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Seropositivity of HAV and HEV among Febrile Hepatitis Cases at a Tertiary Care Hospital.

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Abstract:
Background: *Enterically transmitted Hepatitis A virus (HAV) and Heptitis E virus (HEV) can cause acute liver disease both sporadically and in epidemics in developing countries. Cases are not clinically distinguishable and specific diagnosis can be made by detection of serum IgM antibodies of HAV and HEV.**Aim:**The present study was undertaken to know the incidence of HAV and HEV seropositivity in acute hepatitis cases attending tertiary care hospital, Hyderabad during June 2018 to May 2019 after obtaining institutional ethical committee approval.*
Material & Methods: *A total of 150 serum samples from 133 provisionally diagnosed acute hepatitis cases and 17 healthy persons were collected after taking informed consent and tested for IgM antibodies of HAV and HEV by ELISA method and screened for HBsAg by immunochromatography. The results of liver function tests were noted.*
Results: *Among 133febrile hepatitis samples 21 (15.79%) were HAV IgM positive, 22 (16.54%) were HEV IgM positive while both HAV & HEV IgM positivity was observed in 9 (6.76%)samples. Male: female ratio of 1.7:1 was observed.Commonest age groups affected were 11-20 years and 21 – 30 yearswith 13.5% each followed by 6% in 31 – 40 years.Samples of 17 healthy persons were negative for both HAV IgM & HEV IgM. Serum bilirubin levels of 3-6mg/dL was seen in 33 (25%) cases while >6 mg/dL was seen in 39 (29.6%) cases.*
Studying local incidence of HAV & HEV among acute febrile hepatitis cases helps in improving the preventive measures such as safe water supply, sanitation as well as vaccination.
Key words: *Hepatitis, seropositivity, IgM antibodies, sporadic, serum bilirubin.*

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I. Introduction

Hepatitis A virus and hepatitis E virus cause acute self -limiting infection that may vary in severity from inapparent to fulminant hepatitisand is indistinguishable clinically without serological testing. Co-infection with two or more viruses may lead to serious complications and increased mortality.Both HAV and HEV are water borne pathogens transmitted by feco-oral route. Incubation period of HAV is 14 – 28 days while mean incubation period of HEV is 6 weeks [1,2]. Typical signs and symptoms of hepatitis include mild fever, reduced appetite, nausea, vomiting lasting for few days, jaundice (yellow discoloration of skin and sclera)with dark urine and pale stools and slightly enlarged liver [3].

HAV is single stranded positive sense RNA virus belonging to Picornaviridae family. It persists in the environment and can withstand food production processes that are used routinelyto inactivate or control bacterial pathogens. In developing countries with poor sanitary conditions and hygiene practicesmost children get infected with HAV before the age of 10 years. In developed countries with good sanitary & hygienic practices infection rates are low. [2,4]

HEV was first recognized in 1978 during an epidemic in Kashmir valley, Northern India with 52,000 cases of hepatitis resulting in 17,000 deaths [1]. HEV is a single stranded positive sense RNA virus with 4 human genotypes of which 1 & 2 exclusively infect humans and can lead to endemic HEV or outbreaks in countries with poor sanitation system. Genotypes 3 & 4 can infect humans along with animals and can result in sporadic infection [5]. HEV infection during pregnancy is characterized by more severe infection that sometimes results in fulminant hepatitis and increase in maternal and fetal mortality (approximately 20%).Recombinant HEV proteins production led to the development of serologic diagnostic tests. Chronic HEV infection with genotype 3 or 4 was reported in immunosuppressed people [5,6].

Definitive diagnosis of HAV or HEV infection is usually based on detection of specific IgM antibodies to the virus in the person's blood. Additional tests like Real Time Polymerase Chain Reaction (RT- PCR) to detect virus in blood or stool is needed in cases with chronic HEV infection [6].

World Health Organization (WHO) organizes "World Hepatitis Day" on 28th July every year to increase awareness & understanding of viral hepatitis. With a vision of eliminating viral hepatitis as a public health problem WHO adopted "Sustainable Development Agenda 2030" with global targets of reducing new viral hepatitis infections by 90% and reducing deaths due to viral hepatitis by 65% by the year 2030 [1].

The Aim of the present study is to detectthe HAV and HEV IgM antibodies in febrile jaundicecases attending tertiarycare hospital, Hyderabadand to determine the age specific seropositivity rates of HAV and HEV.

II. Material and Methods

Serum samples were collected from 133 persons suffering with fever, jaundice and provisionally diagnosed as acute hepatitis after taking informed consent during June 2018 to May 2019. Serum samples were also collected from 17 healthy persons without any present complaints. Patient details including age, gender, history of present illness, past illness and family history were noted. Results of liver function tests were also noted. All the 150 serum samples were tested for HBsAg by immunochromatography method and for IgM antibodies of HAV & HEV by ELISA method using HEPAVASE MA-96, GB Corp (IgM capture immunoassay) and HEV IgM ELISA 3.0, MP diagnostics (indirect immunoassay) kits respectively following the manufacturer's guidelines.

III. Results

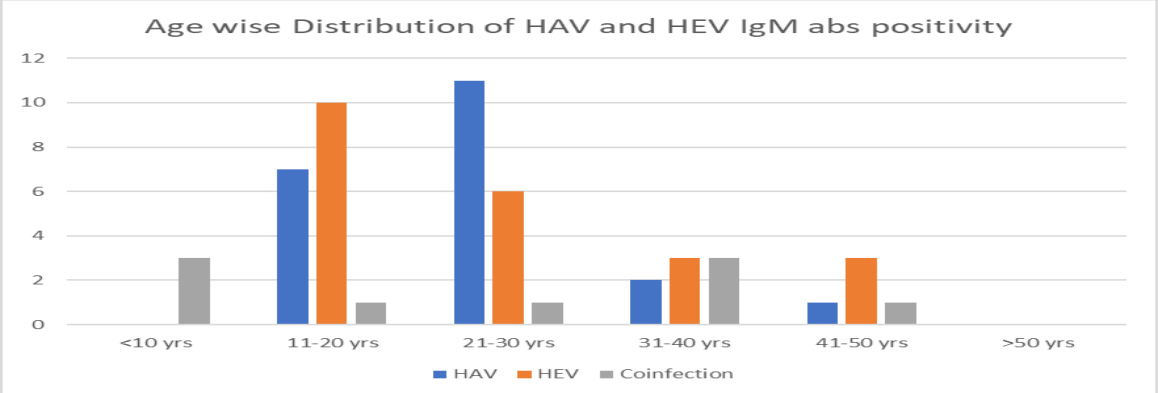
The 150 serum samples include 133from acute hepatitis cases and 17 from healthy persons. Among 133 hepatitis cases 84 were male and 49were female with male: female ratio of 1.7: 1.Of all the133samples one sample from 31 – 40 yearsage group was positive for HBsAg.HAV IgM Abs were positive in 21 (15.79%) samples and 22(16.54%) were positive for HEV IgM Abs, whereas 9(6.76%) were positive for both antibodies(Table: 1).

Table No: 1 Distribution of HAV & HEV IgM abs in febrile hepatitis samples (n=133).

Age group in years	M	F	HAV IgM Abs			HEV IgM Abs			Both HAV & HEV		
			M	F	Total	M	F	Total	M	F	Total
< 10 yrs	1	2	--	--	--	--	--	--	1	2	3
11 – 20	24	10	6	1	7	6	4	10	1	--	1
21 – 30	27	24	9	2	11	1	5	6	1	--	1
31 – 40	16	8	2	-	2	2	1	3	2	1	3
41 – 50	12	5	1	-	1	1	2	3	1	--	1
> 50 yrs	4	--	--	--	--	--	--	--	--	--	--
Total	84	49	18	3	21	10	12	22	6	3	9

Maximum number of HAV positivity was in the age group of 21 – 30 yrs(8.27%) followed by 11 – 20 yrs(5.26%). For HEV positivity most affected age group was 11 – 20 yrs (7.5%) followed by 21 – 30 yrs, (4.5%). Samples from less than 10 yrs age group were 3 and all of them were positive for both HAV & HEV IgM Abs. Samples from>50 yrs agewere negative for HAV & HEV(Fig:1).All the 17 healthy controls were negative for HBsAg, HAV IgM Abs and HEV IgM Abs. Serum bilirubin levels of 133 samples ranged from 2.2 to 12 mg/dL. Serum Bilirubin level of <3mg / dL was seen in 61 (45.4%) samples, whereas>3 to 6 mg / dL in 33 (25%) and >6 mg / dL in 39 (29.6%) samples.

Fig:1 Age wise distribution of HAV & HEV IgM abs in febrile hepatitis samples (n=133).



IV. Discussion

The epidemiology of HAV is complex, and is shifting in countries that are making improvements to public health and sanitation. In developing countries where sanitary conditions are variable, children often escape infection thus higher susceptibility in older age groups and may lead to outbreaks of HAV disease[7]. Global prevalence rates of antibody to Hepatitis-E virus (anti-HEV) that vary by region, population, and circulating genotypes of HEV with unexpectedly high seropositivity in some developed settings [8,9].Co-infection has emerged as a leading cause of morbidity due to liver diseases throughout the world.

In the present study16.54% were having HEV IgM Abs and 15.79% were having HAV IgM Abs and the co-infection of HAV and HEV was seen in 6.76% samples and similar were reported in study by Joon A et.Al. from Mangalore [10]. The results of various studies were shown in Table. 2.

Table No.2: Seropositivity for IgM antibodies of HAV and HEV among various studies.

S.No.	Study	year of study	HAV IgM Abs	HEV IgM Abs	Both HAV & HEV
1	Joon A, Rao P, Shenoy SM, Baliga S. 2015 [9]	2 years	19.31%	10.54%	11.5%
2	Tripurari Kumar et al. 2015 [10]	2011–2013	7.4%	10.4%	1.3%
3	Prabhat Kiran Khatri et al. 2017 [11]	2016	13.79%	4.02%	1.15%
4	Manoj V. Murhekar et al. 2018 [12]	2014-2017	12.6%	16.1%	1.3%
5	Arghadip Samaddar et al. 2019 [13]	2015-2017	6.96%	9.63%	2.07%
6	Yashik Bansal, et al. 2022 [14]	2011-2018	16.9%	14.9%	1.6%
7	Present Study	2018-2019	15.79%	16.54%	6.76%

In areas with high disease endemicity, symptomatic infection is most common in young adults aged 15 – 40 yrs. Although infection occurs in children, they often have either no symptoms or only mild illness without jaundice. In the present study HAV IgM positivity was high in 21-30 yrs age group (8.27%) whereas HEV IgM positivity was high in 11-20 yrs age group (7.5%). Haesun Yun et. Al. in their study showed high seroprevalence for both HAV & HEV in the age group of 30s [15].

In the present study the samples of 17 non symptomatic persons were negative for IgM antibodies of HAV and HEV. T. Lopes et. Al. determined the prevalence of anti HAV and anti HEV antibodies in blood donors in Western Cape, South Africa as 61% and 26% respectively [16]. Sadaf Asaei et. Al. studied among healthy population in Shiraz, Southern Iran and found total anti HAV and IgM Abs in 66.2% and 0.6% whereas total anti HEV and IgM Abs in 13.4% and 0.9% respectively [17].

V. Conclusion

Seropositivity for HAV and HEV together with co infection was significant in the present study. Continuous surveillance helps in detection of mono infection and co infection and helps in implementing preventive measures like vaccination & hygienic practices to reduce the risk of transmission.

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