ETIOLOGY AND OUTCOME OF ACUTE HEPATIC FAILURE - A STUDY OF 40 CASES

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Abstract:

Acute hepatic failure (ALF) is a medical emergency and infrequently presented in the hospitals and may be associated with high mortality rate. Its etiology shows considerable geographical variations. The viral causes are the most common worldwide, [whilst acetaminophen (Paracetamol) induced hepatotoxicity forms the most common precipitant in many developed countries.]

A total forty (40) patients of ALF were studied during the period of January 2003 to July 2004 to evaluate the etiology and outcome. The patients were admitted in different tertiary care hospitals in Bangladesh. The patients were selected randomly by the diagnostic criteria. The selected patients presented with jaundice and hepatic encephalopathy of varying grades. Almost all the cases the causative agents were viruses. Among these, the hepatitis E virus (HEV) was the top most causative agent followed by hepatitis B virus (HBV) in this study. Despite good effort of conservative treatment, the mortality rate was 77.5%. The mortality rate was higher in grade-III and grade-IV encephalopathy patients whereas the prognosis is better in grade-I and grade-II encephalopathy patients.

Introduction

Acute hepatic failure (ALF) is characterized by the development of hepatic encephalopathy within eight weeks after onset of acute liver disease[1]. There is a wide range of causative agents of ALF with geographical variations, the viruses ranking the top[2]. Besides these, drugs, chemicals, poisonous mushroom, shock, hyper and hypothermia, Budd Chiary syndrome and so on may causes ALF[1].

Clinical profile of ALF depends upon the causative agents Viral hepatitis is common in Bangladesh. Acute hepatic failure is a frequent complications of acute viral hepatitis. The common viruses that causes hepatitis are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis E virus (HEV), hepatitis C virus (HCV), hepatitis delta virus (HDV). All these viruses can cause of acute liver failure. Acute liver failure is characterized by disturbances in consciousness, behaviour and personality changes, fluctuating neurological sign, flapping tremor and disturbances in electroencephalographic change[3]. Altered mental status in a jaundice patient is the hallmark of fulminant hepatic failure. Neuropsychiatric changes may develop even before jaundice[4].

The aim and objective of the present study were to evaluate the etiology and outcome of acute hepatic failure patients admitted in different tertiary care hospitals in our setting. We have given emphasis particularly to search the viral markers and find out the outcome by providing modern facilities for biochemical, haematological and serological investigation as well as medical care.

Materials and Methods

The study comprises 40 patients with acute hepatic failure. The patients were admitted in different tertiary care hospitals. Among these, twenty four (24) patients from Dhaka Medical College Hospital (DMCH), five (5) patients from Bangabandhu Sheikh Mujib Medical University (BSMMU) and Eleven (11) patients from Jahurul Islam Medical College (JIMCH) were observed during the period of January 2003 to July 2004. The patients were selected randomly on the basis of diagnostic criteria. Chronic hepatitis cases have been excluded in this study by doing serology, USG of abdomen specially hepatobiliary system & in some cases endoscopic examination of upper gastrointestinal tract. The following criteria were used to diagnose acute hepatic failure[5].

a. Biochemical and haematological features suggestive of hepatitis (Raised serum bilirubin, raised serum transaminase and prolonged prothrombin time).

b. Hepatic encephalopathy within 8 weeks from the onset of acute hepatitis.

c. No pre-existing liver disease.

The selected patients presented with jaundice and hepatic encephalopathy. The clinical grades of hepatic encephalopathy were done by following ways of "Modified Conn & Liebeerthal grading system" [4].

Grade I : Confused, altered mood or behavior, psychometric defects, disordered sleep pattern.

Grade II : Dorwsy, lethargy, inappropriate behaviour, personality change.

Grade III : Stuporous but speaking and obeying simple commands. Inarticulate speech, marked confusion, amnesia & occasional fits.

Grade IV : Coma.

All the patients were thoroughly investigated biochemically and for viral markers to search for the causes of ALF. The clinical profile and investigations results of each patients were recorded on a predesigned data collection form. All the patients

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were treated conservatively and monitored periodically. The mean duration of observation was four (4) weeks.

Observation and Results

A total 40 patients were studied on the basis of diagnostic criteria for acute hepatic failure. All the patients presented with mild to severe jaundice and features of hepatic encephalopathy.

In this study, majority of the patients (87.5%) presented within the 4th weak of illness but only (17.5%) patient presented within the 1st weak of illness. The death rate was lower (42.86%) in those presented within 1st week but higher (84.85%) of those presented after 1st week (Table-I).

Seven (17.5%) patients presented with hepatic encephalopathy of grade-IV and ten (25%) patients had grade-III encephalopathy. Only two patients from grade-III were survived and rest of the patients from grade-III and all patients from grade-IV hepatic encephalopathy died in this study (Table-II).

Serum bilirubin level, serum alanine aminotransferase (ALT) level, serum albumin level and prothrombin time were measured in all the studied patient. Thirty three (82.5%) patients had bilirubin level between 85-340 mmol/L, two (5%) patient had bilirubin level below 85 mmol/L and five (12.5%) patients had bilirubin level above >340 mmol/L (Table-III). ALT level was less than 100 U/L in seven (17.5%) patients, between 100-1000 U/L in thirty two (80%) patients and only one (2.5%) patient had ALT level above 1000 U/L (Table-IV). Twenty one patients (52.5%) had prothrombin time between 15-30 seconds and ten patients (25%) had more than 50 seconds (Table-V). Fourteen (35%) patients had serum albumin level below 35 gm/L and the rest twenty six (65%) patients had above 35 gm/L (Table-V). The mortality rates were 80% and 90% of those patients having higher bilirubin level (>340 mmol/L) and prothrombin time (>50 seconds) respectively. The mortality rate was 64% in those having lower albumin level (<35 gm/L).

Viral markers for hepatitis B, hepatitis C hepatitis E and hepatitis A viruses were done in all cases. Marker for hepatitis B and hepatitis E virus were found positive in fourteen (35%) and sixteen (40%) cases respectively. Both hepatitis B and hepatitis E viral markers were positive in eight (20%) cases. Marker for hepatitis A virus was positive in one case. All viral markers were negative in one (2.5%) case (Table-VII). Marker for hepatitis D virus could not be done in this study. The causative agent could not be indentified in one case. Inspite of optimum conservative management, thirty one (77.5%) patients were died and nine (22.5%) patients were recovered in this study (Table-VIII).

Table-I: *Duration of illness and death in patients of acute hepatic failure in this study (n=40).*

Duration of illness (week)	Admitted patients Number	Death of patients Number	Percentage
<1	7	3	42.85
1-2	13	10	76.92
3-4	15	13	86.67
>4	5	5	100

Table-II: *Distribution of grades of hepatic encephalopathy and death in patients of acute hepatic failure in this study (n=40).*

Grades of hepatic encephalopathy	Admitted patients Number	Death of patients Number	Percentage (%)
Grade-I	8	5	62.50
Grade-II	15	11	73.33
Grade-III	10	8	80.00
Grade-IV	7	7	100.00

Table-III: *Serum bilirubin level in patients of acute hepatic failure at presentation in this study (n=40).*

Serum bilirubin level (mmol/L)	Number of patients	Percentage (%)
<85	2	5.0
85-170	12	30.0
171-340	21	52.5
341-510	3	7.5
>510	2	5.0

Table-IV: *Serum alanine aminotransferase level in patients of acute hepatic failure at presentation in this study (n=40).*

Serum ALT (U/L)	Number of patients	Percentage (%)
<100	7	17.5
100-300	21	52.5
301-500	8	20
501-1000	3	7.5
>1000	1	2.5

Table-V: *Prothrombin time in patients of acute hepatic failure at presentation in this study (n=40).*

Prothrombin time (seconds)	Number of patients	Percentage (%)
15-17	9	22.5
18-30	12	30
31-50	9	22.6
>50	10	25

Table-VI: *Serum albumin levels in patients of acute hepatic failure at presentation in this study (n=40).*

Serum albumin (gm/L)	Number of patients	Percentage (%)
<35	14	35
35-45	22	55
>45	4	10

Table-VII: *Distribution of viral markers in patients of acute hepatic failure in this study (n=40)*

Viral markers	Number of patients	Percentage (%)
HEV (positive)	14	35
HBV (positive)	16	40
Both HEV & HBV (positive)	8	20
HAV (positive)	1	2.5
All viral markers (negative)	1	2.5

Table-VIII: *Outcome of treated patients of acute hepatic failure in this study (n=40).*

Outcome	Number of patients	Percentage (%)
Recovered	9	22.5
Expired	31	77.5

Discussion

Acute hepatic failure is a critical condition. This study evaluated the etiology and outcome of acute hepatic failure patients admitted in three medical institutes of Bangladesh.

All the patients investigated thoroughly and also searched for viral markers. All the patients were treated conservatively and monitored periodically.

Varying grades of hepatic encephalopathy is the hallmark of acute hepatic failure in this study. The death rate was lower (70%) in grade-I and grade-II encephalopathy but higher (89%) in grade-III and grade-IV encephalopathy. This is similar to other studies. The death rate of patients with grade-III and grade-IV hepatic encephalopathy of those studies were 75.8% and 81% respectively[6].

In this study the mortality rate were higher in those patients having high serum bilirubin level (>340 mmol/L), high prothrombin time (>50 seconds) and less serum albumin (<35 gm/L). The total number of these groups of patients were 5, 10 and 14 and the mortality rates were 80%(5), 90%(9) and 64%(9) respectively. These findings are closely related to other studies. They reported more than 90% death in case of high serum bilirubin and prothrombin time[7].

Viral markers were done in all the patients in this study. Hepatitis E virus was positive in sixteen (40%) cases and hepatitis B in fourteen (35%) cases. Co-infection with hepatitis B and hepatitis E viruses were positive in eight (20%) patients. Report from developing countries showed that HEV is the main cause of acute hepatic failure which is lower in western countries[8,9]. A study from UK reported only 16.6% cases of acute hepatic failure due to HEV infection but a study from India reported 62% cases[8]. HBV causes acute hepatic failure in 30-40% cases in western countries[10,11]. In two other studies reported 40% and 28.5% cases of acute hepatic failure were due to HBV infection[12,13]. Data is not available about the co-infection with HBV and HEV in acute hepatic failure[8]. Hepatitis A virus was positive in one (2.5%) case and the causative agent could not be identified in only one case in this study. A study reported that hepatitis A virus infection complicating acute liver failure was less than 1% case[12]. In USA about one third of adult have Anti HAV antibodies and about 100 death per year are attributed to HAV related acute liver failure[14].

By providing optimum conservative management, the survival rate in patients of acute hepatic failure in this study was 22.5%. This was almost similar to other studies[4]. Survival rate was higher (57.14%) in patient admitted within 1st week of illness and lower (15.15%) in those admitted after 1st week. This is also similar to other studies. The survival rate were 53.3% and 14.9% in patients admitted within 1st week and after 1st week of illness respectively in those studies[15,16].

Summary & Conclusion

Clinical and biochemical profile of 40 patients with acute hepatic failure were studied. The patients were admitted in three tertiary care hospitals. Features of hepatitis, encephalopathy and increased prothrombin time in the absence of any features suggestive of pre-existing liver diseases were the key indicators

for the diagnosis of acute hepatic failure. All patients had jaundice and features of encephalopathy ranging from grade-I to grade-IV. All the patients were thoroughly investigated and provided optimum conservative management and monitored periodically.

Raised prothrombin time, serum bilirubin and alanine aminotransferase were found in all patients. Serum albumin was slightly low in 35% patients. Anti HEV was positive in 40% patients and HBsAg positive in 35% patients. Both anti HEV and HBsAg were positive in 20% of patients. HAV was positive in only one case in this study. Causes could not be identified in one case. Only 22.5%a patients were recovered completely and 77.5% patients expired. The mortality rates were higher with those patients presented after 1st week of illness, with hepatic encephalopathy grade-III and grade-IV, very high serum bilirubin, high prothrombin time and less serum albumin. Although there are some minute variations in some parameters, most of the findings in the present study are similar as suggested by other authors. However further study with larger samples, with improved investigations and management techniques is suggested to evaluate the strength or weakness of this study.

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