

Six Year Tale of Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) at a Tertiary Care Centre in Punjab: A Retrospective Study from 2018 to 2023

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ABSTRACT

BACKGROUND: Acute viral hepatitis, primarily hepatitis A (HAV) and hepatitis E (HEV) carry a significant health burden in India, raising substantial public health concerns due to their link with inadequate hygiene and sanitation practices.

AIM: The study aimed to investigate the prevalence of Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) among patients presenting with acute viral hepatitis at a tertiary care centre in Punjab, North India.

MATERIAL AND METHOD: A total of 3793 serum samples suspected acute viral hepatitis for collected from tertiary care hospital during six years (2018- 2023) were analyzed for IgM antibodies against HAV and HEV using Rapid diagnostic tests.

RESULTS: The results revealed a higher incidence of HAV IgM positivity (13.4%) compared to HEV IgM positivity (8.7%). The combined prevalence of HAV and HEV infections was 22.15%. Gender-wise analysis showed a higher incidence of Hepatitis A in males, while Hepatitis E was more prevalent among females. Age-wise distribution indicated a higher proportion of HAV-positive cases in patients < 20 years (76.9%) and HEV-positive cases in young adults of age group 21-30 years (50%). Seasonal variation demonstrated the prevalence of both viruses throughout the year, with peaks in cases observed at the end of the monsoon season and the beginning of winter in this geographical region.

Keywords: Acute Viral Hepatitis; Hepatitis A Virus; Hepatitis E Virus; Rapid diagnostic tests

INTRODUCTION

The enterically transmitted hepatitis A and hepatitis E viruses are two significant etiological agents that are the main causes of acute viral hepatitis posing substantial public health concerns globally.^[1] They are linked to inadequate hygiene and sanitation, communicable diseases represent a large

health burden and raise important public health problems in our nation.^[2] India is hyperendemic for both the hepatitis A virus (HAV) and the hepatitis E virus (HEV), according to numerous researches from different states that have documented incidences of viral hepatitis in the nation.^[3] HEV and HAV are members of the non-

enveloped RNA virus family Hepeviridae. HEV and HAV belong to distinct genera within the family Hepeviridae (HEV) and Picornaviridae (HAV), respectively. HEV is classified into Orthohepevirus A genus, while HAV belongs to the Hepatovirus genus. Despite their differences, both viruses share common features in their genomic organization, including a 5' untranslated region (UTR), open reading frames (ORFs), and a 3' UTR. Variations in the HEV genome have led to the classification of distinct genotypes and subtypes, each exhibiting unique epidemiological and clinical characteristics. These viruses mainly spread through the fecal-oral route by consumption of contaminated items, owing to poor personal hygiene and sanitation practices.^[4] Serum amino-transferase activity elevation during acute sickness is indicative of both HEV (anti-HEV) and HAV (anti-HAV) antibodies. IgM class antibodies are the main responders at first and continue for a few months.^[5] Hepatitis A and E outbreaks and isolated cases have been documented globally; there is a clear correlation shown in areas with contaminated water supplies, poor sanitation, unhygienic living conditions, restricted access to medical care, and low levels of health literacy.^[6] In India, particularly in regions like Punjab, where rapid urbanization, population density, and socioeconomic disparities prevail, the prevalence of HEV and HAV infections remains noteworthy. Factors such as inadequate access to clean water, improper waste management systems, and overcrowded living conditions contribute to the heightened risk of viral hepatitis transmission.

This study aims to determine the prevalence of HAV and HEV. This research will contribute to better risk assessment, management and future prevention of acute liver hepatitis cases. In India, the liver illness associated with hepatitis A is very rare and mostly affects children; while acute viral hepatitis and acute liver failure (ALF) in adults are primarily caused by HEV.^[7]

This suggests that HEV has a major role in liver disease development in India, especially in adult populations. Research on acute viral hepatitis has shown co-infection with both the HEV and HAV viruses at rates ranging from 7% to 24%. There are concerns that this type of co-infection could exacerbate the illness and result in a poor prognosis.^[8]

MATERIALS & METHODS

The six-year retrospective study is based on laboratory records which were carried out from January 2018 to December 2023, at a tertiary care centre located in Punjab, North India to check the prevalence of HAV and HEV infection among patients of different age group suffering with acute viral hepatitis. During this specific timeframe, a total of 3793 individuals with clinically suspected cases of acute viral hepatitis, comprising patients from both the outpatient department (OPD) and the inpatient department (IPD), were included as subjects in the study. The serum samples were analyzed for IgM anti-HAV and IgM anti-HEV using commercially available RDTs (CTK Biotech.), as per manufacturer's instructions.

Inclusion Criteria: Samples with request of both HAV IgM and HEV IgM were included in this study.

Exclusion Criteria: Samples with request of either HAV IgM or HEV IgM were not included in this study.

RESULT

The present study was performed over the period of 6 years from January 2018 to December 2023 in the Malwa region Tertiary Care Centre, Patiala, Punjab. The study was conducted on 3793 individuals with clinically suspected infections presented to the outpatient and in-patient department at Tertiary Care Hospital. There was varied number of cases in each year which has been tested as shown in Table 1. It was observed that maximum numbers of positive cases for HAV were found in year 2019, followed by 2023, 2022 and 2018

while in 2020 and 2021 few cases were found to be positive. Similar trend was seen in HEV positive case, highest number of cases was found in year 2019, followed by 2022, 2018 and 2023. Similarly, few cases were observed in 2020 and 2021. Overall average positivity rate of HAV cases was

found to be 14.5% and HEV positivity rate was observed as 12.5%. Combined positivity rate of HAV and HEV was found to be 27% in the Malwa region of Punjab. Co-infection of HAV and HEV was observed only in year 2018 (5.1%) and 2019 (4.8%).

Table 1: Annual Statistics of HAV and HEV Testing and Co infection Rates at VRDL, GMC Patiala (2018-2023)

HAV and HEV Tests done in VRDL, GMC, Patiala in five years (From: 2018 to 2023)						
YEAR	Total No. of HAV tests	HAV Positive	Total No. of HEV test	HEV Positive	Total positive cases of HAV+HEV	Co infection of HAV and HEV
2018	292	58 (19.9%)	292	40 (13.7%)	98 (33.6%)	5 (5.1%)
2019	484	77 (15.9%)	510	69 (13.5%)	146 (29.4%)	7 (4.8%)
2020	219	14 (6.4%)	216	24 (11.1%)	38 (17.5%)	0
2021	265	11 (4.2%)	251	16 (6.4%)	27 (10.5%)	0
2022	483	65 (13.5%)	273	42 (15.4%)	107 (28.8%)	0
2023	325	75 (23.1%)	183	24 (13.1%)	99 (36.2%)	0
TOTAL	2068	300 (14.5%)	1725	215 (12.5%)	515 (27.0%)	12 (2.3%)

Month wise percentage of positive cases distribution has been shown in Figure 1. In year 2018, it was observed that HAV and HEV positive cases upsurge were established in the month of January, February and June. In the year 2019, highest positive cases were found from the month of April to August for both HAV and HEV. For the year 2020 and 2021 only few cases

were found to be positive in between the whole years. In 2022, difference in the trend of positivity was observed, HAV cases were found to be high during the month of May to August while HEV cases were found to be highest during January to March. In 2023, positivity was highest in the month of October to December.

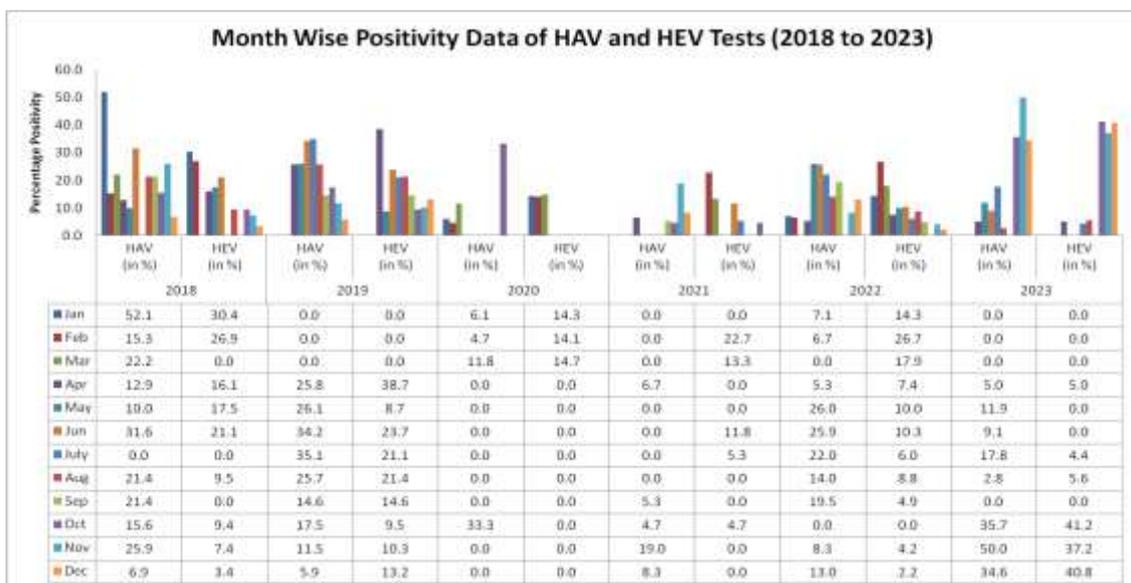


Figure 1: Month-wise distribution of HAV and HEV tests conducted at VRDL, GMC Patiala from January 2018 to December 2023. Each cell shows the percentage of positive tests for HAV and HEV for each month within the respective year. Percentages reflect the proportion of positive results out of the total tests conducted for that month. The data highlights fluctuations in the prevalence of HAV and HEV throughout the year and across different years.

Age Distribution: Age of the patients were divided into different age groups ranging from 0-10 to >50 as shown in Table 2 and Table 3. For HAV highest number of positive cases was observed in the age group of 0-10, 11-20, 21-30 while for HEV

highest number of cases was found in age group of 11-20 and 21-30. Few patients with higher age group were infected with both the virus. Results indicate that young individuals are more prone to HAV/HEV viral infection than elders.

Table 2: Age-wise Distribution of HEV Positive Cases at VRDL, GMC Patiala (2018-2023)

Distribution of HAV positive cases							
Age group (years)	2018	2019	2020	2021	2022	2023	TOTAL
0-10	22	29	2	2	29	15	99
11-20	19	24	5	5	21	25	99
21-30	14	19	2	3	14	20	72
31-40	3	2	2	1	1	7	16
41-50	0	2	2	0	0	5	9
>50	0	1	1	0	0	3	5
Total	58	77	14	11	65	75	300

Table 3: Age-wise Distribution of HEV Positive Cases at VRDL, GMC Patiala (2018-2023)

Distribution of HEV positive cases							
Age group (years)	2018	2019	2020	2021	2022	2023	TOTAL
0-10	2	7	2	0	0	2	13
11-20	13	18	3	3	12	8	57
21-30	12	22	10	6	21	7	78
31-40	6	9	5	5	9	5	39
41-50	6	9	3	1	0	1	20
>50	1	4	1	1	0	1	8
Total	40	69	24	16	42	24	215

Among these age groups, HAV infection there were more in males (59.3%) than females (40.7%) whereas HEV infection was found to be more in females as shown

in Table 4 and Figure 2. Co infection was more in males (2018: 3.1% and 2019: 2.7%) than females (2018: 2% and 2019: 2.1%) in year 2018 and 2019 respectively.

Table 4: Gender Distribution of HAV and HEV Positive Cases and Co-infections at VRDL, GMC Patiala (2018-2023)

YEAR	GENDER	HAV	HEV	COINFECTION
2018	M	30.6%	17.3%	3.1%
	F	25.5%	23.5%	2%
2019	M	28.8%	19.2%	2.7%
	F	24%	28.1%	2.1%
2020	M	28.9%	28.9%	0
	F	2.1%	34.2%	0
2021	M	18.5%	25.9%	0
	F	22.2%	33.3%	0
2022	M	38.3%	14%	0
	F	22.4%	25.2%	0
2023	M	49.5%	15.2%	0
	F	26.3%	9.1%	0

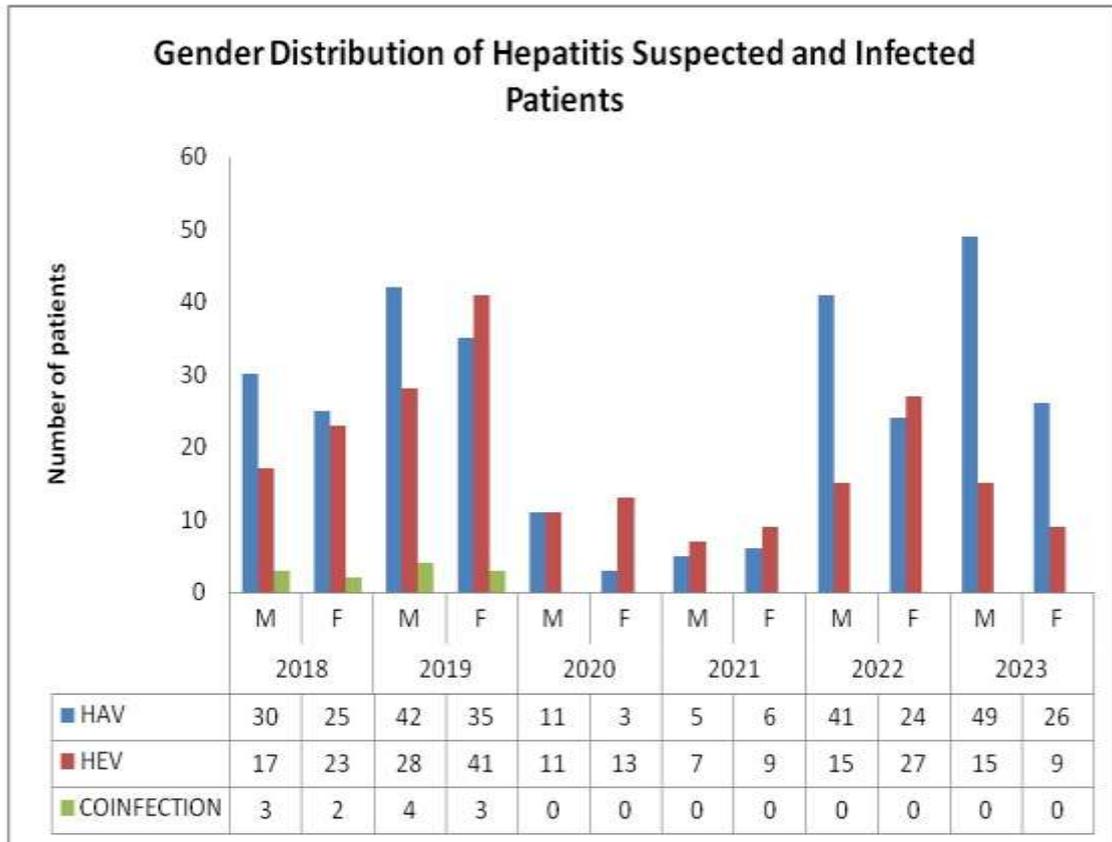


Figure 2: This figure presents the prevalence rates of Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) infections, disaggregated by gender (Male (M) and Female (F)) across the years 2018 to 2023. The data are represented as the percentage of cases out of the total number of infections reported for each gender in each year.

DISCUSSION

Over a span of six years, from January 2018 to December 2023, the study offers a thorough assessment of Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) infections in the Malwa area of Punjab. A significant surge in infection rates as well as the greatest number of positive cases for both HEV and variations in the frequency of viral hepatitis, frequently associated with alterations in public health initiatives, environmental variables, or outbreaks. [9,10]

Many studies which have highlighted the prevalence of HAV and HEV aligns with the present study with prevalence ranging from 12.6% to 78.6% in case of HAV while 1.7% to 67% in case of HEV. [11-14] Co-infection rate was also found to be less in several studies reported. A study conducted in North west Punjab showed the similar trends of prevalence. They found that 68.42% of patients had HEV infection and 2.1% had HAV was recorded. This aligns

with several research investigations that have detected annual and seasonal HAV while 6.31% were coinfected with both HAV and HEV. [13] The co-infection rates of HAV and HEV, observed primarily in 2018 and 2019, are relatively low compared to the overall infection rates. This is consistent with other studies that have documented lower co-infection rates due to the distinct transmission routes and epidemiological patterns of these viruses. [14] The findings suggest that while co-infections can occur, they may be less common and potentially influenced by specific outbreak conditions or individual susceptibility factors. Co-infection of HAV and HEV has been documented but is relatively rare. A study by Shinde et al. (2020) found that co-infection rates were generally low and often confined to specific outbreaks or regions. [15] The co-infection rates observed in the current study are consistent with these findings, suggesting that while co-infection

can occur, it is not the predominant outcome in most cases.

Significant trends and variations in infection rates are shown in the results, with clear changes seen over time and within various demographic groups. Seasonal and annual variations in HAV and HEV infections have been shown in a number of investigations. For instance, a study found that HEV infections are more common during colder seasons, but HAV infections frequently show seasonal peaks, usually in warmer months.^[16]

The observed monthly variation in positivity rates further supports the notion of seasonal patterns. Peaks in HAV cases in 2018 and 2019 were observed during the first half of the year, while HEV cases in 2022 showed a distinct peak during the winter months. Such trends have been previously reported, with HEV infections often showing higher incidence during the colder months.^[17] The resurgence of cases in late 2023, particularly from October to December, may indicate a cyclical pattern or a delayed impact of environmental factors or changes in public health measures.

The COVID-19 pandemic may have had an influence on the dynamics of viral transmission by reducing public gatherings and improving cleanliness, which may have contributed to the comparatively lower number of cases in 2020 and 2021.^[18] Another study revealed a significant decline in viral hepatitis cases during the COVID-19 pandemic due to improved sanitation and reduced social interactions.^[19] These findings align with the observed trends in this study, reinforcing the impact of external factors like pandemics on infection rates.

The study highlights that young individuals (0-30 years) are more susceptible to HAV and HEV infections, with a higher incidence of HAV in the age groups of 0-10, 11-20, and 21-30, and HEV mainly affecting the population with the age range of 11-30 years. This aligns with existing literature which suggests that younger populations are more at risk due to factors such as limited vaccination coverage, lower immune

response, and potentially higher exposure rates in community settings.^[20,21] Consistent with our findings, research by Grover et al. (2024) found that HAV infections predominantly affect younger populations, particularly children and adolescents.^[22] Similarly, a study by Palewar et al. (2022) observed that HEV infections also showed higher prevalence in young adults, which could be attributed to lifestyle and exposure factors.^[23] These results corroborate the higher incidence rates of HAV and HEV in younger age groups as seen in the current study.

In terms of gender distribution, the study found a higher prevalence of HAV infections in males and a predominance of HEV infections in females. Previous research has shown variable gender distribution patterns for viral hepatitis, often influenced by socio-cultural practices, healthcare access, and differing exposure risks.^[24,25] The observed co-infection rates, being higher in males, could be due to differential exposure or health-seeking behaviors between genders. Previous research presents mixed findings on gender differences in hepatitis infections which has reported higher incidence rates of HAV in males, which aligns with the current study.^[26] However, the predominance of HEV in females is less commonly reported. Research noted varying gender distributions for HEV infections, sometimes showing higher rates in pregnant females.^[27] The gender-specific differences in infection rates might reflect variations in exposure risks, healthcare access, or socio-cultural factors.

The findings from the current study align well with previous research, confirming established trends in HAV and HEV infections. The observed seasonal variations, age-specific susceptibilities, and gender differences are consistent with global and regional studies. The impact of the COVID-19 pandemic on infection rates also supports findings from other studies indicating disruptions in typical infection patterns. Further research is necessary to understand the underlying causes of these

trends and to develop targeted public health interventions to manage and prevent viral hepatitis in different demographic groups.

The results of this study emphasize the need for continued surveillance and targeted public health interventions to address the seasonal and demographic variations in HAV and HEV infections. Enhanced vaccination programs, particularly for younger populations and regions with identified peaks, could help in reducing infection rates. Additionally, public awareness campaigns focusing on hygiene practices and safe drinking water could be crucial in preventing future outbreaks.

Additional research is needed to explore the underlying causes of the observed trends, including the impact of environmental changes, healthcare infrastructure, and socio-economic factors. Investigating the genetic diversity of HAV and HEV strains in this region could also provide insights into the patterns of transmission and co-infection dynamics.

CONCLUSION

Hepatitis A and E remain significant causes of acute viral hepatitis in Punjab, with HAV affecting mainly children and HEV young adults. Seasonal peaks during post-monsoon and winter highlight the role of sanitation and water quality. Strengthened surveillance, vaccination, and hygiene measures are vital to reduce their burden.

Declaration by Authors

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