Original Research Article

Hepatitis-E: Clinical profile and outcome assessment from India

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Abstract

Background: Hepatitis E is the most common cause of acute viral hepatitis in the adult population in India. Hepatitis-E has self-limiting clinical course, but can be life threatening in certain high risk groups like pregnancy and alcoholic liver disease. . The present study evaluated the predictors of mortality in patients with acute Hepatitis-E cases at a tertiary care center from India. **Methods:** This cross sectional study including cases of viral Hepatitis E was done at tertiary care hospital at Mysore during January 2016 to November 2016. A total of seventy nine patients diagnosed with HEV infection using IgM anti-HEV enzyme-linked immunosorbent assay (ELISA) kits were included in the study. **Results:** Out of seventy nine, forty two (53.2%) patients were males and thirty seven (46.8%) were females. The mean age of our study group was 44.3±13.47 years. Out of seventy nine Hepatitis E patients, six had coinfection, two with Hepatitis A (2.5%) and four (5.1%) were HBsAg positive. A total of seventy three (92.4%) patients survived while six (7.6%) patients expired during the course of the illness. Among six fatal cases, four (66.7%) died of acute on chronic liver failure and two (33.6%) died of acute liver failure (ALF). **Conclusion:** Pre-existing chronic liver disease was found to be significantly associated with mortality in patients suffering from viral Hepatitis E. Increased bilirubin, Low serum albumin, alcohol use, were also associated with increased mortality due to acute viral hepatitis E. Pregnancy was not a determinant of mortality in Hepatitis-E patients in this study.

Key Words: Acute viral Hepatitis E, Chronic Liver Disease, HEV, ALF, FHF.

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INTRODUCTION

Outbreaks of hepatitis have been documented for centuries, but the first description of epidemic jaundice due to hepatitis was written by Hippocrates.[1] Acute Viral Hepatitis (AVH) is mainly caused by hepatitis A virus (HAV), hepatitis B virus (HBV) and hepatitis E virus (HEV). They can be recognized by serological tests only.[2] Hepatitis E is an significant cause of acute clinical hepatitis in Asian adult population including Indian adults.[2] The disease was first documented as a distinct clinical entity in the 1980s when persons affected during a large water-borne epidemic of viral hepatitis during 1955-56 in Delhi and another epidemic in Kashmir during 1978 were tested negative for serological markers of acute hepatitis A and B. [3] It spreads through fecal contamination of drinking water. HEV infection, a common cause of water-borne epidemics, is endemic and frequently responsible for acute viral hepatitis in developing countries. [4] According to the South-East Asia Regional Office of the World Health Organization (WHO), hepatitis E is widespread in developing countries, accounting for upto 60-70% of all sporadic cases of acute viral hepatitis. [5] Viral hepatitis is a major public health problem in India too, which is hyper endemic for both HAV and HEV. [6] Most reports from India implicate HEV as the major cause, ranging from

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12.6-78.6% in both sporadic and epidemic hepatitis from different parts the country.[7,8] In men and non-pregnant women; the disease is usually self-limited and has a case-fatality rate of < 0.1%. Conversely, in pregnant women, predominantly from certain geographical areas in India, HEV infection is more severe. HEV causes high mortality in pregnant women, 20-30% as compared to 0.2-1% in general population.[9] It has been implicated as an important etiological agent for sporadic fulminant hepatic failure (FHF) in developing countries. [10] Etiology of acute viral hepatitis cannot be distinguished on the basis of mode of presentation alone; confirmation is done serologically. With this background the present study assessed the clinical profile, laboratory profile and outcome of acute viral hepatitis E.

METHODOLOGY

This cross sectional study including cases of acute viral Hepatitis E was conducted at tertiary care hospital in Mysore. The study was conducted from January 2016 to November 2016 during which Out of four hundred sixty samples of patients presenting with history suggestive of viral Hepatitis were analyzed. Seventy nine adult patients had Hepatitis-E infection diagnosed using IgM anti-HEV enzyme-linked immunosorbent assay (ELISA) kits (manufactured under license from ImmunoVision USA) and were included in the study. After obtaining written consent, all patients included in study were interviewed and subjected to clinical and laboratory examination. Detailed history regarding complaints with which the patient presented and any other significant past history including use of alcohol were taken. Clinical examination included general physical examination and systemic examination, with special emphasis on presence of jaundice, blood pressure, presence of organomegaly, ascites, pregnancy and presence of signs of hepatic encephalopathy. Laboratory investigations included complete hemogram, renal and liver function tests. Viral markers for Hepatitis B virus, Hepatitis A Virus, Hepatitis C Virus, Hepatitis E Virus were done by hepatitis B surface antigen (HBsAg), IgM anti-HAV, anti-HCV and IgM anti-HEV antibodies respectively. Symptomatic improvement, patients feeling better, and progressive decline in the level of liver enzymes were considered as criteria for recovery. Final outcome was recorded in the form of recovery or death. A comparison was then made between the patients in these two outcome groups based on their demographic profile, clinical parameters and serum laboratory values. The chronic liver disease (CLD) patients were subdivided on the basis of their Child Pugh score into Class A, B, and C. It is used to assess the prognosis of chronic liver disease. Diagnosis of CLD was made based on ultrasound, upper GI endoscopy and laboratory findings. We defined FHF when there is development of encephalopathy and deranged prothrombin time (PT) by more than four seconds of control. The management of all ALF patients was done in the ICU as per standard guidelines. Data were analyzed using SPSS version 15.0. A $\chi 2$ test was applied to identify statistical significance between various categorical variables. Paired t test was used to compare the difference between mean quantitative parameters at initial and later stage of disease. Similarly, an independent sample t test was used to compare parameters between those patients who died to those who survived. A P value less than 0.05 was considered statistically significant.

RESULTS

Out of Four hundred sixty samples analyzed, 79 (17%) adult patients diagnosed as having Hepatitis-E infection were included in the study. Among them forty two (53.2%) patients were men and thirty seven (46.8%) were women. The mean age was 44.3±13.47 years. The most common symptom was jaundice, found in 82.3% cases, followed by fever (58.2%) and pain in abdomen (38%). Diarrhea and GI bleeding was found in two cases (Table 1). Basic parameters of the study group are presented in Table 2.Table 3 shows characteristics present among study participants. Out of seventy nine Hepatitis E patients, two (2.5%) were Hepatitis A positive, four (5.1%) were HBsAg positive while none had Hepatitis C. Diabetes was more common (22.8%) than hypertension (7.6%) among cases. There were three (3.8%) pregnant patients in this study. A total of seventy three (92.4%) patients were discharged after symptomatic improvement with mean hospital stay of 5.52 days. Six (7.6%) patients succumbed during the course of the illness. No fatality was seen among pregnant women with HEV in the present study. Significant differences were found between total bilirubin and serum albumin values for discharged and expired patients. (p values < 0.05). (Table 4)Out of six patients who died, four (66.7%) died of chronic liver disease and two (33.6%) died of acute liver failure. Out of seven patients with chronic liver disease, three patients were having Child Pugh class B and four were having class C. Among them, three (42.8%) patients survived while four (57.2%) patients succumbed to disease where three were having advanced liver disease (Child Pugh C). Infection with acute Hepatitis E in CLD patients was found to be associated with mortality (p value 0.001) as summarized in table 5.

Table 1: Chief complains of the study cases

Symptoms	Frequency	Percentages
Jaundice	65	82.3
Pain in Abdomen	30	38.0
GI Bleeding	2	2.5
Fever	46	58.2
Vomiting	21	26.6
Diarrhea	2	2.5
Renal impairment	9	11.4

Table 2: Mean value of basic parameters in Hepatitis E patients

Variable	Mean	SD
Age (in years)	44.3	13.47
Hemoglobin (gm/dl)	13.4	2.31
Platelet count (lac/microliter)	2.42	0.95
Total Leukocyte count (per cumm)	9239	4321
S. Creatinine (mg/dl)	1.11	0.91
Hospital Stay (days)	5.52	4.76

Table 3: Patient characteristics

Characteristics	Frequency (n=79)	Percentage
Hepatitis A	2	2.5
Hepatitis B (HBsAg)	4	5.1
Hepatitis C	Nil	Nil
Ascites	3	3.8
Pregnancy	3	3.8
Hepatomegaly	16	20.3
Splenomegaly	8	10.1
Diabetes	18	22.8
Hypertension	6	7.6
Chronic Liver Disease(CLD)	7	8.8
Acute Liver Failure (ALF)	2	2.5

Table 4: Comparison between recovered and expired patients

Variables	Recovered (n=73) (Mean ± SD)	Expired (n=6) (Mean ± SD)	P value
Age (years)	43.9 ± 13.43	48.8 ± 15.52	0.395
Gender			
Male	42 (57.5%)	4 (66.7%)	0.282
Female	37 (42.5%)	2 (33.3%)	
Hb (mg/dl)	13.5 ± 2.28	11.95 ± 2.53	0.112
PLT (lac/cumm)	2.46 ± 0.96	1.68 ± 0.53	0.111
TLC(per cumm)	8810 ± 3709	14107 ± 7817	0.004
S. Creat (mg/dl)	0.96 ± 0.32	2.53 ± 2.53	< 0.001
T. Bilirubin (mg/dl)			
Initially	10.9 ± 6.81	24.9 ± 5.40	< 0.001
Later	5.4 ± 6.01	15.0 ± 8.90	0.001
Albumin (g/dl)			
Initially	3.6 ± 0.46	2.8 ± 0.40	< 0.001
Later	3.6 ± 0.62	2.4 ± 0.58	< 0.001

Table 5: Chronic liver disease patients

Variables	Recovered (n=3)	Expired (n=4)	p value
Age (years)	41.12 ± 14.51	44.68 ± 15.02	0.765
Chronic liver disease			
Child Pugh A	0	0	0.001
Child Pugh B	2 (66.6%)	1 (25.0%)	
Child Pugh C	1 (33.3%)	3 (75.0%)	
Days Hospitalized	5.26 ± 2.1	11.21 ± 3.5	0.049

DISCUSSION

In the present study, a total of seventy nine adult patients diagnosed as having Hepatitis E infection age ranging from 17 years to 66 years were included in the study. Among them, Forty two (53.2%) patients were males and thirty seven (46.8%) were females showing male preponderance which is in accordance with similar studies done in North India (Punjab)[11] , China[12] , Taiwan[13] , and Bangladesh[14] . However it was found to be 1:1 in an epidemic outbreak in Africa.[15] The mean age of our study group were 44.3±13.47 years with the majority of patients (82.27%) older than 30 years of age, whereas a lower mean age (28.8 years) was seen in a study from North India.[16] Out of 460 samples analyzed total seventy nine adult patients were diagnosed as having Hepatitis-E infection, six patient had co-infection, two (2.5%) had Hepatitis A, four (5.1%) were HBsAg positive while none had Hepatitis C which is comparable to the findings of a study done in Pakistan.[17] All of them recovered, however recovery was delayed in these patients compared to other patients (5.52vs 10.2 days). In a study involving 165 south-east Asian adult patients with Acute viral Hepatitis (from India, Nepal, Pakistan), a specific etiologic diagnosis was made in 122 (74%) patients where acute hepatitis E occurred in 40%, HAV in 18.7%, HBV in 11.5%, HCV 1.2%, and combined infection in 4.2%. No viral etiology could be confirmed in the rest 43 (26%) cases.[18] The finding of a higher mortality in the pregnant population with Hepatitis-E virus is well-documented consistently in the past in various studies through the years. The causes of mortality have been attributed to Fulminant Hepatic Failure and obstetric complications such as hemorrhage. [19, 20] Studies from Karachi, where Hamid SS *et al*[21]. Evaluated the clinical course along with the maternal and fetal outcome in 12 pregnant women who presented with FHF, showed maternal mortality to be at 16.6%. Several previous studies have consistently documented the association between HEV infection during pregnancy and mortality.[22] In contrary to published studies, none of 3 pregnant women included in our study died due to HEV infection, our observations were similar to observation by Harshad *et al*.[23]. Deranged Liver function with increased biluribin and transaminases are consistent finding with the clinical features of HEV infection. [24] Total Protein and Albumin values do not change significantly over the course of disease.In our study, case fatality rate due to HEV infection was found to be 7.6% which is consistent with the finding of the study done in western India (7.0%)[25] whereas it was higher than the finding of study done in North-east India (2.0%).[26] Values of total bilirubin, serum albumin and creatinine for expired patients were significantly altered in comparison to the patients who were survived which was in line with the findings of other studies.[24,10] These laboratory investigations can be used as markers of poor prognosis among HEV patients. In our study, out of six patients who died, four (66.7%) died of acute on chronic liver failure which shows pre-existing chronic liver disease to be significantly associated with mortality in patients suffering from Hepatitis E[29]. The results of our study in the CLD group to be significantly associated with mortality, is consistent with literature. Kumar *et al*[27]compared 107 cirrhotic patients super infected with HEV to 200 (non-cirrhotic) controls. They found HEV infection in cirrhotics to be associated with rapid hepatic decompensation as well as higher mortality, citing HEV positive status to be an independent risk factor for mortality in cirrhotics.I n another study from Nepal[28] . Superinfection with HEV was a significant predictor of morbidity and mortality in patients with chronic liver disease.

CONCLUSION

Pre-existing chronic liver disease was found to be significantly associated with mortality in patients suffering from viral Hepatitis E. Increased bilirubin, Low serum albumin, alcohol use, were also associated with increased mortality due to acute viral hepatitis E. Small number of study population and non-availability of Genotyping are the limitations of our study.

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