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Original Research Article

Seroprevalence of Hepatitis A and Hepatitis E in Patients Suffering From Acute Viral Hepatitis in a Tertiary Care Hospital of Rajasthan

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Abstract:

Introduction: Viral hepatitis refers to a primary infection and inflammation of the liver by any of the heterogeneous group of hepatitis virus types A, B, C, D and E. The condition can be self-limiting or can progress to fibrosis (scarring), cirrhosis or liver cancer. Viral hepatitis is a cause for major health care burden in India and is now equated as a threat comparable to the "big three" communicable diseases – HIV/AIDS, malaria and tuberculosis. Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are predominantly enterically transmitted pathogens and are responsible to cause both sporadic infections and epidemics of acute viral hepatitis (AVH). Around 400 million people all over the world suffer from chronic hepatitis and the Asia-Pacific region constitutes the epicenter of this epidemic.

Aims & Objectives: This prospective, cross-sectional study will be conducted on all symptomatic patients of acute viral hepatitis attending the tertiary-care hospital in Jhalawar, Rajasthan. The aim of this study is to - 1) determine the occurrence of specific IgM antibodies to HAV and HEV in acute viral hepatitis cases in our institution 2) assess the validity of an algorithm based on liver function test (LFT) for differential diagnosis of acute viral hepatitis in jaundiced patients 3) correlate the results thus obtained from LFT and IgM HAV & HEV to determine the incidence & seroprevalence of HAV & HEV infection.

Study Site: The study was conducted at Viral Research & Diagnostic Laboratory in the Department of Microbiology of S.R.G Hospital & Jhalawar Medical College, Jhalawar, Rajasthan.

Study Duration: The study was carried out for a period of 1 year i.e. November 2018 to November 2019 after approval from the institutional ethical committee.

Study Subjects: After obtaining informed consent, complete clinical and epidemiological history of the all the patients satisfying the inclusion and exclusion criteria were recorded.

Inclusion Criteria: All patients suspected of Acute Viral Hepatitis attending the Outpatient & Inpatient Departments of Medicine, Paediatrics and Obstetrics & Gynaecology were included in this study.

Exclusion Criteria: (1). Patients with Chronic viral hepatitis with underlying with Hepatitis B and Hepatitis C. (2). Non-infective cases of jaundice (physiological, hereditary & acquired haemolytic anaemias, blood transfusion reactionary anemia, obstructive jaundice, alcoholics, drug & toxin reactions, malignancies, as a complication of some primary disease). (3). Non-hepatotropic viral etiological cases of jaundice. (4). Non-viral etiological cases of jaundice. (5). Neonatal cases of jaundice.

Sample Collection: 5-8 ml of venous blood was collected with sterile and aseptic precautions in plain vacutainers which was allowed to clot for around 20 minutes and transported to Viral Research & Diagnostic Laboratory (VRDL) in the Department of Microbiology, where it was centrifuged at for 10 mins, serum was separated and stored at -20*C till analysis. IgM antibodies to HAV & HEV were detected from the serum by the principle of Enzyme Linked Immunosorbent Assay (ELISA) employing commercially available ELISA kit (DIA.PRO, Italy).

Observation & Results: This study was conducted on a total of 267 patients of which 52% (138/267) patients were found to be suffering from Acute Viral Hepatitis either due to HAV or HEV. HAV IgM antibodies were detected in 67 subjects, with an overall seroprevalence rate of 25.09%. HEV antibodies were detected in 81 subjects, with an overall seroprevalence rate of 30.33%. The overall incidence of HEV was found to be higher in the study population as compared to HAV. HAV & HEV co-infection was found to be 3.74%.

Keywords: Hepatitis, HAV, HEV, ELISA, Viral.

Introduction

Viral hepatitis refers to a primary infection and inflammation of the liver by any of the heterogeneous group of hepatitis virus types A, B, C, D and E. 1 These 5 types are of greatest concern because of the burden of illness and death they cause and the potential for outbreaks and epidemic spread. In particular, types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer. Viral hepatitis is a cause for major health care burden in India and is now equated as a threat comparable to the "big three" communicable diseases – HIV/AIDS, malaria and tuberculosis.

Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are predominantly enterically transmitted pathogens and are responsible to cause both sporadic infections and epidemics of acute viral hepatitis (AVH). Around 400 million people all over the world suffer from chronic hepatitis and the Asia-Pacific region constitutes the epicenter of this epidemic. [1] HAV & HAE is typically caused by ingestion of contaminated food or water. Acute infection may occur with limited or no symptoms or may include symptoms such as jaundice (yellowing of the skin and eyes), dark urine, extreme fatigue, nausea, vomiting and abdominal pain.

HAV is a non-enveloped 27-nm, heat-, acid-, and ether-resistant RNA virus in the genus Hepatovirus of the family Picornaviridae. HEV is a non-enveloped, single-stranded positive-sense RNA virus in the genus Hepevirus family Hepeviridae and is the major cause of waterborne hepatitis in tropical and subtropical countries. HEV has at least 4 different types: genotypes 1, 2, 3 and 4. Genotypes 1 and 2 have been found only in humans. Genotypes 3 and 4 circulate in several animals (including pigs, wild boars, and deer) without causing any disease, and occasionally infect humans. Genotype 1 is usually observed in developing countries and causes community-level outbreaks, while Genotype 3 is usually reported in developed countries and does not cause outbreaks.

HAV & HEV infections are usually subclinical or acute and remain self-limited and do not progress to chronic liver disease. They spread via the feco–oral route and are closely associated with poor sanitary and bad hygienic conditions. HAV infections account for 1.4 million new cases per year worldwide, and the risk of infection is inversely proportional to levels of sanitation and personal hygiene.[2] According to the WHO estimates by Havelaar et al., HAV resulted in 13.7 million illnesses and 28000 deaths in 2010. With improved sanitation and provision of HAV vaccination, areas or populations with high HAV endemicity show patterns of declining endemicity.[3] In a study done by Agrawal & Goel in 2015, based on the different age-specific HAV seroprevalence profiles, the world can be divided into countries of high, intermediate, low, and very low HAV endemicity. In countries of high endemicity, most people acquire HAV in their early childhood and are immune to the virus. On the contrary, adults from low endemic areas are first exposed to HAV during travel to or residence in endemic areas, or being engaged in risky behaviors, such as contact with infected persons, being men who have sex with men (MSM) or using illicit drugs.[4]

Fulminant hepatitis due to HEV occurs more during pregnancy, especially during the third trimester, especially with genotype [1]. The mortality rate among pregnant females is high and sometimes can reach 15% - 20%. It is a self-limiting disease and hospitalization is required for patients with fulminant hepatitis and it should also be considered in symptomatic pregnant females.[5]

Although the mechanism of liver injury is not yet clear, it is possible that interplay of hormonal and immunologic changes during pregnancy, along with a high viral load of HEV, renders the woman more vulnerable. Immunologic changes during pregnancy promote the maintenance of the fetus in the maternal environment by suppression of T cell–mediated immunity, rendering pregnant women more susceptible to viral infections like HEV infection.[6]

Serology

Serological testing for the detection of immunoglobulin M (IgM) antibodies to HAV (anti-HAV) & HEV (anti-HEV) is required to confirm the diagnosis. IgM anti-HAV is usually detectable when symptoms appear and concentrations decline to undetectable levels within 6 mo for most patients.

However, cases of patients that test positive for IgM anti-HAV more than 1 year after infection have been reported. Immunoglobulin G (IgG) anti-HAV appears early in the course of the infection and remains detectable throughout the person's lifetime.

Total anti-HAV tests are often used in epidemiological investigations or to detect susceptibility to HAV but they do not identify acute infection. Vaccines, available since the early 1990s, are not yet widely used, therefore most individuals with anti-HAV acquired immunity through infection.[7]

Two serological markers can be used to investigate the presence of past or recent HEV infection. The

first is anti-HEV IgM, which indicates the acute phase, and the second is anti-HEV IgG, which indicates current infection when observed together with anti-HEV IgM detection or past contact when it is detected alone.[8]

Indian Scenario

The last decade has witnessed tremendous change in our understanding of the virus in epidemiology, clinical features, diagnostic modalities, treatment options and the need for vaccination. As the virus continues to perplex clinicians and virologists alike, this review attempts to discuss the nuances in our understanding of this virus, its pathogenesis and diagnosis, especially with reference to the Indian scenario. Viral hepatitis is increasingly being recognized as a public health problem in India. Keeping this in mind the National Viral Hepatitis Surveillance Programme has been initiated by the Government of India. The National Centre for Disease Control is the nodal agency for the implementation of the scheme "The National Programme on Surveillance of Viral Hepatitis". This central sector scheme is an ongoing scheme under the 12th FYP. The Standing Finance Committee (SFC) has approved the continuation of the on-going scheme for the FY 2017-2020. Ten sites have been identified which will be responsible for implementing the program in the initial two years.

Objectives:

- To establish laboratory network for laboratory-based surveillance of viral hepatitis in different Geographical locations of India.
- To ascertain the prevalence of different types of viral hepatitis in different zones of the country.
- To provide laboratory support for outbreak investigation of hepatitis through established network laboratories.
- To develop technical material for generating awareness among healthcare providers and in the community about waterborne and blood borne hepatitis.

Targets:

- Establishment of laboratory-based surveillance for viral hepatitis in the country for collection of data.
- Development of testing and surveillance guidelines and its dissemination.
- A network of laboratories with quality testing for hepatitis markers will be established covering the entire country
- Training of manpower/health care providers in 10 regional labs including NCDC i.e. the reference lab.
- Development of IEC for providers and community.
- Establishment of baseline data for hepatitis to see the impact

In India, the estimated burden of viral hepatitis is very high, necessitating focus on prevention and control measures of hepatitis to mitigate the morbidity and mortality due to hepatitis. As these viruses continue to perplex clinicians and virologists alike, this review attempts to discuss the nuances in our understanding of this virus, its pathogenesis and diagnosis with reference to the Indian scenario.

Due to paucity of data, the exact burden of disease for the country is not established. Data thus obtained from this study will be essential for planning of future vaccination strategies and better sanitation program in this part of the country.

Aims & Objectives

This prospective, cross-sectional study will be conducted on all symptomatic patients of acute viral hepatitis attending the tertiary-care hospital in Jhalawar, Rajasthan. The aim of this study is to -

1) Determine the occurrence of specific IgM antibodies to HAV and HEV in acute viral hepatitis cases in our institution
2) Assess the validity of an algorithm based on liver function test (LFT) for differential diagnosis of acute viral hepatitis in jaundiced patients
3) Correlate the results thus obtained from LFT and IgM HAV & HEV to determine the seroprevalence of HAV & HEV infections

Material and Methods

Study site: The study was conducted at Viral Research & Diagnostic Laboratory in the Department of Microbiology of S.R.G Hospital & Jhalawar Medical College,

Jhalawar, Rajasthan.

Study duration: The study was carried out for a period of 1 year i.e. November 2018 to November 2019 after approval from the institutional ethical committee.

Study subjects: After obtaining informed consent, complete clinical and epidemiological history of the all the patients satisfying the inclusion and exclusion criteria were recorded. The inclusion and exclusion criteria were as follows —

Inclusion criteria: All patients suspected of Acute Viral Hepatitis attending the Outpatient & Inpatient Departments of Medicine, Paediatrics and Obstetrics & Gynaecology were included in this study.

Exclusion criteria:

1. Patients with Chronic viral hepatitis with underlying with Hepatitis B and Hepatitis C
2. Non-infective cases of jaundice (physiological, hereditary & acquired haemolytic anaemias, blood transfusion reactionary anemia, obstructive jaundice, alcoholics, drug & toxin reactions, malignancies, as a complication of some primary disease)
3. Non-hepatotropic viral etiological cases of jaundice
4. Non-viral etiological cases of jaundice
5. Neonatal cases of jaundice

Sample collection:

5-8 ml of venous blood was collected with sterile and aseptic precautions in plain vacutainers which was allowed to clot for around 20 minutes and transported to Viral Research & Diagnostic Laboratory (VRDL) in the Department of Microbiology.

Where it was centrifuged at 4000 rpm for 10 mins, serum was separated and stored at -20*C till analysis. IgM antibodies to HAV & HEV were detected from the serum by the principle of Enzyme Linked Immunosorbent Assay (ELISA) employing commercially available ELISA kit (DIA.PRO, Italy).

Observation & Results

Study Population Characteristics

This study was conducted, after obtaining clearance from institutional ethics committee, on a total of 267 patients comprising of 154 (57.67%) Males & 113 (42.32%) Females within age groups ranging from 3months to 80 years of age. Out of 113 females, 27 (15.04%) cases were pregnant. Out of 267 cases, a total of 102 (38.02%) patients were hospitalised.

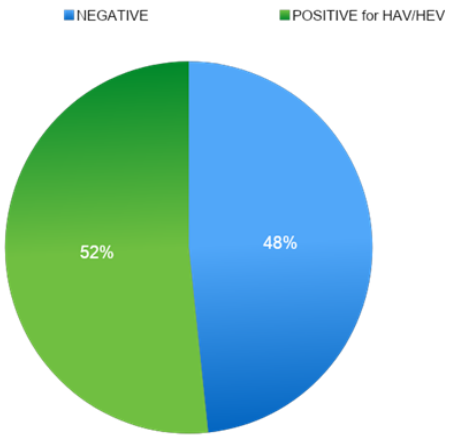

Figure 1: Total Seroprevalence of AVH due to HAV/HEV

In this study, 52% (138/267) patients were found to be suffering from Acute Viral Hepatitis either due to HAV or HEV, which implies that more than 50% burden of AVH comprises of HAV & HEV infection. (Fig 1)

Table 1: Seroprevalence of HAV & HEV -

HAV	21.34% (57/267)
HEV	26.59% (71/267)
HAV + HEV coinfection	3.74% (10/267)
Total Affected Population	51.68% (138/267)

HAV IgM antibodies were detected in 67 subjects, with an overall seroprevalence rate of 25.09%. HEV antibodies were detected in 81 subjects, with an overall seroprevalence rate of 30.33%. The overall incidence of HEV was found to be higher in the study population as compared to HAV. HAV & HEV co infection was found to be 3.74%. [Table 1] (Fig 2)

Table 2: Gender wise distribution of HAV & HEV infected population

Sex	HAV	HEV
Males	**17.53%** (27/154)	**33.11%** (51/154)
Females	**35.39%** (40/113)	**26.54%** (30/113)
Total	67	81

The seropositivity rate of HAV IgM was significantly higher in females **(35.39%)** as compared to males **(17.53%).** Whereas, the seropositivity rate of HEV IgM was found to be higher in males **(33.11%)** as compared to males **(26.54%).** [Table 2] (Figure 3)

Table 3: Gender comparison between HAV infected individuals -

	HAV +ve	HAV -ve	TOTAL
Males	27	127	154
Females	40	73	113
Total	67	200	267

Table 4: Gender comparison between HEV infected individuals - Chi squared equals 10.137 with 1 degrees of freedom

	HEV +ve	HEV -ve	Total
Males	51	103	154
Females	30	83	113
Total	81	186	267

The gender comparison showing females to be more prone to HAV infection than males was found to be statistically significant. (P value equals 0.0015) [Table 3] Gender comparison in HEV infection was however not found to be statistically significant. [Table 4]

Table 5: Age wise distribution of cases in HAV & HEV positive population

Age (years)	HAV +ve	HEV +ve	HAV+HEV
<10	**80.76%** (42/52)	**7.69%** (4/52)	**5.76%** (3/52)
11-20	**36.17%** (17/47)	**27.65%** (13/47)	**6.38%** (3/47)
21-30	**7.35%** (5/68)	**42.64%** (29/68)	**4.41%** (3/68)
31-40	0/39	**46.15%** (18/39)	0/39
41-50	**4.16%** (1/24)	**33.33%** (8/24)	**4.16%** (1/24)
51-60	**5.55%** (1/18)	**27.77%** (5/18)	0/18
>60	**5.26%** (1/19)	**21.05%** (4/19)	0/19
Total	67	81	10

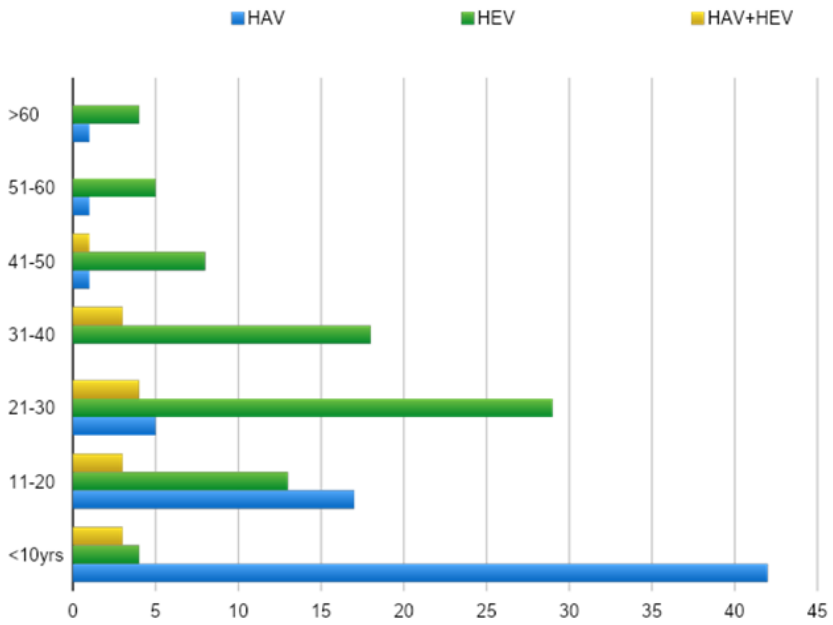

Figure 2: Age wise distribution of cases in HAV & HEV positive population

Table 6: Age wise distribution in HEV infected population

Population	HEV +ve	HEV -ve	TOTAL
Pediatric	11.11% (9)	64	73
Adult	88.88% (72)	122	194
Total	81	186	267

Table 7: Age wise distribution in HAV infected population

Population	HAV +ve	HAV -ve	TOTAL
Pediatric	79.10% (53)	16	69
Adult	20.89% (14)	184	198
Total	67	200	267

Chi squared equals 128.718 with 1 degrees of freedom. The overall prevalence of HAV infection is predominantly higher in the pediatric population as compared to adults and is considered to be extremely statistically significant. (P value is less than 0.0001) [Table 7] Chi squared equals 12.761 with 1 degree of freedom. The two-tailed P value equals 0.0004.

The overall prevalence of HEV infection is predominantly higher in adults as compared to the pediatric population and is considered to be extremely statistically significant. [Table 6]

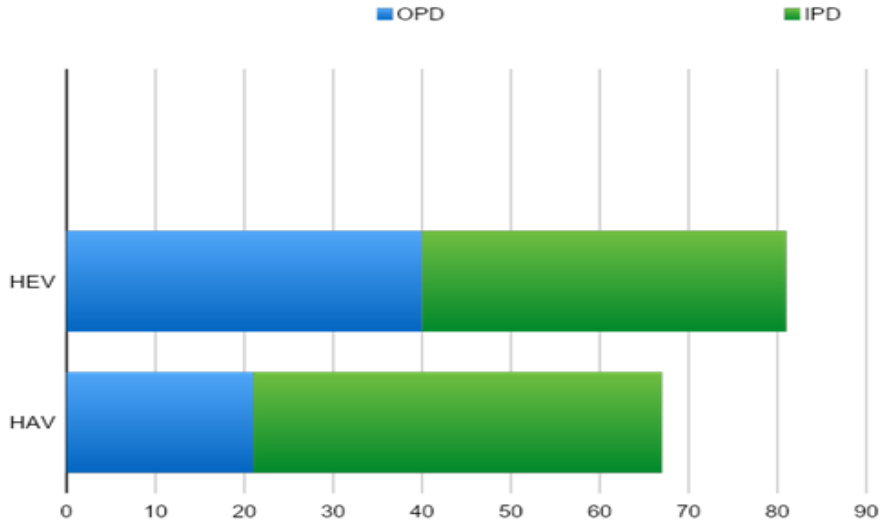

Figure 3: History of admission (OPD/IPD) in HAV & HEV infected population

Chi squared equals 30.629 with 1 degrees of freedom. The rate of hospital admission as in-patient (IPD) was found to be higher in HAV (45.09%) infected individuals as compared to outpatient (OPD) visit and this comparison was found to be statistically significant. (P value is less than 0.0001) (Figure 3)

Chi squared equals 6.855 with 1 degrees of freedom. The rate of hospital admission as in-patient (IPD) seemed to be higher in HEV (40.19%) infected individuals as compared to outpatient (OPD) visit and the comparison was found to be statistically significant. (P value is less than 0.0088) (Figure 3).

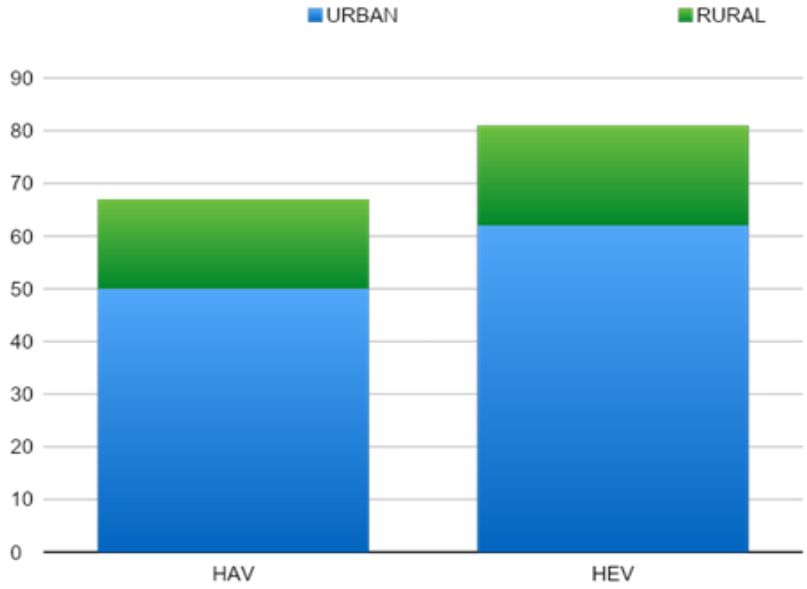

Figure 4: Area wise distribution (Urban/Rural) of HAV & HEV infected population

In this study, the seropositivity rate of HAV and HEV in Urban (25.64% & 31.79%) population was slightly higher than rural areas (23.61% & 26.38%) respectively. However this difference was not found to be statistically significant. (Chi squared equals 0.006 with 1 degrees of freedom. The two-tailed P value equals 0.9378)

In this study, the rate of hospital admission as in-patient (IPD) was found to be higher in HAV (45.09%) infected individuals as compared to outpatient (OPD) visit. The rate of hospital admission as in-patient (IPD) was found to be higher in HEV (40.19%) infected individuals as compared to outpatient (OPD) visit.

However this comparison was not found to be statistically significant. (Chi squared equals 0.006 with 1 degrees of freedom. The two-tailed P value equals 0.9378) (Figure 4)

Table 8: Source of drinking water in HAV & HEV infected population

Source	HAV	HEV
Local Tubewell	**17.69%** (20/113)	**34.51%** (39/113)
Open well	**57.14%** (4/7)	**71.42%** (5/7)
Filtered tap water	0/18	**27.77%** (5/18)
Tap water	**33.33%** (43/129)	**24.80%** (32/129)
TOTAL	67	81

The overall incidence of HAV & HEV infection was found to be considerably higher in people utilising Open Well as the source of drinking water, with HEV (71.42%) infection predominating HAV (57.14%), as compared to Tap water, Local tube well and Filtered tap water. [Table 8]

Table 9: History of Open Defecation in population infected with HAV & HEV

Open Defecation	HAV +ve	HEV +ve
Yes	59.70% (40/67)	64.19% (52/81)
No	43.28% (27/67)	35.80% (29/81)
Total	67	81

Amongst the study population of this study, those patients who openly defecated were more prone to acquire HAV (59.70%) & HEV (64.19%) infection as opposed to those utilising proper sanitation. [Table 9]

Table 10: Month wise distribution of HAV & HEV infected population

Month	HAV	HEV	HAV+HEV	Total
November	9.52% (2/21)	19.04% (4/21)	14.28% (3/21)	42.85% (9/21)
December	0/27	29.62% (8/27)	7.40% (2/27)	37.03% (10/27)
January	0/19	57.89% (11/19)	0/19	57.89% (11/19)
February	0/9	55.55% (5/9)	11.11% (1/9)	66.66% (6/9)
March	12.50% (1/8)	37.50% (3/8)	12.50% (1/8)	62.50% (5/8)
April	7.69% (1/13)	38.46% (5/13)	0/13	46.15% (6/13)
May	19.14% (9/47)	23.40% (11/47)	2.12% (1/47)	44.68% (21/47)
June	33.33% (11/33)	18.18% (6/33)	3.03% (1/33)	54.54% (18/33)
July	23.80% (5/21)	28.57% (6/21)	0/21	52.38% (11/21)
August	25% (6/24)	12.5% (3/24)	0/24	37.5% (9/24)
September	58.33% (14/24)	20.83% (5/24)	0/24	79.16% (19/24)
October	38.09% (8/21)	19.04% (4/21)	4.76% (1/21)	61.90% (13/21)
Total	67	81	10	158

According to this study, HAV and HEV were seen to be prevalent all around the year with predominance seen towards the end of monsoons and beginning of winters and more so even the co-infection showed a similar seasonal trend. A peak in HEV was also noted in the beginning of rainy season. [Table 10]

Table 11: Clinical manifestations of HAV & HEV positive patients

	HAV	HEV
Duration of illness		
<7d	71.64% (48/67)	90.12% (73/81)
>7d	28.35% (19/67)	9.87% (8/81)
Fever	62.68% (42/67)	62.96% (51/81)
Nausea/vomiting	85.07% (57/67)	85.19% (69/81)
Loss of appetite	82.08% (55/67)	75.30% (61/81)
Jaundice	94.02% (63/67)	92.59% (75/81)

Dark Urine	79.10% (53/67)	62.96% (51/81)
Abdominal Pain	25.37% (17/67)	18.51% (15/81)
Hepatomegaly	16.41% (11/67)	11.11% (9/81)

Table 12: Liver Function tests of HAV & HEV positive patients

Liver Function Tests	HAV +ve	HEV +ve
AST/ALT >1 <1	 **79.10%** (53/67) **20.89%** (14/67)	 **67.90%** (59/81) **27.16%** (22/81)
Elevated Bilirubin	**100%** (67/67)	**100%** (81/81)
Mean Bilirubin	45.79	41.06
Elevated ALP	**70.14%** (47/67)	**71.60%** (58/81)

Clinical characteristics of individuals infected with either HAV or HEV had deranged liver function tests with elevated transaminases, bilirubin & ALP levels. [Table 11]

The mean bilirubin of HAV infected patients were 45.79 IU/L , whereas those infected with HEV had their mean bilirubin around 41.06 IU/L. [Table 12]

Discussion

In the present study, 52% (138/267) patients were found to be suffering from Acute Viral Hepatitis either due to HAV or HEV. In 2016, a study done by Agrawal et al. on 475 samples, 181 samples were positive for HAV and/or HEV infection with an overall prevalence of 38.1%, which was comparatively lower than our study.9 However in 2014, a population based cross-sectional study conducted by Vitral et al., 359 out of 397 cases were found to be infected with HAV/HEV with an overall seropositivity rate of 90.42% which is higher when compared to our study.[10]

In this study, HAV IgM antibodies were detected in 67 subjects, with an overall seroprevalence rate of 25.09% and HEV antibodies were detected in 81 subjects, with an overall seroprevalence rate of 30.33%. When compared with a study done in 2018 by Netra et al., out of a total of 1751 serum samples, 908 serum samples were tested for IgM HAV and 843 serum samples were tested for IgM HEV. Of these 908 suspected HAV cases, IgM antibodies were detected in 73 (8.03%) serum samples. Among 843 suspected HEV cases, 185 (21.94%) serum samples were positive for IgM antibodies, which is comparatively lower than our study finding.[11]

The rate of co-infection in present study was found to be 3.74% which is in accordance with a recent study done in 2019 by Samaddar et al., [12] with a co-infection rate of 2.07% and is much lower than the study conducted in 2018 by Netra et al., [11] depicting HAV & HEV co-infection rate of 11.5%.

In this study, the overall prevalence of HAV infection was predominantly higher in pediatric population 79.10% (53/67) as compared to adults 20.89% (14/67) whereas the overall prevalence of HEV infection was predominantly higher in adults 88.88% (72/81) as compared to pediatric population 11.11% (9/81). Probability of lower HEV infection rates in children may be due to: (1) Anicteric HEV infections, therefore, children can go unnoticed.[2] (2) Subclinical HEV infections in the endemic area make children more immune and adult more vulnerable for HEV infection.[13,14] That justifies the preponderance of HEV infection in its respective age group that is in older children and young adults still remain the same.

Community- based studies revealed that among schoolchildren; by the age of 5 years nearly 80% of children were found with anti-HAV antibodies and by the age of 16 years nearly all children had protective anti- HAV antibodies. Findings by Kamal et al. in 2010 13 and Pelosi et al. in 2008 14 also agree with the results found in this study.

In the present study, considering the source of drinking water of the cases included in our study, the overall incidence of HAV & HEV infection was found to be considerably higher in people utilizing Open Well as the source of drinking water, with HEV (71.42%) infection predominating HAV (57.14%), as compared to Tap water, Local tube well and Filtered tap water. In a population based cross-sectional study conducted by Vitral et al in 2014, the source of water utilized by their study subjects were either open well or river stream, amongst which only 308/379 subjects utilized filtered water as their source of drinking water out of which 83.40% were positive for HAV IgM and out of 302 subjects utilizing filtered water as their source of drinking water, 13.20% were positive for HEV IgM.[10] Also, in 2013, Kumar et al., in a study conducted in Punjab found that persons with jaundice were more likely to report foul-smelling piped water (adjusted odds ratio [AOR], 4.0, 95% confidence interval [CI], 2.2–7.2) and used piped water for drinking (AOR, 5.1; 95% CI, 2.2–11.4) than persons without jaundice. Among 14 cases tested, all had anti-hepatitis E virus IgM, and none had anti-hepatitis A virus IgM. Additionally, 21/23 tap water samples from affected households had detectable fecal coliforms. An environmental investigation found that water pipelines were

damaged during sewer construction and likely led to contamination of drinking water with hepatitis E virus.[15] Coming to the comparison between Urban & Rural areas, the seropositivity rate of HAV and HEV in Urban (25.64% & 31.79%) population was slightly higher than rural areas (23.61% & 26.38%) areas respectively. In 2018, a study done by Netra et al.[11], there was no significant difference in occurrence of HAV & HEV among rural (48% & 51.90%) and urban (52% & 48.10%) area, while according to viral hepatitis surveillance- India (2011– 2013) two-thirds of outbreaks were reported from rural areas (Kumar et al., 2015).[11]

According to this study, HAV and HEV were seen to be prevalent all around the year with predominance seen towards the end of monsoons and beginning of winters and more so even the co-infection showed a similar seasonal trend. A peak in HEV was also noted at the beginning of the rainy season. This seasonal variation in transmission of acute viral hepatitis might be probably due to mixing of contaminated soil into wells, rivers and other common sources of drinking water during periods of heavy rains or floods. In a very recent study conducted by Samaddar et al. in 2019, HAV and HEV infections were prevalent all-round the year with maximum number of cases seen from May to September, that is, during summer and rainy seasons.[12] Also in 2018, a study done by Netra et al., maximum positive cases of HAV and HEV were found in from month April to September as summer and rainy season.[11] In the present study, the clinical characteristics of people affected with HAV & HEV were evaluated under the following parameters, such as, duration of illness, fever, nausea & vomiting, loss of appetite, jaundice, dark urine, abdominal pain & hepatomegaly. Studies conducted by Kamaal et al., Vitral et al., & Radhakrishnan et al. also showed similar observations.[13,10,17]

In this study, individuals infected with either HAV & HEV had deranged liver function tests with elevated transaminases (79.10% & 67.90%), bilirubin & ALP (70.14% & 71.60%) levels. The mean bilirubin of HAV infected patients were 45.79 IU/L, whereas those infected with HEV had their mean bilirubin around 41.06 IU/L. In a recent study done by Samaddar et al. in 2019, the total serum bilirubin (normal range: 0.2–1.2 mg/dL), AST (normal range: 10–40 U/L), ALT (normal range: 7–56 U/L) and ALP (normal range: 20–140 IU/L) levels were raised in 68.1%, 61.7%, 59.6% and 74.5% of the HAV-positive patients and in 78.5%, 72.3%, 61.5% and 70.8% of the HEV-positive patients, respectively. In HAV-HEV co-infection, it was observed that ALP level was raised in all patients while total bilirubin, AST and ALT levels were raised in 85.7%, 64.3% and 85.7% cases, respectively. Three patients with co-infection had very high levels of liver enzymes (AST and ALT >2000 IU/L). This suggests that dual infection with HAV and HEV can lead to severe disease manifestations such as acute liver failure and hepatic encephalopathy.[12] Netra et al. in a recent study in 2018 found that, IgM HAV positive patients elevated levels of AST (aspartate aminotransferase), ALT (alanine aminotransferase), ALP (alkaline phosphatase) and GGT (gamma-glutamyl transpeptidase) was seen in 71.23%, 79.45%, 84.93% and 75.34% cases respectively, while among IgM HEV positive patients it was found in 89.72%, 77.29%, 82.16% and 74.59% cases respectively.[11]

Conclusion

Even though the therapeutic options are limited in HAV and HEV infections, emphasis on regular testing of HAV and HEV in patients of AVH on a routine basis is required, especially for the management of severe infections in HAV-HEV coinfections, high-risk groups like pregnant females, chronic liver diseases, and immunosuppressed patients. With a feco-oral route of transmission, periodic surveillance, especially in monsoon and post-monsoon, is of utmost importance for early diagnosis and curtailment of outbreaks and epidemics by the public health sectors through proper sanitization, hygiene, and public awareness.

As these viruses continue to perplex clinicians and virologists alike, this review attempts to discuss the nuances in our understanding of this virus, its pathogenesis and diagnosis with reference to the Indian scenario. Also, the knowledge of the strength and limitations of ELISA will allow the rational use and interpretation of results and it will be of immense help in arriving at a probable diagnosis of Acute Viral Hepatitis. Data thus obtained from this study will be essential for planning of future vaccination strategies and better sanitation programs in this part of the country.

The **'National Viral Hepatitis Control Program'** launched on 28th July 2018 on the occasion of World Hepatitis Day by the Ministry of Health & Family Welfare (GOI) aims to achieve significant reduction in the infected population, morbidity, mortality associated with Hepatitis A, B, C, D, and E and achieve countrywide elimination of Hepatitis C by 2030.

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