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Original Research Article

Etiology, Clinical Manifestations, Management, and Prognosis of Acute Liver Failure in Paediatric Patients at Burdwan Medical College PICU

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Abstract

Introduction: Acute liver failure (ALF) in children is a rare but life-threatening condition with varied etiology and rapid progression. Understanding its clinical profile, management, and outcomes is crucial for timely intervention and improving prognosis.

Aims and Objectives: To analyze the etiology, clinical features, management strategies, and outcomes of pediatric acute liver failure cases admitted to the Pediatric Intensive Care Unit (PICU) of Burdwan Medical College.

Materials and Methods: This hospital-based prospective observational study was conducted in the Department of Pediatrics and Pediatric Intensive Care Unit (PICU) at Burdwan Medical College and Hospital, West Bengal, India, over a period of one year from July 2022 to August 2023. The study included 100 children aged 1 month to 12 years who were admitted to the PICU with a diagnosis of acute liver failure (ALF).

Results: The most affected age group was 1–5 years (40%), with highest mortality in children <1 year (60%). Viral hepatitis was the most common etiology (35%), followed by indeterminate causes (30%) and metabolic disorders (15%). Hepatic encephalopathy (60%), coagulopathy (70%), and hypoglycemia (25%) were significantly associated with higher mortality ($P < 0.05$). Use of N-acetylcysteine improved survival (75%, $P = 0.005$), while the need for mechanical ventilation and presence of cerebral edema were linked with poor prognosis ($P < 0.001$). Overall mortality was 40%, with only 8% referred for liver transplantation.

Conclusion: Pediatric ALF in this region is predominantly due to viral hepatitis and indeterminate causes, with significant mortality, especially in infants and those with metabolic etiologies. Early diagnosis, identification of poor prognostic indicators, and aggressive supportive care are essential to improving outcomes. Strengthening metabolic screening and expanding transplant access remain critical challenges.

Keywords: Pediatric Acute Liver Failure, Etiology, Hepatic Encephalopathy, Coagulopathy, N-Acetylcysteine, Liver Transplant, PICU.

Introduction

Acute liver failure (ALF) in children is a rare but life-threatening clinical syndrome characterized by the rapid deterioration of liver function, resulting in coagulopathy and hepatic encephalopathy in a previously healthy child [1]. It represents a diagnostic and therapeutic emergency, demanding early identification and intensive management due to its high morbidity and mortality. Unlike adults, where drug-induced liver injury—particularly acetaminophen toxicity—predominates, the etiology in children is more heterogeneous and age-specific, including viral hepatitis, metabolic disorders, autoimmune hepatitis, and indeterminate causes [2,3]. The burden and pattern of ALF vary significantly across regions, influenced by differences in infectious agents, vaccination coverage, availability of medical care, and genetic predispositions [4]. In India, ALF remains a significant cause of pediatric mortality, especially in tertiary care settings, with infections such as Hepatitis A and E being predominant causes in younger age groups [5]. However, recent years have witnessed a shift in the spectrum of etiologies, with an increase in indeterminate causes and

metabolic liver diseases being recognized with advancing diagnostic capabilities [6]. In neonates and infants, inborn errors of metabolism (IEM) account for a considerable proportion, while in older children, autoimmune hepatitis and Wilson's disease are also important contributors [7].

The clinical presentation of ALF in children is often nonspecific initially, with symptoms such as jaundice, vomiting, lethargy, and anorexia. As the disease progresses, encephalopathy, coagulopathy, hypoglycemia, and multiorgan dysfunction may ensue [8]. Pediatric hepatic encephalopathy poses particular diagnostic challenges due to age-related variability in mental status assessment, making timely recognition and grading crucial for prognosis [9]. Early identification and comprehensive management—including intensive supportive care, neuroprotection, management of coagulopathy, and consideration for liver transplantation—are vital to improving outcomes.

Management in a Pediatric Intensive Care Unit (PICU) is multidisciplinary, involving hemodynamic stabilization, correction of metabolic derangements, nutritional support, and infection control. Artificial liver support systems and extracorporeal therapies may serve as a bridge to transplantation or recovery [10]. Nevertheless, access to liver transplantation remains limited in many regions of India due to socioeconomic constraints, donor shortages, and logistic hurdles, making early diagnosis and aggressive supportive care even more essential [3].

Outcome in pediatric ALF is variable and largely determined by the underlying etiology, degree of hepatic encephalopathy, presence of multiorgan failure, and timely access to specialized care. While survival has improved with advances in critical care and transplantation, mortality remains significant in resource-limited settings. Studies from Indian tertiary centers have shown that with timely intervention, survival without liver transplant is achievable in a notable proportion of cases, particularly in viral and drug-induced ALF [5,6]. Despite its clinical importance, there is a paucity of region-specific data on pediatric ALF in Eastern India, particularly in rural and semi-urban populations. Burdwan Medical College, serving as a referral center for a large pediatric population in West Bengal, offers a unique opportunity to evaluate the demographic profile, etiology, clinical features, management strategies, and outcomes of ALF in this region. Understanding the local epidemiology and outcome predictors can guide early diagnosis, optimize PICU management protocols, and inform public health strategies aimed at reducing preventable causes.

This study aims to fill this knowledge gap by systematically analyzing the clinical spectrum and outcome of pediatric ALF admitted to the PICU of Burdwan Medical College. It seeks to identify the predominant causes, assess the efficacy of current management practices, and explore the factors influencing survival and recovery in this vulnerable group.

Materials and Methods

Study Design: Hospital-based, prospective observational study.

Study Setting: Department of Pediatrics and Pediatric Intensive Care Unit (PICU), Burdwan Medical College and Hospital, West Bengal, India.

Study Duration: Conducted over a period of 1 year (July 2022 August 2023).

Study Population: Children aged 1 month to 12 years admitted to PICU with a diagnosis of acute liver failure (ALF).

Inclusion Criteria:

Patients fulfilling the Pediatric Acute Liver Failure (PALF) Study Group criteria:

- Evidence of acute liver dysfunction (e.g., elevated liver enzymes).
- Coagulopathy (INR >1.5 with encephalopathy or INR >2.0 without encephalopathy).
- No evidence of pre-existing chronic liver disease.

Exclusion Criteria:

- Children with known chronic liver disease.
- Patients with incomplete clinical or laboratory data.
- Children discharged or referred before diagnosis or without complete workup.

Sample Size: 100 patients

Study Parameter

- Age (months/years)
- Sex (Male/Female)
- Area of residence (Urban/Rural)
- Nutritional status (Well-nourished/ Undernourished)
- Viral hepatitis (Hepatitis A, B, E)
- Drug-induced (e.g. paracetamol, anti-TB drugs)
- Metabolic disorders (e.g. Wilson's disease, galactosemia, tyrosinemia)
- Autoimmune hepatitis
- Sepsis-related
- Indeterminate (no definitive cause found)
- Duration of symptoms before admission
- Jaundice
- Vomiting
- Altered sensorium (encephalopathy)

- Bleeding manifestations (e.g. melena, hematemesis)
- Hepatomegaly
- Ascites
- Fever
- Seizures
- Grading of hepatic encephalopathy (Grade I–IV)
- Serum bilirubin (mg/dL)
- SGPT/ALT (IU/L)
- INR
- Serum ammonia (µmol/L)
- Blood sugar (mg/dL)
- Serum creatinine (mg/dL)
- Platelet count (×10⁹/L)
- Viral serology (HAV, HBV, HEV)
- Metabolic screening (TMS, urine GCMS, etc.)
- Supportive care (IV fluids, electrolytes, glucose)
- Mechanical ventilation
- Use of mannitol/lactulose for encephalopathy
- N-acetylcysteine therapy
- Plasma/FFP transfusion
- Antibiotics/antivirals
- Dialysis (hemodialysis or peritoneal)
- Referral for liver transplant
- Survival without liver transplant
- Death
- Referred for liver transplantation
- Duration of PICU stay
- Complications (e.g. cerebral edema, renal failure, sepsis)

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data.

Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Age Distribution and Outcome of Pediatric ALF Cases (n = 100)

Age Group	Number of Patients (%)	Recovered (n)	Died (n)	P-value
<1 year	20 (20%)	8	12	0.042
1–5 years	40 (40%)	30	10	
6–12 years	40 (40%)	28	12	

Table 2: Etiology-wise Distribution and Outcome

Etiology	No. of Cases (%)	Recovered (n)	Died (n)	P-value
Hepatitis A	20 (20%)	18	2	0.006
Hepatitis E	15 (15%)	12	3	
Drug-induced (ATT)	10 (10%)	7	3	
Inborn Errors of Metabolism (IEM)	15 (15%)	5	10	
Autoimmune Hepatitis	10 (10%)	6	4	
Indeterminate	30 (30%)	15	15	

Table 3: Clinical Features and Their Association with Mortality

Clinical Feature	Present (n)	Recovered (n)	Died (n)	P-value
Hepatic Encephalopathy	60	30	30	0.001
Coagulopathy (INR >2)	70	35	35	0.012
Hypoglycemia	25	10	15	0.018
Cerebral Edema (clinically suspected)	15	3	12	<0.001
Ascites	40	30	10	0.089

Table 4: Management Modalities and Outcomes

Management Strategy	No. of Patients	Survived (n)	Died (n)	P-value
Mechanical Ventilation	30	10	20	<0.001
NAC (N-acetylcysteine)	40	30	10	0.005
Antibiotics	60	40	20	0.214
Mannitol for raised ICP	10	2	8	0.004
Liver Transplant Referral	8	3	5	0.331

Table 5: Prognostic Factors and Outcome (Univariate Analysis)

Variable	Survivors (n=60)	Non-survivors (n=40)	P-value
Median serum ammonia (µmol/L)	68	140	0.001
Mean INR	1.9 ± 0.5	3.2 ± 0.7	<0.001
Mean ALT (IU/L)	850 ± 400	720 ± 380	0.203
Median bilirubin (mg/dL)	9.5	12.2	0.041
Duration of hospital stay (days)	8.2 ± 3.1	5.6 ± 2.7	0.006

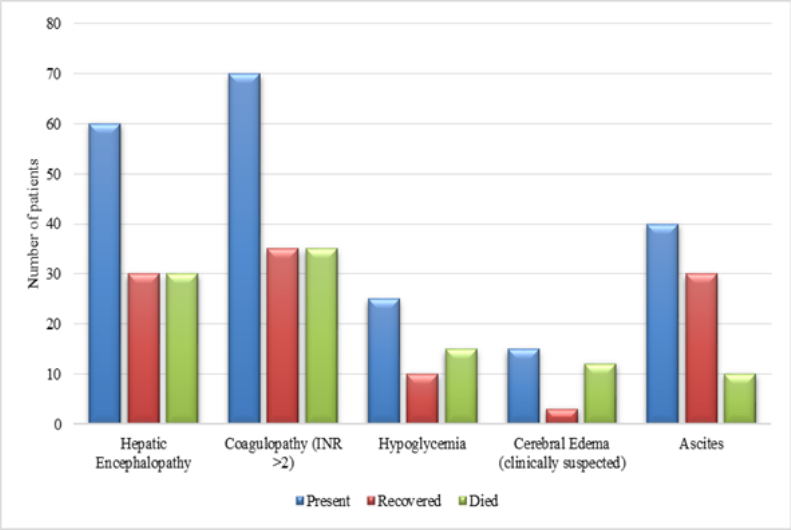

Figure 1: Clinical Features and Their Association with Mortality

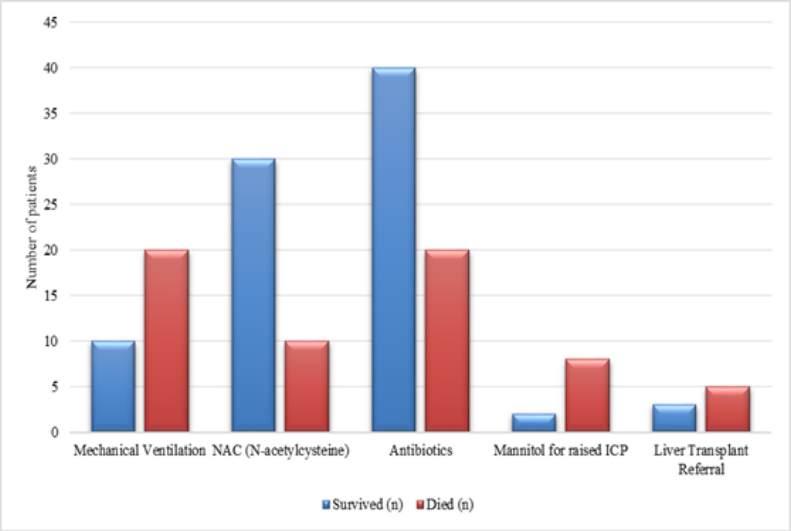

Figure 2: Management Modalities and Outcomes

A total of 100 pediatric patients with acute liver failure (ALF) were included in the study. The analysis was focused on demographic patterns, etiology, clinical features, management strategies, and their correlation with patient outcomes. As shown in Table 1, the majority of patients were aged between 1–5 years (40%), followed by 6–12 years (40%), and <1 year (20%). The mortality was highest in the <1 year age group, where 12 out of 20 children (60%) died. In contrast, children aged 1–5 years had the best outcomes, with 75% (30/40) recovering. The difference in mortality across age groups was statistically significant (P = 0.042), suggesting younger age, particularly infancy, as a poor prognostic indicator. Table 2 demonstrates that viral hepatitis was the most common identifiable cause, with Hepatitis A (20%) and Hepatitis E (15%) comprising 35% of cases. Hepatitis A had a high recovery rate (90%), while inborn errors of metabolism (IEM) were associated with the worst outcomes—10 out of 15 children with IEM died (66.7%). Among the 30 patients with indeterminate etiology, mortality was also high (50%). The association between etiology and outcome was statistically significant (P = 0.006),

underscoring the importance of early and accurate identification of the underlying cause.

The clinical presentation varied, but certain features were strongly associated with higher mortality (Table 3). Hepatic encephalopathy was present in 60 patients and significantly associated with poor outcomes (50% mortality, P = 0.001). Similarly, coagulopathy (INR >2) was seen in 70 children and was linked to a mortality rate of 50% (P = 0.012). Hypoglycemia, another critical feature, was associated with a significantly higher risk of death (P = 0.018). Cerebral edema, though present in only 15 patients, carried the highest case fatality—80% mortality (P < 0.001). On the other hand, ascites did not show a statistically significant correlation with outcome (P = 0.089).

Management modalities had varied impacts on survival outcomes (Table 4). Children requiring mechanical ventilation had poor prognosis, with a 66.7% mortality rate (P < 0.001), suggesting that need for respiratory support is a marker of severe disease. N-acetylcysteine (NAC) administration was associated with a significantly higher survival rate (75%, P = 0.005), indicating its potential benefit even beyond acetaminophen-induced liver failure. While the use of antibiotics was common (60 patients), it was not statistically linked to improved survival (P = 0.214). Use of mannitol for suspected raised intracranial pressure was associated with poor outcomes (80% mortality), likely reflecting the severity of hepatic encephalopathy in those patients (P = 0.004). Referral for liver transplant was limited to 8 children, with a survival of 3 out of 8; however, this was not statistically significant (P = 0.331), possibly due to the small sample size and late referral.

As shown in Table 5, several laboratory and clinical markers were statistically associated with survival. Median serum ammonia levels were significantly higher in non-survivors (140 µmol/L) compared to survivors (68 µmol/L) (P = 0.001). Similarly, mean INR was markedly elevated among non-survivors (3.2 ± 0.7) compared to survivors (1.9 ± 0.5) (P < 0.001), reaffirming the prognostic value of coagulopathy. While ALT levels did not differ significantly (P = 0.203), total serum bilirubin was higher in non-survivors (12.2 mg/dL vs 9.5 mg/dL; P = 0.041). Notably, the average duration of hospital stay was significantly shorter among those who died (5.6 ± 2.7 days), suggesting early deterioration and poor prognosis in more severe cases (P = 0.006).

Discussion

This study provides important insights into the clinical spectrum, etiology, management, and outcome of pediatric acute liver failure (ALF) in a tertiary care PICU setting in Eastern India. With an overall mortality of 40%, the study highlights the critical need for early identification of high-risk cases and timely intervention to improve outcomes.

Our findings show that the 1–5 years age group had the highest survival rate, while infants (<1 year) had the worst prognosis, a result consistent with previous studies. Bhaduri and Mieli-Vergani reported a similar age-related trend, emphasizing the higher vulnerability of infants due to immature immune systems, delayed recognition of symptoms, and a higher incidence of metabolic disorders in this group [11]. Moreover, Sundaram et al., in a multicenter U.S.-based study, also noted increased mortality in infants and highlighted the diagnostic challenges and limited transplant eligibility in this age group [12].

The etiological profile in our study showed viral hepatitis (especially Hepatitis A and E) as the most common cause, accounting for 35% of cases. This aligns with data from developing countries, where viral etiologies remain dominant due to poor sanitation and lower vaccination coverage [13]. In contrast, in high-income countries, drug-induced ALF, particularly from acetaminophen overdose, is more prevalent [14]. Interestingly, inborn errors of metabolism (IEM) were the leading cause of death in our cohort, with a 66.7% mortality rate. This finding supports the observations of Dhawan et al., who identified metabolic causes as significant contributors to mortality in infants and stressed the importance of early metabolic screening [15].

Clinically, the presence of hepatic encephalopathy, INR >2, and hypoglycemia were strongly associated with poor outcomes in our study. These findings reinforce the well-established understanding that coagulopathy and encephalopathy are key prognostic markers in ALF, as reported in previous studies [11,12]. The strong association between cerebral edema and mortality (80%) is alarming, and reflects the fatal consequences of raised intracranial pressure—a complication commonly associated with severe hepatic encephalopathy and delayed treatment [12].

Management outcomes also revealed valuable trends. The use of N-acetylcysteine (NAC) significantly improved survival (75%, P = 0.005), even in non-acetaminophen ALF cases. This is supported by studies like that of Squires et al., who demonstrated the benefit of NAC in improving transplant-free survival, especially in early stages of encephalopathy [14]. Conversely, mechanical ventilation was associated with high mortality, reflecting the severity of systemic illness in these patients. Similarly, mannitol use, while theoretically helpful in managing cerebral edema, was linked to poor outcomes—likely due to its use in more advanced disease stages rather than any

direct harm. Univariate analysis in our study showed that higher serum ammonia and INR were strong predictors of mortality—both of which are consistent with international consensus on poor prognostic markers [12,14]. Shorter hospital stay among non-survivors suggests rapid progression of disease, underlining the narrow therapeutic window available in ALF cases. Despite advances in supportive care, liver transplantation remains the only definitive treatment for irreversible ALF. However, only 8% of patients were referred for transplant in this study, and just 3 survived. This low referral and transplant rate highlight the resource limitations, lack of transplant facilities, financial constraints, and late presentation of patients—challenges commonly faced in low- and middle-income countries, as echoed by Bhattacharya et al. in their regional study [13]. Overall, this study reinforces the importance of early diagnosis, aggressive supportive care, and etiology-specific interventions in improving outcomes in paediatric ALF. The findings are in line with existing literature but also emphasize region-specific challenges such as late presentation, limited access to liver transplant, and higher incidence of metabolic and viral causes.

Conclusion

This study highlights the diverse etiological spectrum, clinical presentations, and prognostic factors associated with pediatric acute liver failure (ALF) in a tertiary care setting. Viral hepatitis, especially Hepatitis A and E, emerged as the most common causes, while inborn errors of metabolism were associated with the highest mortality. Key clinical and biochemical markers such as hepatic encephalopathy, elevated INR, hyperammonemia, and hypoglycemia were significantly associated with poor outcomes. The use of N-acetylcysteine showed promising survival benefits, whereas the need for mechanical ventilation and presence of cerebral edema indicated severe disease and higher mortality. Limited access to liver transplantation remains a major challenge in resource-constrained settings. Early recognition of high-risk features, prompt supportive care, and targeted investigations are crucial to improving survival in pediatric ALF. Region-specific data such as this can inform clinical protocols and help guide timely referrals and policy planning for liver transplant accessibility.

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