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RESEARCH ARTICLE OPEN ACCESS

Co-infection of Hepatitis A and Hepatitis E Viruses among the Acute Viral Hepatitis Cases in Tertiary Care Hospital –A Four Years Retrospective Study

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Abstract

Acute viral hepatitis(AVH) is caused by Hepatitis A (HAV) and Hepatitis E(HEV). It is major health burden in India. Both the viruses HAV and HEV are primarily transmitted via the faeco-oral course. Study was conducted to determine the seroprevalence of HAV, HEV and rate of co-infection in AVH patients attending rural tertiary care centre. A retrospective laboratory record based study was carried out in rural tertiary health care center located in Western Maharashtra. Laboratory and Medical records of suspected acute viral infection patients were analyzed during study. Study period was June 2014 to July 2018. Commercially available ELISA kits of IgM anti-HAV and IgM anti-HEV were used to analyze serum samples of suspected study participants. Tests were carried out as per the manufacturer's instructions. A total of 778 acute viral hepatitis cases were included in the study from July 2014 to July 2018 among which 85/778 (10.9 %) detected positive for HAV and 121/778 (15.6%) detected positive for HEV. Co-infection was identified in 6/778(0.8 %). Jaundice, fever fatigue and hepatomegaly were common clinical presentation in HAV, HEV and confection with both viruses in acute viral hepatitis patients. Study indicated low exposure to HAV in childhood bellow 16 years. Co-infection rate was detected high in 16-25 years age group. Vaccination policy against HAV in adolescent age group needed as there is change epidemiological shift of HAV which has been observed in the current study. These data will helps for planning future vaccination strategies, better implementation sanitation program, and safe water supply in this geographic area.

Keywords: Co-infection, hepatitis A virus, hepatitis E virus, seroprevalence

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INTRODUCTION

Acute viral hepatitis mainly caused by HAV and HEV andis a major problem worldwide[1]. Communicable diseases are the major health burden in our country. Viral hepatitis due to primary Hepatitis viruses is endemic in developing and less developed country[2]. Various studies in different states have been reported cases of viral hepatitis in the country[3].Hepatitis A, B, C and E are the four major hepatotropic viruses causing viral hepatitis. HAV and HEV is a non-enveloped RNA virus of the genus Hepetovirus and family Hepeviridae. Both HAV and HEV are primarily spread via the faeco-oral route. Many studies published earlier revelled HAV exposure is common in kids while HEV common among youth. Both the viruses generally cause self-restricting infections. They may confound as fulminant hepatitis which prompts high casualty particularly noted in pregnant females who contracted HEV contamination especially in the second and third trimester. Co-infection with numerous hepatotropic infections has been accounted in different investigation studies carried in intense viral hepatitis with a rate fluctuating from 7-24%. There has been forecast that this co-infection may build the seriousness of the illness and may have bad prognosis.[4] Outbreaks and sporadic instances of hepatitis A and E detailed all around the world ,however there is firm association connected with hazardous drinking water, insufficient sanitation, poor cleanliness, lack of wellbeing administrations and absence of wellbeing training in asset restricted countries.[5-7]It is difficult to diagnose co-infection clinically and by biochemical analysis, serology and PCR needed to help in timely diagnosis and identification of causative agent .[8-9]This study will help in anticipation of risk and the management of acute liver failure in youngsters and grown-up. This study was planned to know the magnitude of HAV, HEV and co-infection, its clinical profile in patients with intense (Acute) viral hepatitis in this geographical area.

MATERIALS AND METHODS

After a study protocol presentation and endorsement from institutional ethics committee(ref. no. KIMSDU/IEC/06/2018), a retrospective laboratory record based study was conducted in rural tertiary health care center located in Western Maharashtra. The document in laboratory and medical records were reviewed and analyzed to retrieve the Demographic data, Clinical data,and laboratory data. Study period was June 2014 to July 2018. A sum of 778 acute viral hepatitis patients was our study population in a time bound study period. Serum samples included in study were analyzed for IgM anti-HEV for the detection HEV infection and anti -IgM antibody detection for HAV, using commercially available ELISA kits (Recombilisa CTK Biotch,Inc). Tests were carried out as per the manufacturer's instructions.

Clinical Criteria

An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine.

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. Tests requested for other viral markers such as hepatitis B surface antigen and HCV were also excluded.

Statistical Analysis

The data is summarized into numbers and percentages. Association is tested by applying Chi-Square test. The level of significance was 5%.

RESULTS

Our study revealed overall higher prevalence of HEV(15.6%) than that of HAV (10.9%)in suspected cases of Acute Viral hepatitis. The study also revealed significant association between HEV and HAV in Acute Viral Hepatitis (Chi-Square = 4.541, p = 0.0331). Significantly high proportion of positive HEV were negative for HAV

Table 1. Co-relation between HAV, HEV and Co-infection of both (A&E)

	Hepatitis E		
Hepatitis A	Positive (%)	Negative (%)	Total (%)
Positive	6 (0.8)	79 (10.1)	85(10.9)
Negative	115 (14.8)	578 (74.3)	693 (89.1)
Total (%)	121(15.6)	657 (84.4)	778

Table 2. Age specific etiology of acute viral hepatitis

Age in years	Hepatitis A (%) n=85	Hepatitis E (%) n=121	Co-infection (A&E) n=6
0-4	07 (8.2)	0 (0)	0(0)
5-15	15(17.6)	03(2.4)	0(0)
16-25	38(44.5)	47(38.8)	3(50%)
26- 35	09 (10.5)	49 (40.4)	2(33.3)
36-45	07(8.2)	16(13.2)	1(16.0)
46-55	03(3.5)	03(2.4)	0(0)
>55	06(7)	03(2.4)	0(0)

HAV high seroprevalence was noted in 16-25 years age group (44.5%), HEV seroprevalence was observed in 26-35 years age group (40.4%).Co-infection was high in 16-25 years age group. Lowseroprevalence rate was observed in 0-4 year and above 55years age group.

Table 4. Serum alkaline phosphatase in patients with hepatitis

Serum alkaline phosphatase (IU/L)	Hepatitis A n=85	Hepatitis E n=121	Co-infection (A&E)n=6
up to 169	65	66	0
170-180	8	6	1
181 - 540	10	45	5
>540	2	4	0

In co-infection with HAV and HEV serum alkaline phosphatase was high in the range of 181-540 IU/L.

Table 3. Sex distribution of CO- infection, HAV and HEV in patients presenting acute viral hepatitis

Sex	Number positive cases n=6 (%)	Hepatitis A (%) n=85	Hepatitis E (%) n=121
Male	4(66.6)	46(54.1)	75(61.9)
Female	2(33.3)	39(45.8)	46(38.6)
Total	6	85	121

Male population have higher rate of co-infection rate (66.6%) in comparison with females (33.3%).

Table 5. Clinical features

Clinical features	Hepatitis A (n=85)(%)	Hepatitis E n=121(%)	Co-infection (A&E)n=6(%)
Jaundice	85(100)	121(100)	6 (100)
Fever	45(52.9)	96 (79.3)	5 (83.6)
Pruritus	18(21.17)	83 (68.3)	4(66.6)
Fatigue	39(45.8)	89(73.4)	5(83.6)
Pain in abdomen	16(18.8)	32(26.4)	4(66.6)
Nausea/ vomiting	36(42.3)	56(46.2)	3(50)
Hepatomegaly	85(100)	121(100)	6(100)
Splenomegaly	5 (5.8)	8(6.6)	2(33.3)

Common clinical presentation with Jaundice, hepatomegaly (100%) was observed in patients followed by fever (52.9%) fatigue (45.8%) in HAV, HEV and confection with both viruses in acute viral hepatitis study group.

and significantly high proportion of positive HAV were negative for HEV. This resulted in low rate of co-infection, 0.8%, in Acute Viral Hepatitis.

DISCUSSION

Hepatitis A virus (HAV), and hepatitis E virus (HEV) are responsible for sporadic and epidemic forms of acute hepatitis across globe,especially common in developing countries including India. Co-infection with multiple virus in acute hepatitis is not uncommon. HAV is commonly considers as enterically transmitted etiological agent for AVH Worldwide with high seroprevalence. However, our study identified HEV high seroprevalence (15.5%) then that of HAV (10.9%) in suspected acute viral hepatitis patients. Our study results of single virus infectivity with either HAV or HEV are in concordance with different investigations from various locality in the nation, prevalence ranging from 12.6% to 78.6%.[11-13] Arvindkumar et al.[10] (2006) reported high rate of co-infection 24.4 % ,Monika et al.[4] reported low rate of co-infection 5.2% in 2016. Few studies are done in rural health setup, one of them was Gitanjali Sarangi et al.[15] (2019) reported confection rate 2.2% in Odisha Eeastrn India. Co-infection with both HAV and HEV in present study is less (0.8%) as compare Gitanjali Sarangi et al.[15] Reason may be due to low suspicion of co-infection or improved socioeconomic status and improved sanitation in recent years. . This decreased tread in rate of co-infection (HAV & HEV) from 2006 to 2019 may be due to high prevalence of HAV antibody or vaccine against HAV and improved socioeconomic status of community in the country[15].

Table 6. Different studies in India

Author	year	Place	No. AVH cases	Co-infection (%)
Arvind Kumar et al.[10]	2006	Lucknow	122	30(24.6)
Monika Agrawal et al.[11]	2016	New Delhi	475	25(5.2)
Shikha Handa et al.[4]	2018	Dehradun	125	13(10.4)
Gitanjalisarangi et al.[15]	2019	Odisha Eastern India	499	11(2.2)
Present study	2019	Western Maharashtra	778	6(0.8)

Table shows frequency and changing trend of co-infection in different geographical areas in India.

A total of 778 number of acute viral hepatitis cases were included in the study population from July 2014 to July 2018 among which85/778 (10.9 %) positive for HAV and 121/778 (15.5%) positive for HEV. Co-infection was identified in 6/778(0.77 %). HAV high seroprevalence was noted in 16-25 years age group (44.5%), HEV seroprevalence was observed in 26-35 years age group (40.4%). Co-infection was high in 16-25 years age group. Male population have higher rate of co-infection rate (66.6%) in comparison with females (33.3%). Jaundice, fever fatigue and hepatomegaly are common clinical presentation in HAV, HEV and confection with both viruses in acute viral hepatitis.[14]Frequency of co-infection with HAV and HEV varies in differ studies conducted in India. Although it is known that serum alkaline phosphates level increases in acute viral hepatitis, the range is towards higher sides(above 181 IU/L) when patient having co-infection with HAV and HEV.

CONCLUSION

Our study revelled overall higher prevalence of HEV (15.5%) then that of HAV (10.9%)in suspected cases of Acute Viral hepatitis. HAV high seroprevalence was noted in 16-25 years age group (44.5%), this show low exposure to HAV in childhood (bellow 16 years)which result in lack of heard immunity in this age group and susceptible to hepatitis A virus infection . HEV seroprevalence was observed in 26-35 years age group (40.4%). Co-infection was high in 16-25 years age group. There is a need for community based serosurvilance of HAV and HEV among the general population. Also there is need to strengthen the viral diagnosis laboratory at periphery. High clinical suspension in AVH patients especially among pregnant women to reduce morbidity and mortality. Health education to improving levels of personal hygiene. This study observation will help Authority to develop local policy for investigation protocol in AVH patient, also helps in future studies which are aimed to address the outcome issue in AVH patient with single virus infection / mixed viral infection. This data information will be help for planning future vaccination strategies, better implementation sanitation program, and safe water supply in this geographic area of the country.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

RVS is principal investigator of the research project and corresponding author of the research paper. STM, ARS, SRP guided for design the research project and conduction of the work during study period. ADP provided Microsoft excel knowledge and its applications for assessment and data analysis. Dr. SKP contributed for English editing of the manuscript and online submission of the research paper.

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ETHICS STATEMENT

Present study was record based. We did not require any animal experiment for the study, however the study was approved by Institutional Ethics Committee of Krishna Institute Medical sciences "Deemed to be" University Karad.

DATA AVAILABILITY

All datasets generated during this study are included in the manuscript.

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