Original Research Article

Study of acute viral hepatitis with special reference to fulminant hepatic failure

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ABSTRACT

Background: Fulminant hepatic failure is a complication of viral hepatitis and is one of the leading causes of death in hospitalized children with viral hepatitis in India.

Methods: All the patients suspected to have acute viral hepatitis and/or fulminant hepatic failures with hepatic encephalopathies were included in the study and the diagnosis was made on the basis of history, clinical examination including a detailed neurological examination. Triage scoring, Glasgow coma scale, encephalopathy grading were recorded at the time of admission and necessary investigations were carried out.

Results: The occurrence of acute viral hepatitis and fulminant hepatic failure was 200 (2.004%) and 40 (0.401%) respectively during study period. Highest occurrence of 35.50% in the age group of 4-6 years, yellowish discoloration of the eyes or the urine was the most common presenting complaint. Only 45 % of the children who had fulminant hepatic failure survived and mortality was found to be 100% in those children who had grade 4 hepatic encephalopathy. Mortality was higher in those children who had duration of more than 10 days between the onset of jaundice and encephalopathy. Mortality was higher in those with prothrombin time between 41 to 50 seconds and with serum ammonia level more than 200 mmol/l. Hepatitis A virus was the most common cause of fulminant hepatic failure and Hepatitis E virus with hepatic encephalopathy was associated with 100 % mortality.

Conclusions: Hepatitis A infection though associated with a good prognosis, younger age group (< 6 years) and co infection with Hepatitis E virus have a poor prognosis. Good hygiene practices and early immunization could be a step towards the prevention of Hepatitis A infection.

Keywords: Fulminant hepatic failure, Hepatic encephalopathy, Viral hepatitis

INTRODUCTION

Viral hepatitis is a major health problem in developing and developed countries. Hepatotropic viruses are designated as hepatitis A, B, C, D, E and G viruses.

Many other viruses can cause hepatitis as one component of a multisystem disease, including herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus, Varicella-zoster virus, human immunodeficiency virus (HIV), rubella, adenoviruses, enteroviruses, parvovirus B19, and arboviruses.1,2,3

The six hepatotropic viruses are a heterogenous group that cause similar acute clinical illness, except for HGV, which appears to cause no or mild disease. HBV is a DNA virus, whereas HAV, HCV, HDV, HEV and HGV are RNA viruses. HAV and HEV are not known to cause acute illness, whereas HBV, HCV and HDV viruses can cause important morbidity and mortality through chronic
illness. HGV can cause chronic infections but with little mortality or morbidity. HAV appears to cause most cases of hepatitis in children.\textsuperscript{1,2}

Fulminant hepatic failure is a complication of viral hepatitis and is one of the leading causes of death in hospitalized children with viral hepatitis in India. The condition is very distressing as it occurs acutely in previously healthy children and progresses rapidly despite all modern treatment.\textsuperscript{3}

Fulminant hepatic failure is strictly defined as a clinical syndrome resulting from massive necrosis of hepatocytes or from severe functional impairment of hepatocytes in a patient who does not have a preexisting liver disease. The disorder usually evolves over a period of less than 8 weeks. Synthetic, excretory, and detoxifying functions of the liver are severely impaired; with hepatic encephalopathy as the essential diagnostic criterion.\textsuperscript{1}

Viral hepatitis continues to be a major cause of morbidity and mortality. In India fulminant hepatic failure in children is associated with very high mortality rate of 70 to 80%. Most cases in our setup are due to waterborne hepatotropic viruses.\textsuperscript{3}

The present study was done to evaluate various clinical, biochemical and serological parameters, to determine the prognosis and outcome of acute viral hepatitis and fulminant hepatic failure.

**METHODS**

The present study was conducted at a teaching institute over a period of 1 year and 9 months. A total of 200 patients were included in the study.

All the patients admitted in the pediatric wards who were suspected to have acute viral hepatitis and/or fulminant hepatic failures with hepatic encephalopathy were included in the study. All the patients of chronic hepatitis, chronic liver disease, cirrhosis, obstructive jaundice and neonatal jaundice were excluded from the study.

At the time of admission, a detailed history was taken, and a detailed clinical examination was done which was recorded in the proforma. The clinical diagnosis of acute viral hepatitis and fulminant hepatic failure with hepatic encephalopathy was made on the basis of history, clinical examination including a detailed neurological examination.

Triage scoring, Glasgow coma scale and encephalopathy grading were recorded at the time of admission. Investigations were done and recorded in the proforma. Treatment was instituted as early as possible. Daily follow-up examination was done. Improvement or deterioration in clinical status was noted and required investigations were repeated to determine the progression of the illness.

**RESULTS**

The study was conducted among 200 patients of acute viral hepatitis in a tertiary care centre. The incidence of acute viral hepatitis and fulminant hepatic failure was 200 (2.004%) and 40 (0.401%) respectively during study period. Out of 200 patients of acute viral hepatitis 40 patients (20%) developed fulminant hepatic failure.

**Table 1: Incidence of clinical symptoms in acute viral hepatitis.**

| Clinical symptoms       | Total no. of patients (n=200) | Incidence |
|-------------------------|-------------------------------|-----------|
| Yellow sclera/urine     | 196                           | 98.00%    |
| Fever                   | 191                           | 95.50%    |
| Nausea/vomiting         | 148                           | 74.00%    |
| Loss of appetite        | 175                           | 87.50%    |
| Abdominal pain          | 82                            | 41.00%    |
| Abdominal distention    | 15                            | 7.50%     |

Out of 200 patients of acute viral hepatitis, 61 (30.50%) patients were in the age group between 0 to 3 years of age, 71 (35.50%) patients were between 4 to 6 years of age, 43 (21.50%) patients were between 7 to 9 years of age and 25 (12.50%) patients were between 10 to 12 years of age.

**Figure 1: Distribution of causative agents among acute viral hepatitis patients (N=200).**

Out of 200 patients of acute viral hepatitis, 126 (63%) patients were male and 74 (37%) patients were female. Male: Female ratio observed 1.70:1.

Among the 200 patients of acute viral hepatitis, 94 (47%) patients had HAV infection and 15 (7.5%) of the patients had both HAV and HEV infection.

Out of the 40 patients of fulminant hepatic failure, 18 (45%) patients survived and 22 (55%) patients expired. In 3 patients (7.5%) the duration was more than 10 days and all these 3 patients expired.
Out of 40 patients of fulminant hepatic failure, 14 (35.00%) patients had SGPT level less than 500 IU/L, out of which 7 (50.00%) patients expired. 7 (17.50%) patients had between 501 to 1000 IU/L, out of which 5 (71.43%) patients expired. 9 (22.50%) patients had between 1001 to 1500 IU/L, out of which 4 (44.45%) patients expired. 2 (5.00%) patients had between 1501 to 2000 IU/L, all these patients expired. 2 (5.00%) patients had between 2001 to 2500 IU/L, this patient survived. 1 (2.50%) patient had between 2501 to 3000 IU/L, this patient survived. 1 (2.50%) patient had between 3001 to 3500 IU/L, this patient expired. 2 (5.00%) patients had between 3501 to 4000 IU/L, out of which 3 (96.67%) patients expired.

TABLE 2: Distribution of serum ammonia level and mortality in fulminant hepatic failure patients.

| Serum Ammonia (mmol/lit) | Total No. of Patients (n=31) | Mortality |
|--------------------------|-----------------------------|-----------|
| Up to 100                | 12 (38.70%)                 | 4 (33.34%)|
| 101 to 150               | 11 (35.48%)                 | 5 (45.45%)|
| 151 to 200               | 5 (16.13%)                  | 5 (100%)  |
| More than 200            | 3 (9.67%)                   | 3 (100%)  |

Table 3: Distribution of complications and mortality in fulminant hepatic failure patients.

| Complications             | Total no. of patients (n=40) | Mortality   |
|---------------------------|------------------------------|-------------|
| Hypoglycemia              | 6 (15.00%)                   | 5 (83.33%)  |
| Seizures                  | 9 (22.50%)                   | 6 (66.67%)  |
| Gastrointestinal bleeding | 28 (70.00%)                  | 21 (75.00%) |
| Renal failure             | 15(37.50%)                   | 10 (66.67%) |
| No complication           | 8 (20.00%)                   | 0 (0%)      |

DISCUSSION

In this study out of the 200 patients, 30.5% patients were in the age group of 0-3 years, 35.5% patients were in the age group of 3 to 6 years and 34% patients were in the age group of more than 6 years. This was comparable to the results in a study done by Chawan et al in which 34.6% patients were in the age group of 3 to 6 years and 30.7% patients were in the age group of more than 6 years.5

In the present study HAV infection was found in 47% patients, which was comparable with the studies of Surendra Kumar et al (56.37%), Malathi et al (38.6%), Marcus et al (40.18%), T.N.Chau et al (49.3%), pooled Indian data (53%).6-10 HAV was the leading cause of Acute Viral Hepatitis in all the studies.

In our study HBV infection was found in 3.5% patients, which was comparable with the study of Chadha et al (5.4%).11 The incidence of HBV infection in studies of Malathi et al was 13.4%, Marcus et al was 31.77%, T.N. Chau et al was 37.6%,7-9

Combined HAV+HEV infection were present in 7.5% patients. The incidence of combined HAV+HEV infection in the studies of Surendra Kumar et al was 19.46%, Malathi et al was 13.4%, pooled Indian data was 11.17%.6,7,10

In the present study, mortality rate was 10% in patients with hepatic encephalopathy grade I and II which was comparable with the study of Bendre et al (9.09%).4 In the study of Poddar et al no mortality was found in patients with hepatic encephalopathy grade I and II. In the present study, mortality rate was 70% in patients with hepatic encephalopathy grade III and IV which was comparable with the study of Bendre et al (85.72%).4 In the study of Poddar et al mortality rate was 47.22% in patients with hepatic encephalopathy grade III and IV.12

Table 4 shows that, in the present study the mortality rate observed was 66.67% in the patients with seizures, 75% mortality rate was observed in the patients with gastrointestinal bleeding, and all patients without any complications were survived.
Table 5: Comparison of different complications in patients with fulminant hepatic failure.

| Study                | Complications | Gastrointestinal bleeding | No complication |
|----------------------|---------------|--------------------------|-----------------|
| Present study N = 40 | Total no.     |                          |                 |
| of patients          | 9 (22.50%)    | 28 (70%)                 | 8 (20%)         |
| Survived             | 3 (33.33%)    | 7 (25%)                  | 8 (100%)        |
| Expired              | 6 (66.67%)    | 21 (75%)                 | 0 (0%)          |
| Bendre et al N = 36  | Total no.     |                          |                 |
| of patients          | 3 (8.33%)     | 8 (22.22%)               | 19 (52.77%)     |
| Survived             | 0 (0%)        | 2 (25.00%)               | 19 (100%)       |
| Expired              | 3 (100%)      | 6 (75.00%)               | 0 (0%)          |

In the study of Bendre et al, showed that 100% mortality rate was observed in the patients with seizures, 75% mortality rate was observed in the patients with gastrointestinal bleeding, and all patients without any complications were survived.4

In the present study, hypoglycemia was associated with high mortality (83.33%). In the study of Srivastava et al, which showed that blood glucose level less than 45 mg/dl was associated with poor outcome.13 So seizures, gastrointestinal bleeding and hypoglycemia were associated with high mortality in patients of fulminant hepatic failure.

Hepatic encephalopathy grade, duration between onset of jaundice and encephalopathy, liver size, serum bilirubin level, prothrombin time and presence of complications are important prognostic indicators in patients with fulminant hepatic failure.

CONCLUSION

From the present study authors concluded that hepatitis A virus is the commonest causative agent of acute viral hepatitis and fulminant hepatic failure. Although Hepatitis A infection is associated with a good prognosis, younger age group (<6 years) and co-infection with Hepatitis E virus have a poor prognosis. Prothrombin and ammonia levels were found to have a good correlation with the incidence of morbidity and mortality. Good hygiene practices and early immunization could be a step towards the prevention of Hepatitis A infection.

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