related disease burden. Educating the people about vaccination against HBV, will help in the prevention of disease and increase the herd immunity.

Limitations:

1. Anti-hepatitis B core IgG and IgM antibodies could not be tested, which would have aided to diagnose cured / occult HBV infections.
2. Due to limited resources, genotyping of HBV and HCV could not be carried out.

REFERENCES:

1. Mukherjee PS, Dutta E, Das DK, Ghosh S, Neogi S, Sarkar A. Knowledge about hepatitis B and hepatitis C virus infection and consequences: a cross-sectional assessment of baseline knowledge among infected patients in West Bengal, India. *Hepatology, Medicine and Policy*.2017;2(6):1-9.
2. Grewal US, Walia G, Bakshi R, Chopra S. Hepatitis B and C viruses, their coinfection and correlations in chronic liver disease patients: A tertiary care hospital study. *Int J App Basic Med Res*. 2018;8:204-9.
3. Dharmadhikari CA, Kulkarni RD, Kulkarni VA, Udgaonkar US, Pawar SG. Incidence of hepatitis B surface antigen in liver diseases and voluntary blood donors. *J Indian Med Assoc*.1990;88:73-5.
4. Banker DD. Viral hepatitis (Part-2). *Indian J Med Sci*. 2003;57:415-24.
5. Hoofnagle JH, Heller T. Hepatitis C. In: Zaxim D, Boyer TD. (eds.) *Hepatology: A textbook of liver disease*. 4th edition. Volume 2. Philadelphia: Saunders Publishers; 2003. p.1017-24.
6. Chowdhary A. Epidemiology of hepatitis B virus infection in India. *Hepat B Annu*. 2004;1:17-24.
7. Chandra M, Khaja MN, Farees N, Poduri CD, Hussain MM, Aejaz Habeeb M, et al. Prevalence, risk factors and genotype distribution of HCV and HBV infection in the tribal population: A community based study in South India. *Trop Gastroenterol*. 2003;24:193-5.
8. Devi KS, Singh NB, Mara J, Singh TB, Singh YM. Seroprevalence of hepatitis B virus and hepatitis C virus among hepatic disorders and injecting drug users in Manipur. A preliminary report. *Indian J Med Microbiol*.2004;22:136-37.
9. Jindal N, Bansal R, Grover P, Malhotra R. Risk factors and genotypes of HCV infected patients attending tertiary care hospital in North India. *Indian J Med Microbiol*. 2015;33:189-90.
10. Saha D, Pal A, Biswas A, Panigrahi R, Sarkar N, Sarkar J, et al. Characterization of treatment-naïve HIV/HBV co-infected patients attending ART clinic of a tertiary healthcare centre in Eastern India. *PLoS One*. 2013; 8(8): e73613. <https://doi.org/10.1371/journal.pone.0073613>; e73613.
11. Kumarasamy N, Solomon S, Flanigan TP, Hemalatha R, Thyagarajan SP, Mayer KH, et al. Natural history of human immunodeficiency virus disease in Southern India. *Clin Infect Dis*. 2003; 36:79-85.
12. Roy A, Praveen S, Devi KS, Haokip P, Laldinmawii G, Damrolien S. Seroprevalence of hepatitis B and hepatitis C in people who inject drugs (PWID) and other high risk groups in a tertiary care hospital in Northeast India. *Int J Community Med Public Health*. 2017;4:3306-9.
13. Chowdhary A. Epidemiology of hepatitis B virus infection in India. *Hepat B Annu*. 2004;1:17-24.
14. Dutta S. An overview of molecular epidemiology of hepatitis B virus (HBV) in India. *Virology*. 2008;5:156.
15. Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clin Microbiol Infect*. 2011; 17:107–15.
16. Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. *Clin Liver Dis*. 2010;14:1–21.
17. Agarwal L, Singh AK, Agarwal A, Singh RP. Incidental detection of hepatitis B and C viruses and their coinfection in a hospital-based general population in tertiary care hospital of Uttar Pradesh. *J Family Med Prim Care*. 2018;7:157-61.
18. Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: A systematic review of data published between 1965 and 2013. *Lancet*. 2015;386:1546-55
19. Sood S, Malvankar S. Seroprevalence of hepatitis B surface antigen, antibodies to the hepatitis C virus and human immunodeficiency virus in a hospital-based population in Jaipur, Rajasthan. *Indian J Community Med*. 2010;35:165-9.
20. Shyamala R, Rao J. The study of prevalence of hepatitis B surface antigen in a tertiary care hospital in South India. *Der Pharmacia Lett*. 2013;5:11-2.
21. Quadri SA, Dadapeer HJ, Arifulla KM, Khan N. Prevalence of hepatitis B surface antigen in hospital based population in Bijapur, Karnataka. *Al Ameen J Med Sci*. 2013;6:180-2.
22. Kaur R, Singh A, Singh GP. Increasing prevalence of hepatitis among transfusion transmitted infections: A tertiary care centre experience. *J Evol Med Dent Sci*. 2012;1:875–81.
23. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of

- hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology*. 2013;57: 1333–42.
24. Jayasekera CR, Barry M, Roberts LR, Nguyen MH. Treating hepatitis C in lower-income countries. *N Engl J Med*. 2014;370:1869-71.
 25. Schwarz TF, Dobler G, Gilch S, Jäger G. Hepatitis C and arboviral antibodies in the Island populations of Mauritius and Rodrigues. *J Med Virol*. 1994; 44:379-83.
 26. Desikan P, Khan Z. Prevalence of hepatitis B and hepatitis C virus co-infection in India: A systematic review and meta-analysis. *Indian J Med Microbiol*. 2017; 35:332-9.
 27. Saravanan S, Velu V, Nandakumar S, Madhavan V, Uma S, Kailapuri G, et al. Hepatitis B virus and hepatitis C virus dual infection among patients with chronic liver disease. *J Microbiol Immunol Infect*. 2009;42:122-8.
 28. Liu Z, Hou J. Hepatitis B virus (HBV) and hepatitis C virus (HCV) dual infection. *Int J Med Sci*. 2006; 3:57-62.
 29. Kruse RL, Kramer JR, Tyson GL, Duan Z, Chen L, El-Serag HB, et al. Clinical outcomes of hepatitis B virus coinfection in a United States cohort of hepatitis C virus-infected patients. *Hepatology*. 2014; 60:1871-8.
 30. Devi KS, Singh NB, Mara J, Singh TB, Singh YM. Seroprevalence of hepatitis B virus and hepatitis C virus among hepatic disorders and injecting drug users in Manipur – A preliminary report. *Indian J Med Microbiol*.2004; 22:136-7.
 31. Puri P. Tackling the hepatitis B disease burden in India. *J Clin Exp Hepatol*. 2014; 4:312-9.
 32. Tandon BN, Gandhi BM, Joshi YK. Etiological spectrum of viral hepatitis and prevalence of markers of hepatitis A and B virus infection in North India. *Bull World Health Organ*.1984; 62:67-73.
 33. Reddy GA, Dakshinamurthy KV, Neelaprasad P, Gangadhar T, Lakshmi V. Prevalence of HBV and HCV dual infection in patients on haemodialysis. *Indian J Med Microbiol*. 2005; 23:41-3.
 34. Javadi A, Ataei B, Kassaian N, Nokhodian Z, Majid Y. Co-infection of human immunodeficiency virus, hepatitis C and hepatitis B virus among injection drug users in drop in centers. *J Res Med Sci*. 2014; 19(1):17-21.
 35. Locarnini S, Chen D-S, Shibuya K. No more excuses: viral hepatitis can be eliminated. *Lancet*. 2016; 387(10029):1703–1704.