Research Article

Acute hepatic failure with encephalopathy in children

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Abstract

Introduction: Hepatic encephalopathy is a serious and likely to be reversible neurophyschiatric state in the patient of liver failure. Acute hepatic failure is a life-threatening condition in children. **Objectives**: The study analyses the clinical spectrum, prognosis and factors determining the prognosis of children with acute hepatic failure and associated encephalopathy in a tertiary level hospital. **Methodology**: Thirty two children (18 males and 14 females) were presented with the diagnosis over a two year period. It is a Prospective study. **Results**: The commonest cause of acute hepatic failure was hepatitis A virus found in 30% of cases. Only 30% (9 out of 32) children could be survived, in which mostly came in hepatic encephalopathy Stage I and II. Hemorrhagic manifestations were significantly more (P=0.002) in died in contrast to survived. **Conclusion**: Hepatic failure is a condition associated with high mortality primarily in absence of hepatic transplantation facilities. Focus of efforts should be in providing preventive steps such as immunization and society education.

Key words: Acute hepatic failure, Hepatic encephalopathy

Introduction

Hepatic encephalopathy is a serious and likely to be reversible neurophyschiatric state in the patient of hepatic failure. Acute hepatic failure is a life-threatening condition in children with varied etiology such as hepatotropic viruses (A,B,C,D and E), metabolic conditions, drugs and toxins[1]. The accurate reason of the disease is unclear in a large proportion of patients primarily in the underprivileged section because of absence of proper diagnostic facilities.

The end result of the disease is also poor primarily in the area where there is lack of the liver transplantation facilities [2].

Therefore it is necessary to evaluate the clinical spectrum and markers influencing the prognosis of patients with hepatic encephalopathy. There is a scarcity of data about the spectrum of manifestation and prognosis of children with hepatic encephalopathy especially in developing countries. Therefore the study was tried at a tertiary level center to analyse the clinical and biochemical spectrum of manifestation, prognosis and markers determining the prognosis in children with acute hepatic encephalopathy.

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Methodology

It was a tertiary level centre based prospective descriptive study, where evaluation of the case records was done of children came to the Department of Pediatrics at Gandhi Medical College Bhopal MP with of Acute Hepatic Failure with hepatic encephalopathy between June 2013 and July 2015. The hepatic encephalopathy as a diagnosis was formed in those children who came with declined level of consciousness in association with acute liver involvement manifesting as icterus due to conjugated / unconjugated hyperbilirubinemia.

An elaborate history which included likelihood of ingestion of toxins and drugs was enquired to the parents or guardians. Elaborate clinical examination which included neurological examination was performed in all patients. On the basis of history and clinical examination, staging of hepatic encephalopathy [3] was done. In every patient tests was done which involved blood cell counts, peripheral blood smear for malarial parasite, liver function tests [Serum Asparatate aminotrasferase, Alanine aminotransferase, Direct and Total Bilirubin, Serum Albumin, Prothrombin time (PT), INR, Serum electrolytes, Blood urea, Serum creatinine and blood culture.

Tests for Viral markers was done which included hepatitis B surface antigen (HBsAg) and antibodies against hepatitis A virus and hepatitis C virus (HCV). Ophthalmological checkup for Kaysner-Fleisher ring (K-F ring) was done depending on the child's condition. X-ray chest, ultrasonography abdomen, and urine analysis were performed as per the need. Evaluation for several causes

of hepatic encephalopathy was not possible in detail such as Hepatitis E and metabolic disorders because of paucity of diagnostic facilities and un affordability of patients. All patients were admitted in the Pediatric Intensive Care Unit (PICU) or pediatric wards. Vital parameters were monitored and the treatment given in form of intravenous fluids, systemic antibiotics, H2 blockers, mannitol and GI wash. Fresh frozen plasma and/or blood transfusions were administered as required.

The end result was determined in form of survival (improvement and successful discharge after the encephalopathy has been resolved), death and leave against medical advice (LAMA). Results were subjected to Descriptive analyses. Numeric data were compared by Students t test while proportions were compared by Chi-square and Fischer exact tests.

Results

Thirty two children (18 males and 14 females) were came with a diagnosis of acute hepatic failure with associated encephalopathy who were involved in the study. Patients age ranged from 1 year to 12 years with mean (SD) age of 7.38 (4.18) years. The duration of icterus before hospitalization was 13 days with mean (SD) duration of 17 days while the mean (SD) duration of declined level of consciousness was 1.7 (1.9) days. Seven patients were came with Stage I encephalopathy, five patients in stage II, ten patients in stage III and ten in stage IV encephalopathy. Hemorrhagic manifestations were observed in many (21 out of 32) of the patients.

Table 1: Shows Characteristics of patients with Hepatic Encephalopathy (n=32).

Parameters	Mean	Standard Deviation (SD)
Age	7.38	4.2
Icterus (duration)	13.30	17.01
Declined level of consciousness (duration)	1.70	1.87
Hemoglobin	8.79	2.60
TLC	1.94	0.84
Platelet count	1.99	1.28
PT	55.00	33.35
INR	4.20	2.15
SGPT	887.85	887.82
SGOT	701.49	629.62
Alkaline Phosphatase	847.54	442.68
Bilirubin (serum)		
Total	17.04	9.51
Direct	8.01	6.50
Proteins(serum)		
Total	5.98	1.04
Albumin	3.37	1.11
Sodium	130.21	8.80
Potassium	3.98	0.87
Blood Urea	54.51	40.33
Serum Creatinine	1.28	0.97

Table-2: Displaying course on the basis of Encephalopathy's stage.

Stage	Expire	Survival	LAMA
One (n=7)	0	7	0
Two(n=5)	2	3	0
Three (n=10)	4	6	3
Four (n=10)	10	0	4

Hepatitis A virus were the agent responsible for acute hepatic failure observed in ten children as determined by Anti HAV IgM antibodies. No patient was positive for HbsAg or HCV antibodies. K-F ring was not found in any of study patient. The laboratory parameters of the study patients are shown in Table 1. Prolonged PT (INR > 1.5) was observed in 76% of patients. In 24 patients PT was increased, prolonged INR was than 4 in seventeen. In thirty two study patients, 15 (46.8%) children expired while 12(37.5%) patients improve and discharged. Five (16%) patients given leave against medical advice(LAMA). Table 2 shows course of patients on the basis of encephalopathy's stage. Survival was 100% in stage one and two, 60% in stage three, and 0% in stage IV. Table 3 compares the profile of children who survived with those who died. It may be argued that the children who left against medical advice were also very sick and should be clubbed along with the deaths. Thus, this table also includes the analysis with LAMA included as deaths. In general, the hemoglobin and platelet count were lower whereas the bilirubin, hepatic enzyme levels and PT were higher in deaths in comparison to survivors but these did not reach statistical significance. The serum proteins and albumin levels were significantly lower (p-value = 0.04 and 0.03, respectively) in the children who died when the analysis included LAMA as deaths. The bleeding manifestations were significantly more common in deaths as compared to survivors irrespective of whether LAMA excluded from analysis (p value = 0.002) or included with deaths (p value = 0.000).

Table-3: Compares different Parameters between expired and Survived.

Parameter	Course		*p* value	Course (LAMA plus deaths)		
	Expired (n=16)	Survival (n=16)		Expired (n=23)	Survival (n=9)	*p* value
Age (in year)	7.6 (4.7)	8.4 (4.6)	0.30	8.1 (5.2)	7.2 (4.6)	0.51
Icterus (days)	15.8 (21.9)	7.1 (9.05)	0.21	14.6 (17.1)	7.1 (7.9)	0.17
Declined consciousness (day)	2.1(2.5)	1.6 (1.2)	0.48	2.2 (1.9)	1.4 (1.5)	0.51
Gender (M/F)	10:4	5:1	0.20	14:5	5:1	0.10
Hemorrhage	2	5	0.002	17	5	0.000
Hemoglobin	8.1 (2.0)	9.8 (3.1)	0.12	7.9 (1.9)	10.1 (3.0)	0.23
Total leucocyte count	1.78 (0.88)	1.77 (0.95)	0.78	1.85 (0.79)	1.89 (0.98)	0.89
Platelets	1.54 (0.96)	2.54 (1.58)	0.10	1.60 (1.12)	2.54 (1.42)	0.08
Prothrombin Time	60.9 (31.5)	42.6 (31.4)	0.11	71.1 (42.5)	46.4 (34.1)	0.08
INR	4.58 (1.68)	3.26 (1.89)	0.09	4.87 (2.23)	3.36 (2.01)	0.07
SGPT	1150.4 (948.5)	712.4 (741.6)	0.21	1054.4 (893.8)	754.6 (745.4)	0.38
SGOT	989.7 (661.4)	521.8 (576.3)	0.09	831.8 (546.3)	527.6 (576.3)	0.23
Serum Alk Phosphatase	1002(374.2)	781.3 (511.2)	0.24	889.8 (416.5)	763.6 (518.6)	0.50
Bilirubin						
Total	14.6 (6.8)	13.3 (9.5)	0.61	16.8 (9.1)	13.3 (9.8)	0.27
Direct	6.8 (6.4)	7.1 (5.3)	0.68	8.8 (6.9)	6.7 (5.7)	0.40
Proteins						
Total	6.1 (1.2)	7.1 (1.3)	0.14	5.6 (1.0)	6.4 (1.2)	0.05
Albumin	3.4 (1.3)	3.8 (1.4)	0.13	3.2 (1.1)	4.0 (1.2)	0.04
Sodium	128.4 (9.1)	134.8 (8.5)	0.05	130.1 (9.1)	141.2 (8.8)	0.10
Potassium	4.4 (0.7)	4.2 (1.5)	0.89	4.1 (0.8)	4.2 (1.4)	0.75
Blood Urea	51.4 (34.1)	51.2 (30.5)	0.70	58.8 (46.2)	45.8 (29.7)	0.34
Serum Creatinine	1.3 (0.7)	1.0 (0.4)	0.17	1.6 (1.5)	1.0 (0.4)	0.17

Discussion

Acute hepatic failure is life-threatening condition of varied causes. Clinical scenario of it involves icterus, coagulation abnormality and encephalopathy. Aetiology of it is varied in nature. Common agents are viruses and drugs. Hepatitis A and Hepatitis E are common cause of Hepatic encephalopathy in under-developed nations [4,5,6]. Hepatitis B virus is not a common agent nowadays, probably due to vast coverage of hepatitis B vaccination [7,8].

Evaluation of etiology could not be possible in most (75%) of patients due to scarcity of diagnostic modalities. Still it has been mentioned that etiology is not clear in 45-50% of acute hepatic failure even after detailed investigations[2,9]. These cases known as 'cryptogenic' cases [10] may be due to metabolic disorders or unknown viral agents

Seventy percent of study patients were expired or taken leave against medical advice therefore, survived were thirty percent. This proportion is similar to evidences from other institutions where there is absence of facility for liver transplantation [9,11].

In majority of cases, there were markedly increased PT (INR > 4),which is well known factor to assess prognosis and very long prothrombin time is linked with high mortality[12]. At INR >4, there is the indication for the liver transplantation, especially in small children. Chances of Survival after liver transplantation is 60% to 80% which depends on patient's conditions and facilities and infrastructure which are available[11,12].

The study evaluated the indicators which influences end result of liver failure. Higher the stage of encephalopathy poorer the outcome. Hemorrhage was common in expired. Coagulation derangement is a common picture associated with Acute hepatic failure. There was not an important difference in serum bilirubin ranges, hepatic enzymes and Prothrombin time between survived and expired.

This may be due to small sample size. In a from Turkey based study, stage of encephalopathy, serum bilirubin levels were significantly greater in expired patients[9]. In this study, Sodium levels were lesser in expired patients as compared to those who survived, which may be explained by syndrome of inappropriate secretion of antidiuretic hormone.

Conclusion

Acute hepatic failure is a disease with high mortality rate. This is more so if bleeding manifestations are there. Hepatitis A virus is a common agent of Acute hepatic Failure in children while hepatitis B has become less common. many reasons of Acute hepatic failure still to be established largely due to scarcity of new diagnostic modalities. Facility for liver trans-plantation is still out of reach to a majority of population and where there it is available, it is unaffordable for the most. Therefore focus should be in proper implementation of prevention such as vaccination and society education.

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