



STUDY OF CLINICAL PROFILE, BIOCHEMICAL PROFILE AND OUTCOME IN PATIENTS WITH HEPATITIS E INFECTION

General Medicine

Dr. Anjali G. Rajadhyaksha

Professor and Head of the Unit, Department of General Medicine, Seth G. S Medical College and KEM Hospital Mumbai;400012

Dr. Smit Ghanshyam Ganatra

Senior Resident, Department of General Medicine, Seth G. S Medical College and KEM Hospital Mumbai;400012

Dr. Diksha

Junior Resident, Department of General Medicine, Seth G. S Medical College and KEM

Abhimanyu Bedre* Hospital Mumbai;400012 *Corresponding Author

ABSTRACT

Background: Hepatitis E infection is considered to be the leading cause of fecal-oral infections. Acute icteric hepatitis is the most common form of illness associated with HEV infection. The current study is designed to examine epidemiological, demographic, clinical profile, biochemical parameters and outcomes of HEV-infected patients in the intensive care unit at a tertiary care hospital. **Methodology:** Study was done on 36 patients in age group of more than 12 years, admitted with the confirmed diagnosis of hepatitis E infection based on presence of IgM/IgG, Anti HEV immunoglobulins on Immunoassay. Patients were asked a detailed history including travel history, and food and water intake from outside source and a detailed clinical examination was done. Patient's demographics, examination findings, laboratory parameters, disease related variables and radiology investigations on admission were noted. Patient were followed up till discharge or death. **Results:** Majority of the subjects were females. The mean age of the study subjects was 34.22 ± 14.24 years. Most common symptom among the subjects was Yellowish dis-coloration of sclera (69.44%) followed by nausea and vomiting (55.56%). Most common comorbidity was diabetes (11.11%) followed by hypertension (5.56%). Total protein levels, serum albumin levels, SGOT and SGPT levels as well as alkaline phosphatase levels has significant decline. Most common USG Abdomen finding noted was altered liver echotexture in 77.78% of subjects. 86.11% subjects were discharged, while mortality was 13.89% subjects. Hepatic failure 8.33% was most common cause of death in study subjects, followed by multiorgan dysfunction 2.78% and Respiratory failure 2.78%. Case fatality rate due to HEV infection was 7.6%. Total protein, albumin, BUN, and INR were major risk factors of mortality for HE, which was useful to assess the prognosis of HE. Decreased Albumin and total protein levels on admission was statistically significantly associated with mortality. An increase PT-INR and BUN levels on admission was statistically significantly associated with mortality. **Conclusion:** Majority of the subjects were females of middle age. Most common symptom was Yellowish dis-coloration of sclera. Mortality was observed among 13.89% subjects. Hepatic failure was most common cause of death, followed by multiorgan dysfunction. Case fatality rate due to HEV infection was found to be 7.6%. Total protein, albumin, BUN, and INR were major risk factors of mortality for HE. Decreased Albumin, total protein levels, increase PT-INR and BUN levels on admission were statistically significantly associated with mortality.

KEYWORDS

Clinical profile, Biochemical profile, Hepatitis E infection, Liver function tests, Immunoassay, case fatality Ratio.

INTRODUCTION:

Hepatitis E infection is considered to be the leading cause of fecal-oral infections. Hepatitis E virus (HEV) is a single-stranded RNA virus that contains three open reading frames (ORFs) that combine structural and non-structural proteins⁽¹⁾. A retrospective study in India of acute hepatitis B, originally attributed to hepatitis A virus, suggested a new strain of intestinal hepatitis, later named hepatitis E⁽²⁾. After a member of the research team ingested feces from infected soldiers, he contracted acute hepatitis, and small particles of the virus were detected in his cell by immune electron microscopy. The enzyme immunoassay was also developed to detect antibodies in HEV. The first animal species of HEV, swine HEV, was identified and identified in pigs in the United States⁽³⁾.

In areas of poor sanitation, HEV1 and HEV2 are transmitted through humans through a fecal-oral route, usually through contaminated water. This results in unusual conditions and occasional major outbreaks. HEV is probably the most common cause of acute viral hepatitis in the world⁽⁴⁾. In addition, chronic HEV infections that lead to chronic hepatitis and cirrhosis have been reported in patients who are unable to protect themselves from HEV3-infected infections. The clinical course of HEV infection among pregnant women is known to be very severe and often leads to complete liver failure and mortality up to 20% -25%, especially in those living in developing countries⁽⁵⁾.

The mortality rate was found to be high between the 2nd and 3rd trimester⁽⁶⁾. However, the underlying causes of high mortality during pregnancy are not well understood. Acute icteric hepatitis is the most common form of illness associated with HEV infection. Two stages of the disease have been described: Prodromal phase lasts about 1 to 4 days, characterized by a variable combination of symptoms such as fever, fever, chills, abdominal pain, anorexia, nausea, smoking cessation, vomiting, diarrhea, arthralgias, urticarial rash and asthenia. The current study is designed to examine epidemiological factors

including socioeconomic status, geographical distribution, demographic characteristics such as age and gender and seasonal variability in various cases at delivery, clinical profile of HEV-infected patients, hospitalization in the intensive care unit, a tertiary care hospital, and consequently to link the disease effect with biochemical parameters and the presence of various pre- existing hepatic and metabolic disorders during presentation.

OBJECTIVES:

1. To evaluate the demographic and clinical profile in patients of HEV infection admitted in Medicine ward and Medicine intensive care unit of a tertiary care hospital.
2. To find out presence of various pre-existing hepatic and metabolic disorders at the time of presentation.
3. To correlate outcome of disease with Biochemical parameters of patients at admission.

MATERIALS AND METHODS:

The present observational prospective study was done on 36 patients in Medicine wards & M.I.C.U of a tertiary care hospital. Patients in age group of more than 12 years, admitted with the confirmed diagnosis of hepatitis E infection based on presence of IgM/IgG, Anti HEV immunoglobulins on Immunoassay were included in the study. As Laboratory tests for of IgM/IgG Anti HEV immunoglobulins are not available in institute, hence reports of any ISO 9001 certified lab shall be considered valid. Patients with non-viral causes of hepatitis such as toxic/drug induced, autoimmune hepatitis, Infectious hepatitis except hepatitis E and hepatic steatosis were excluded.

After obtaining permission from institutional ethics committee study was started. Patients or their relatives were asked a detailed history including travel history, and food and water intake from outside source and a detailed clinical examination was done. Patient's demographics like gender and age, history, examination findings, laboratory

parameters, disease related variables such as time since diagnosis, disease duration (time since first symptom) and radiology investigations on admission were noted. Confidentiality of the data & privacy of patient was maintained. Patient were followed up till discharge or death.

Statistical Analysis

Data was analyzed using SPSS version 21. Qualitative data like gender, was presented as frequency and percentage. Quantitative data (like age, creatinine, Bilirubin values) was presented as mean, median, interquartile range and standard deviation. Student T test was used to study association between quantitative variables. Risk factors comparison in mortality and survival group done using univariate analysis. P value < 0.05 was considered statically significant.

RESULTS

Age and gender Distribution of the patients:

In the present study, majority of the subjects were females. The f:M ratio in the current study was 1.25:1. Majority of the study subjects belonged to the age group of 26 to 35 years (36.11%), followed by less than 25 years (33.33%). The mean age of the study subjects was 34.22 ± 14.24 years. 33.33% study subjects were pregnant.

Table 1: Demographic and Clinical Parameters of the study subjects:

Patient Variables		No. of subjects	Percentage
Gender	Female	20	55.56
	Male	16	44.44
Age groups (years)	Less than 25	12	33.33
	26 to 35	13	36.11
	36 to 45	4	11.11
	46 to 55	4	11.11
	More than 55	3	8.33
Pregnant	No	8	22.22
	Yes	12	33.33
	NA	16	44.44
Clinical Presentation	Fever	13	36.11
	Yellowish Discoloration Sclera / Urine	25	69.44
	Malena	3	8.33
	Hematemesis	2	5.56
	Abdominal Pain	11	30.56
	Abdominal Distension	10	27.78
	Edema Feet	8	22.22
	Altered Sensorium	2	5.56
	Anorexia	12	33.33
	Nausea/Vomiting	20	55.56
Comorbidities	Hypertension	2	5.56
	Diabetes	4	11.11
	Blood Transfusion	3	8.33
Water Source	Borewell	3	8.33
	Tap Water	33	91.67
Personal History	Alcohol	10	27.78
	Tobacco	3	8.33
	Smoking	3	8.33
	Travel	2	5.56
	Outside Food	23	63.89

Clinical Presentation:

We observed that fever was reported by 36.11% study subjects, icterus was reported by 69.44% study subjects, malena was reported by 8.33% study subjects, hematemesis was reported by 5.56% study subjects, abdominal pain was reported by 30.56% study subjects, abdominal distension was reported by 27.78% study subjects, edema feet was reported by 22.22% study subjects, altered sensorium was reported by 5.56% study subjects, anorexia was reported by 33.33% study subjects, nausea/vomiting was reported by 55.56% study subjects. Onset of Symptom was 10.86±9.19 months with median of 7.5 months.

Comorbidities

Hypertension was noted among 5.56% study subjects, diabetes was noted among 11.11% study subjects, blood transfusion was given among 8.33% study subjects.

Water Source

Borewell was used among 8.33% subjects, while majority of the subjects used tap water.

Personal History

In the present study we assessed the personal history among the study subjects. We observed that alcohol consumption was observed among 27.78% study subjects, tobacco consumption was observed among 8.33% study subjects, Smoking was observed among 8.33% study subjects, travel was observed among 5.56% study subjects, outside food consumption was observed among 63.89% study subjects.

General Examination

In the present study we assessed the general examination findings among the study subjects. We observed that 8.33% subjects were febrile, pallor was noted among 41.67% study subjects, icterus was noted among 72.22% study subjects, edema was noted among 8.33% study subjects. Mean Pulse, SBP and DBP were 92.28±15.77 per minute, 112.17±10.22 mm of Hg and 74.89±6.31 mm of Hg respectively with median of 90 per minute, 110 mm of Hg and 80 mm of Hg respectively.

Systemic Examination Findings:

Per Abdomen

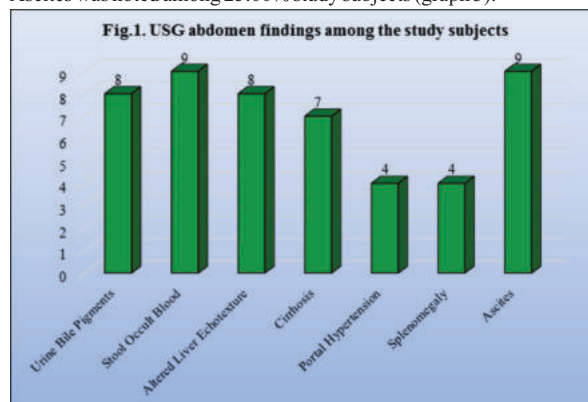
In the present study we assessed the per abdomen findings among the study subjects. We observed that tenderness was recorded among 27.78% study subjects, guarding was recorded among 2.78% study subjects, ascites was recorded among 33.33% study subjects, hepatomegaly was recorded among 8.33% study subjects, splenomegaly was recorded among 5.56% study subjects.

CNS Examination

In the present study we assessed the CNS examination findings among the study subjects. We observed that altered sensorium was noted among 11.11% study subjects, flaps was noted among 8.33% study subjects, hepatic encephalopathy was noted among 13.89% study subjects.

USG Abdomen findings

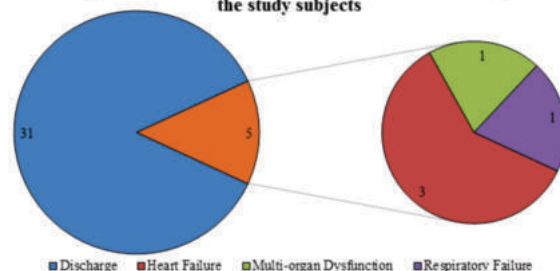
In the present study we assessed the USG abdomen findings among the study subjects. We observed that altered liver echotexture was noted among 77.78% study subjects, cirrhosis was noted among 19.44% study subjects, portal hypertension was noted among 11.11% study subjects, splenomegaly was noted among 11.11% study subjects, Ascites was noted among 25.00% study subjects (graph 3).



Outcomes:

In the present study we assessed the outcomes among the study subjects. We observed that 86.11% study subjects were discharged, while mortality was observed among 13.89% subjects.

Fig 2. Outcomes and Immediate cause of deaths among the study subjects



Immediate Cause Of Death:

In the present study we assessed the immediate cause of death among the study subjects. We observed that hepatic failure was noted among 8.33% study subjects, multiorgan dysfunction was noted among 2.78% study subjects, Respiratory failure was noted among 2.78% study subjects.

Feto-maternal Complications

In the present study we assessed the feto-maternal complications among the study subjects. We observed that IUD was observed among 2.78% subjects' reason for IUD was Preclampsia. We did not observe any maternal death among study subjects.

Comparison of laboratory parameters (on admission Vs on follow up):

In the present study we assessed the hemogram, renal function parameters and liver function parameters among the study subjects on admission as well on outcome. The hemoglobin, Leucocyte counts, Mean platelets counts, BUN and S. Creatinine of both the groups is comparable (all p value >0.05). The mean total Proteins, Mean S. Albumin, Mean SGOT, Mean SPOT levels, Mean Alkaline phosphatase of patients at outcome is significantly lower as compared to on admission. The Total Bilirubin and Mean PT-INR levels of both the groups is comparable

Table 2. Comparison of laboratory parameters (on admission Vs on follow up)

Laboratory parameters	Mean level (On admission)	Mean level (On follow up)	Significance
Hemogram	Hemoglobin (mg/dl)	10.66	0.053
	WBC (per cumm)	11011.47	0.072
	Platelet (Lakhs/cumm)	1.70	0.45
RFT	BUN (mg/dl)	19.92	0.48
	Sr. Creatinine (mg/dl)	1.18	0.48
LFT	Total Protein (GM%)	6.73	0.036
	Albumin (GM%)	3.32	0.0012
	T Bilirubin (MG%)	10.76	0.098
	D Bilirubin (MG%)	7.22	0.16
	SGOT(U/L)	742.46	0.011
	SGPT(U/L)	624.71	0.012
	Alk. Phosphatase (U/L)	181.28	0.034
	PT-INR	1.56	0.48

Table 3. Comparison of biochemical parameters between the deceased group and the survival groups by univariate analysis.

Parameters	Mean Values (Survivors at admission)	Mean Values (Deceased at admission)	P Value
BUN (mg/dl)	15.71	46	0.015
S. Creatinine (mg/dl)	1.15	1.32	0.192
Total Protein (gm%)	6.81	6.18	0.023
Albumin (gm%)	3.38	2.94	0.042
T Bilirubin mg%)	9.97	15.6	0.119
D Bilirubin (mg%)	6.57	11.208	0.388
SGOT(U/L)	776.17	533.4	0.065
SGPT(U/L)	614.46	688.2	0.054
Alk. Phosphatase(U/L)	188.29	137.8	0.051
INR	1.46	2.152	0.01

Table 3 shows comparison of mean biochemical parameters in survivors and deceased at admission and their association with mortality among patients with HEV by. Increased BUN, Decreased S. Total protein, Decreased S. Albumin levels and increased PT-INR at admission is major risk factor for mortality in HEV patients, S. Creatinine, S. T. Bilirubin, S. D. Bilirubin, S. SGPT, Alk. Phosphatase levels are comparable in both Groups.

DISCUSSION

The present study was conducted to assess the clinical profile in patients of HEV infection admitted in Medicine ward and Medicine intensive care unit of a tertiary care hospital, to study various epidemiological factors including socioeconomic status, geographical distribution, demographic factors like age and Gender and seasonal variation of various cases at presentation. To correlate various Biochemical parameters with outcome of disease. And hence to correlate outcome of disease with presence of various pre-existing

hepatic and metabolic disorders at the time of presentation.

Demographic Characteristics

In the present study we observed that majority of the subjects were females. The f:M ratio in the current study was 1.25:1. Majority of the study subjects belonged to the age group of 26 to 35 years (36.11%), followed by less than 25 years (33.33%). The mean age of the study subjects was 34.22 ± 14.24 years. **Aradya VH et al⁽⁶⁾** in their study observed that the mean age of the study subjects was 44.3 years. 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), China, Taiwan, and Bangladesh. **Behera AK et al⁽⁷⁾** in their study observed that twenty-three adult male patients were included in this study with mean age of 32.86 ± 13.34 (range, 18-60 years).

Clinical Presentation

We observed that fever was reported by 36.11% study subjects, YDS/YDU was reported by 69.44% study subjects, melena was reported by 8.33% study subjects, abdominal pain was reported by 30.56% study subjects, abdominal distension was reported by 27.78% study subjects, anorexia was reported by 33.33% study subjects, nausea/vomiting was reported by 55.56% study subjects. In the present study we assessed the pregnancy status among the study subjects. We observed that 33.33% study subjects were pregnant. **Venu H Aradya et al⁽⁶⁾** in their study observed that 3.8% subjects were pregnant.

Sunil Kumar Mudgal et al⁽⁸⁾ in their study observed that All patients presented with jaundice and other associated symptoms, which were nausea/vomiting (88%), anorexia (85%) and abdominal pain (49%). Hepatomegaly was found in 30% of cases. Bleeding diathesis, sleep disturbances and altered level of consciousness were present in 16%, 17% and 14% of patients, respectively. **Behera AK et al⁽⁷⁾** in their study observed that The commonest presenting symptom in these patients was yellowish discoloration of eyes and urine accounting in 19 patients followed by fever (8 patients), abdominal pain (5 patients) and vomiting (3 patients).

Comparison of laboratory parameters (on admission Vs on follow up)

In this study we observed that among liver function parameters, total protein levels, serum albumin levels, SGOT and SGPT levels as well as alkaline phosphatase levels has significant decline on follow up examination. **Sunil Kumar Mudgal et al⁽⁸⁾** in their study observed that on presentation serum bilirubin level was elevated in 100% patients with ALT raised in 86%. We found that 34% of patients presented with bilirubin in range of 2.1-10 mg/dl and 43% with ALT in range of 500-1,000. Values started decreasing by 2nd week and laboratory profile of all survivors became normal by 8th week.

Outcomes:

In the present study observed that 86.11% study subjects were discharged, while mortality was observed among 13.89% subjects. **Sunil Kumar Mudgal et al⁽⁸⁾** in their study observed that Hepatic coagulopathy was the commonest complication; documented in 39% of patients. Only one out of the eight patients who had fulminant hepatic failure survived. Overall mortality was 7%, which correlated with the occurrence of complications and was strongly associated with FHF

Immediate cause of death:

We observed that hepatic failure was noted among 8.33% study subjects, multiorgan dysfunction was noted among 2.78% study subjects, Respiratory failure was noted among 2.78% study subjects. 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. Studies from Karachi, where **Hamid SS et al⁽⁹⁾** 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.

In contrary to published studies, none of 12 pregnant women included in our study died due to HEV infection, our observations were similar to observation by **Harshad et al⁽¹⁰⁾**. Deranged Liver function with increased bilirubin and transaminases are consistent finding with the

clinical features of HEV infection. Total Protein and Albumin values did 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%) and it was higher than finding from study in North-east India (2.0%).

Comparison of biochemical parameters between the deceased and the survival groups:

On comparison of mean biochemical parameters in survivors and deceased at admission and their association with mortality among patients with HEV by Univariate analysis showed that Total protein, albumin, BUN, and INR were major risk factors of mortality for HE, which was useful to assess the prognosis of HE. Decreased Albumin and total protein levels on admission was associated with mortality. An increase PT-INR and BUN levels was associated significantly with mortality.

These findings were in accordance with another similar study by **Shujun Zhang et al.⁽¹¹⁾** in which it was observed that BUN, and INR were major risk factors of mortality of HE based on 210 patients in central of China. **Karkala Achutha Sudharshana Murthy et al.⁽¹²⁾** also observed in their study that Higher mean age, duration of hospital stays, PT-INR, total bilirubin, direct bilirubin, blood urea, were associated with higher mortality, whereas lower mean serum albumin was associated with higher mortality. Diabetics had a higher mean duration of hospital stay.

CONCLUSIONS:

Majority of the subjects were females and mean age was 34.22±14.24 years. Most common symptom was Yellowish dis-coloration of sclera (69.44%). 86.11% study subjects were discharged, while mortality was observed among 13.89% subjects. Hepatic failure 8.33% was most common cause of death, followed by multiorgan dysfunction 2.78% and, Respiratory failure 2.78%. Case fatality rate due to HEV infection was found to be 7.6%.

Total protein, albumin, BUN, and INR were major risk factors of mortality for HE, which was useful to assess the prognosis of HE. Decreased Albumin and total protein levels on admission was statistically significantly associated with mortality. An increase PT-INR and BUN levels on admission was statistically significantly associated with mortality.

Limitations:

This study was conducted in a tertiary care hospital in a metropolitan city hence observations and conclusions of this study cannot be extrapolated to the general population, especially those from rural areas. The sample should have been larger which could give further valuable information related to disease pattern of hepatitis E patients especially in pregnant individuals.

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