www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i9.14

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

An Investigation and Management of Outbreak of Hepatitis E in South-Western India

(Original Article)

Authors
R K Singh[1], Vikas Raj[2], Richa Ranjan[3], Rigvardhan[4], Mukul Bajpai[5]
[1]Assistant Professor, Dept of Paediatrics, Command Hospital (CC) Lucknow-226002
[2]Associate Professor, Dept of Medicine, Military Hospital, Ahmednagar, Maharashtra
[3]Assistant Professor, Dept of Pathology, Command Hospital (CC) Lucknow-226002
[4]Associate Professor, Dept of Pathology, Command Hospital (CC) Lucknow-226002
[5]Assistant Professor, Dept of Pathology, Command Hospital, Lucknow-226002
Institution Where Study Was Carried Out: Military Hospital, Ahmednagar
Corresponding Author
Rigvardhan
Associate Professor, Dept of Pathology, Command Hospital (CC) Lucknow (UP) PIN- 226002
Email: *vardhanrig@yahoo.com*

ABSTRACT

Background: *The term viral hepatitis is reserved for infections of liver caused by a group of viruses having a particular affinity for the liver. A study was carried out to determine the etiological diagnosis, clinical profile, and management outcome in an epidemic of viral hepatitis.*

Methods: *Cases of acute viral hepatitis (n=64) admitted in this hospital were included in the study. Controls who were apparently healthy (n=30) were also evaluated to know the incidence of sub clinical infection. Clinical profile, liver function tests and serological tests were utilized for diagnosis. Management was conservative.*

Results: *Of the 64 cases under study 59 (92.1%) were positive for IgM HEV while 03 out of 30 (10%) controls were positive for IgM HEV. Most of the patients presented with anorexia, jaundice, pain abdomen, and deranged liver function tests. Clinical outcomes were satisfactory in all cases with no deaths or any serious complications.*

Conclusion: *Hepatitis E is common cause for outbreak of epidemic in closed community. A methodical and systemic approach along with high index of suspicion leads to early diagnosis and a concerted approach by medical and administrative authorities helps in containing the epidemic and prevention of complications and fatality.*

Keywords: *Viral hepatitis E, Deranged LFT, IgM HEV.*

Introduction

Hepatitis E virus (HEV) is recognized as a common cause of epidemic and sporadic outbreaks of viral hepatitis especially in Asia and Africa [1]. In addition to civilian cases, hepatitis E outbreaks have been documented in military population of Chad [2], Djibouti [3] and Ethiopia [4]. In India [5, 6, 7] similar outbreaks of non-A, non-B enterically transmitted hepatitis have been reported periodically. HEV is enterically transmitted and causes sporadic outbreaks in young adults predominantly and could be fatal in pregnant women.

In the current report we describe an outbreak of non-A, non-B hepatitis that occurred in Dist Ahmednagar in western part of India recently. This was apparently caused by HEV and was seen in a particular dwelling establishment. The cause was found to be a fecal contamination of the drinking water. The main purpose of this was to study the clinical features, laboratory parameters and methodology with investigations done to contain the epidemic.

Materials and Methods

64 adult males were admitted to the hospital with the diagnosis of acute hepatitis, as manifested by fever, anorexia, nausea, vomiting, malaise, dark colored urine and yellow discoloration of eyes (Tab 1). A detailed history was taken from all patients which included date of onset of symptoms, history of movement, history of working as food handler and other relevant history. As the cases were clustered in a single dwelling unit the possibility of hepatitis occurring due to medications, immunization or due to systemic infections involving liver was ruled out. A total of 30 controls were also subjected to the same history, examination and laboratory investigations. Controls were defined as person who were not ill but lived in the same area and consumed drinking water from the same source. Informed consent was taken. A total of approximately 168 individuals lived in the same area as our cases and controls under study. Blood samples were collected from all the patients on the day of admission to the hospital. Serum was separated and preserved in cold chain until it was tested. Liver function tests were performed in all cases. Serum bilirubin, liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured on unhemolysed blood samples using Siemens kits in Siemens Dimension EXL 200 in accordance with principle based on International federation of clinical chemistry. Quality control measures were strictly followed. In selected cases Prothrombin time (PT) was done using Liquiplastin, Tulip Diagnostics, India kit on semi automated coagulation analyser. Sera were screened within 4 days of collection for the hepatotropic viral markers. Serology for IgM antibodies (Ab) to hepatitis A and E was conducted at virology lab by ELISA (EIA gen Anti-HAV and Dia Pro Diagnostics Bioprobes kits, respectively) [8]. Blood samples of 30 controls were also tested similarly. Serum was also tested for hepatitis B antigen (HBV) using Hepacard kit and anti-hepatitis C Ab (Instachk kit), for cases and controls. All the data was recorded and tabulated.

Water samples from 32 sources in and around the suspected area were tested for fecal contamination using a semi quantitative test. The probable number of coliforms was calculated using McCrady's probability method [9]. Out of 32 water samples, 24 had a probable coliform count over 10 in 100 ml. making them highly contaminated for consumption (fig 1). The free chlorine was absent from these water samples. The free chlorine was accessed using orthotoludine method.

As these cases of viral hepatitis were clustered in a short span of time an epidemic was suspected. Considering that the most common cause of a viral hepatitis outbreak is fecal contamination of drinking water, the water lines in an around the suspected dwelling area were systematically searched. They were dug up methodically and at a particular point a leakage from the sewer line, contaminating the potable water was found. The sewer line was subsequently repaired. After these

corrective measures the peak of viral hepatitis cases declined, proving that there was a temporal association between the disease outbreak and fecal contamination of drinking water.

All patients were managed conservatively. Weekly liver function tests were performed and patients were discharged when the serum bilirubin was in the normal range.

Results

The outbreak reported in this study was short-lived; the majority of the cases occurred within one month.

Patients age ranged from 19 to 22 years, median being 20.5 yrs. All cases were male. Signs and symptoms (tab 1) consisted of fever (100%), anorexia (96%), pain abdomen (55%), icterus (100%) and yellow discoloration of urine (100%) (table 1). Hepatomegaly was seen in 70% of cases and splenomegaly in 10% cases. All patients were treated symptomatically and had uneventful recoveries with no deaths. The median duration of symptoms was 11 to 15 days. The hospital stay ranged from 15 to 48 days.

All 64 cases had abnormal liver function tests suggestive of acute hepatitis .The tests were repeated at weekly intervals. Evaluation revealed raised serum bilirubin (Vanden Bergh direct positive), raised AST and ALT in all cases. These tests were also done in controls and were within normal range. The highest valve of serum bilirubin was 26 mg/dl while the lowest was 1.2mg/dl, the average being 4.61mg/dl. The maximum value for serum AST was 1960 IU/lit, the range being 60 to 1960 IU/L. Serum ALT ranged from 88-2240 IU/L. Prothrombin time done in selected cases showed a range of 12 – 18.5 sec (control was 14 sec). The total leucocyte count ranged from3400/cc-12500/cc while the differential count showed lymphocytosis in 18% of cases (n=28). None of 30 controls had abnormal liver function tests (Tab 2).

Out of 64 cases, 59 were positive for IgM antibodies to hepatitis E virus. Out of the controls, 03 were found to be positive for IgM antibodies to HEV. None of the cases or controls were positive for IgM-hepatitis A virus (HAV). One case was found to have a concurrent HBV and one case had hepatitis C infection. None of the controls showed positivity for hepatic C antibody or hepatitis B antigen (Tab 3).

Out of 32 randomly collected samples of water from various taps in and around the affected area during the outbreak, 24 revealed evidence of inadequate chlorination (≤0.1 ppm) and as per the presumptive coliform count, significant presence of coliform organisms.

Water was tested using semi quantitative methods and random sampling. The results were calculated as per McCrady's probability table. Single and double strength MacConkey's water media was used. The tubes were incubated at 37°C for 48hrs and presence of positive reaction (formation of acid and gas) was noted in each of the tubes (fig 1). The samples were graded as excellent (probable coliform count less than 1in 100ml.), satisfactory (probable coliform count 1-3 in 100 ml.), suspicious (probable coliform count 4-10 in 100ml.) and unsatisfactory (probable coliform count greater than 10 in 100ml.)

Table 1. Signs & symptoms of patients

Symptoms	Patients (%)
Fever	100
Anorexia	96
Icterus	100
Yellowish urine	100
Pain abdomen	55
Hepatomegaly	70
Splenomegaly	10

Table 2. Results of lab investigation

S No.	Lab Parameter	Mean value	Range	Normal range
1	S Bilirubin (mg%)	4.61	1.2-26	<1.0mg%
2	SGOT(IU/lit)	1238.2	60-1960	< 40 IU/lit
3	SGPT(IU/lit)	988.1	88-2240	<40 IU/lit
4	Alk Phosphatase(IU/lit)	83.2	29- 144	<180 IU/lit

Table 3. Lab results in cases and controls

Lab parameter	Cases	Controls
Deranged LFT	64 (100%)	-
IgM HepA	-	-
IgM HepE	59 (92%)	03 (10%)
HBsAg	01 (1.56%)	-
Ab HCV	01 (1.56%)	-

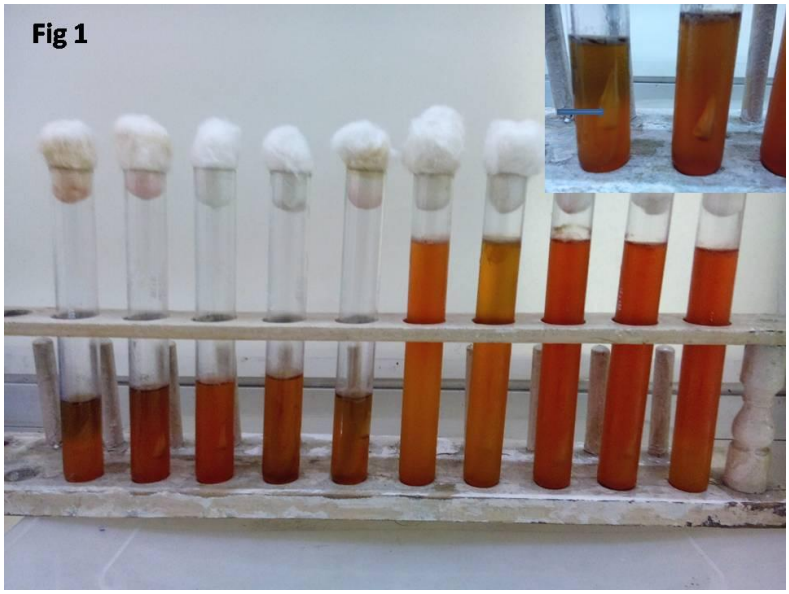

FIGURE 1 Mac Conkey's water media showing unsatisfactory samples with probable coliform count more than 10 in 100 ml with formation of acid and gas (Inset arrow showing gas formation)

Discussion

Contaminated water, as a source of infection, is intimately related to outbreaks of hepatitis due to HEV; which was the cause in this study, similar to several other outbreaks in other places. Cases were clustered around those water supply lines that were found to be crossing the open drains. The clustering of contaminated water sources around the living area of the affected study population led to the outbreak.

A fecal contamination was incriminated as the cause of outbreak of the epidemic in this study, based on the observation that the potable water samples showed significant presence of coliform organisms. Since it is very difficult to isolate actual pathogens like *Salmonella* and *Shigella* species, coliform bacilli are usually selected as an index of pollution, because they are present in large numbers in faeces and have approximately the same survival in water [(9)].

Diagnostic tests with high sensitivity and specificity, such as peptide-based ELISA, have enabled an extensive sero analysis of the epidemic of hepatitis. Analysis of viral markers revealed isolated viral infection in 92.19% cases; co-infection with multiple viruses in 3.12% of patients. The presence of HBV in 1.56% probably reflects sporadic cases in the community. In the

control group 03 out of 30 (10%) showed presence of anti HEV antibody. The 03 cases showing anti HEV Antibodies remained asymptomatic on a 04 week follow up, both subjectively and objectively. Their Serum bilirubin range was 0.6-0.9mg%. Their serum AST and ALT levels were within acceptable limits (< 40IU/L). The age distribution of cases was similar to that described in previous epidemics of hepatitis due to HEV: adults in the age-group of 15-25 years being predominantly affected.

Although HEV and HAV have a common route of transmission, HAV infection was not found in this study as HAV is the predominant form in individuals less than 15 years. Hepatitis due to HAV is considered a childhood disease in developing countries. The case fatality rate was nil in the study possibly because no pregnant females were involved. Prompt hospitalization following the onset of illness and complete rest was important in inducing recovery within a period of 2-6 weeks in the majority of the cases. We did not observe any sequelae suggestive of chronicity.

In our study, dual infection of HEV and HBV was observed in 1.56% of acute hepatitis in adults without any sequelae, while a group of researchers observed dual infection of HEV and HBV in 5.4% of patients of acute hepatitis in adults [(10)]. Tandon *et al.*, have found a higher attack rate of HEV in subjects who are HBsAg carriers [(3)]. However, there is little data available to determine the degree by which HEV infection accelerates or worsens liver damage in people with such chronic hepatitis.

Subclinical infection with HEV in this study was found to be 10% compared to the study by Joe P. Bryan [(1)] which found a subclinical rate of 25%.

Literature on the other hand shows association of HBV and HEV [(9)]. Our results of association of HEV and HBV could be due to two reasons. The population corresponds to mesoendemic zone for HBV; second reason could be attributed to the reactivation of latent HBV due to clinical HEV

Conclusion

HEV is an important cause of acute hepatitis in this part of India. The study revealed many typical epidemiological characteristics of HEV outbreak as reported in the literature. No fatality was reported in the present study. This study found out that around 10% cases of HEV can be subclinical and hence all living around the contaminated source should be screened for HEV infection. This study also emphasizes that preventive measures are most important to prevent such epidemics.

Conflicts of Interest

None identified.

References

1. Bryan JP, Mohammad I et al. Epidemic of hepatitis E in a military unit in Abbottabad, Pakistan. Am. J. Trop. Med. Hyg 2002; 67(6): 662–8.
2. Buisson Y, Coursaget P, Bercion R, Anne D, Debord T, Roue R. Hepatitis E virus infection in soldiers sent to endemic regions. Lancet 1994; 344: 1165–6.
3. Coursaget P, Buisson Y, Enogat N, Bercion R, Baudet JM, Delmaire P, Prigent D, Desrame J. Outbreak of enterically transmitted hepatitis due to hepatitis A and hepatitis E viruses. J Hepatol 1998; 28: 745–50.
4. Tsega E, Krqwczynski T, Hansson BG, Nordenfelt E, Negusse Y, Alemu W, Bahru Y. Outbreak of acute hepatitis E virus infection among military personnel in northern Ethiopia. J Med Virol 1991;34: 232–6.
5. Sarguna P, Rao A, Sudharamana KN. Outbreak of acute viral hepatitis due to hepatitis E virus in Hyderabad. Indian Journal of Medical Microbiology 2007;25: 378-82
6. Mishra B, Srinivasa H, Muralidharan S, Charles S, Macaden RS. Hospital based study of Hepatitis E by serology Department of Microbiology, St. John's

Medical College, Bangalore - 560034, Karnataka, India. Indian J Med Microbiol 2003;21:115-7A.

7. Rao MKK, Nagendra A, Gupta RM, Ohri VC, Raghunath D. An epidemic of hepatitis E in army garrison, Gwalior. Indian J Med Microbiol 1998;14:197-200.
8. Henry JB. Viral infections . Clinical diagnosis and management by laboratory methods. 20th editition, 1065.
9. Laboratory manual of Armed Forces medical services , Vol 2,2009 special techniques , pg 414-415.
10. Tandon BN. Viral hepatitis in tropics and its management. JAMA India - The physicians' Update 2001;4:102-6.