

PCRRT Expert Committee Iconic Practice Points on Prescribing Kidney Replacement Therapy in Critically Sick Children with Acute Liver Failure



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Introduction

- Acute liver failure (ALF) refers to the development of encephalopathy and synthetic dysfunction without a pre-existing liver disease.¹
- The Pediatric ALF Study Group (PALFSG) outlines ALF in the pediatric population as:
 - biochemical evidence of liver injury,
 - absence of known pre-existing chronic liver disease,
 - coagulopathy not corrected by vitamin K administration, and
 - an International Normalized Ratio (INR) >1.5 if the patient has encephalopathy or > 2.0 if the patient does not.²
- The incidence of AKI in PALF can range from 40-85% depending on the etiology.³

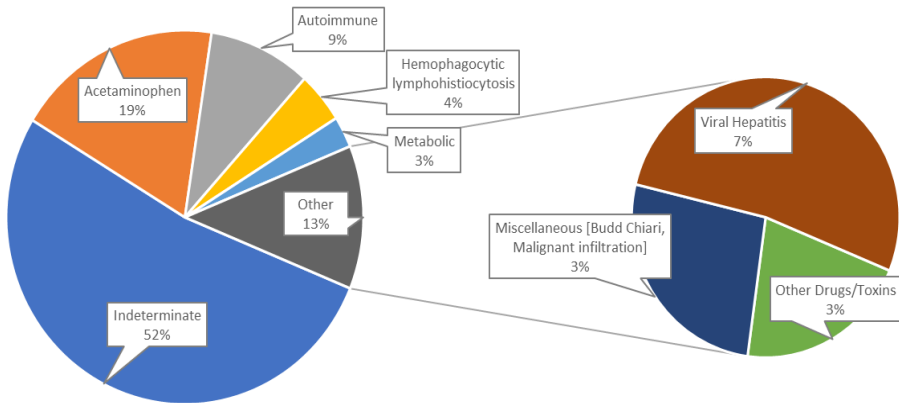


Figure 1. Etiology of ALF in pediatrics⁴⁻⁷

- 52.50%- Indeterminate origins
- 18.70% - Acetaminophen toxicity
- 9.30% - Autoimmunity
- 4.40% - Hemophagocytic lymph histiocytosis
- 6.50% Viral infections
- 2.70% Metabolic diseases
- 2.60% - Other drugs/toxins
- The outcomes of ALF are worse for those who require kidney replacement therapy (KRT) (37%) compared to those without AKI (64%).¹³
- A combination of dialysis modalities may serve an essential role in managing such patients.¹⁹
 - CKRT- Continuous KRT
 - ECLAD’s - Extracorporeal liver-assist devices
 - TPE - Therapeutic plasma exchange
 - MARS - Molecular adsorbent recirculating system
 - SPAD - Single pass albumin dialysis

Objectives

- Inferences can be made from studies about AKI in adult s with ALF and the same techniques can be applied to pediatrics.

Methodology

- Design:** This is a systematic review of AKI in PALF.
- Study Population:** Pediatric patients with acute or chronic liver failure who received Renal Replacement therapy of any form.
- Study Variables:** Mortality/ Survival, Bridge to Transplantation
- Data Collection** Eight studies (one prospective, one case-control, and six retrospective studies) with 196 patients aged 0-18 years old with AKI in PALF were included.

Results

Pediatric Incidence of AKI in ALF		
Study	Event / Sample size	Estimate (95% CI) %
Ferah O et al., 2019 ²⁷	9/51	17.65 (8.40 - 30.87)
Lal BB et al., 2018 ¹²	19/84	22.62 (14.20 - 33.05)
Rodriguez K et al., 2017 ²⁵	29/34	85.29 (68.94 - 95.05)
Moreau R et al., 2013 ²⁸	175/392	44.64 (39.65 - 49.72)
Kulkarnia S et al., 2008 ²⁹	102/583	17.50 (14.50 - 20.83)
Total (random effects)	334/1,144	36.23 (18.76 - 55.82)

Table 1: Meta-analysis of proportion of AKI among ALF patients across different studies

Pediatric Mortality of AKI in ALF		
Study	Event / Sample size	Estimate (95% CI) %
Ferah O et al., 2019 ²⁷	2/9	22.22 (2.81 - 60.01)
Lal BB et al., 2018 ¹²	10/19	52.63 (28.86 -75.55)
Moreau R et al., 2013 ²⁸	26/175	14.86 (9.94 - 21.01)
Total (random effects)	38/203	28.86 (8.10 - 56.00)

Table 2: Meta-analysis of proportion of mortality among AKI patients with ALF across different studies

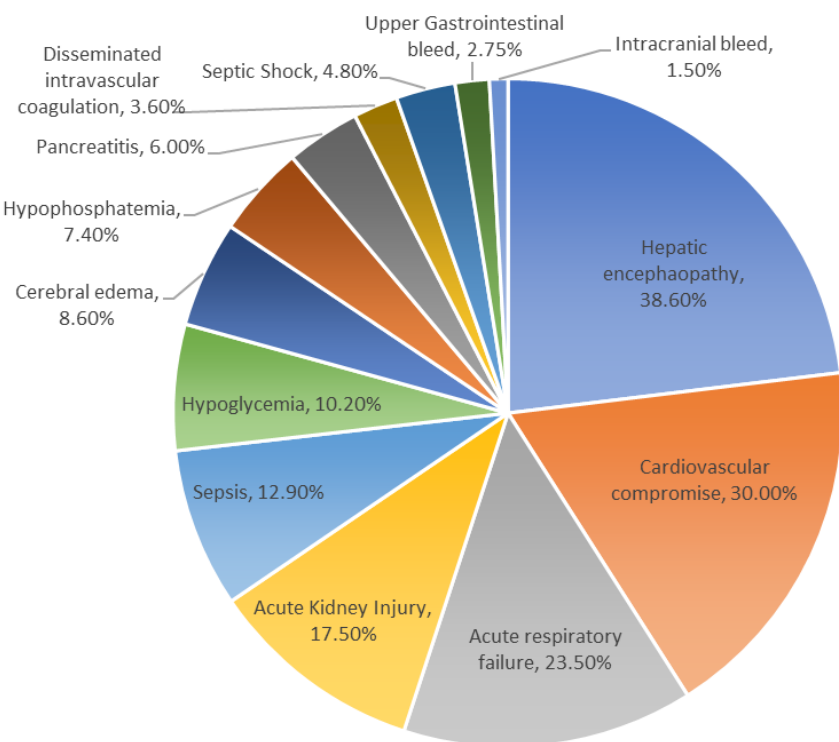


Figure 2. Outcome of ALF in Pediatrics⁴⁻⁷

- 38.60% - Hepatic Encephalopathy
- 30.00% - Cardiovascular compromise
- 23.50%- Acute respiratory Failure
- 17.50% - Acute Kidney Injury
- 12.90% - Sepsis

Discussion

Conservative Management

- There are limited studies on albumin, vasoconstrictors, and vaptans in the pediatric population, but literature regarding their proven efficacy in adults is applicable.
- Albumin infusions have shown to be potentially effective in volume expansion in AKI.
- Large-volume paracentesis in the setting of respiratory compromise or fluid overload may be followed by an albumin infusion

KRT Indicators

- Cystatin-C estimates of eGFR are the most accurate in pediatric ALF with AKI.
- KRT is suggested to be initiated in children with the following conditions:
 - Electrolyte and Metabolic abnormalities resistant to fluid therapy (metabolic acidosis, hyponatremia, hyperkalemia, hypermagnesemia)
 - Hyperphosphatemia (Uremia with bleeding, Elevated lactate level)
 - Hepatic encephalopathy (Grade 3-4)
 - Ammonia >150 μ mol/L and uncontrolled or >200 μ mol/L
 - Fluid overload
 - Severe hemodynamic instability
 - Pericarditis
 - Increased ICP following the failure of mannitol and hypertonic saline treatment

Discussion

Modalities of KRT

- The literature on the use of CKRT’s in PALF with AKI is limited, but positive.
- CKRT is suggested over IHD due to the slower rate of solute removal, gradual correction of hyponatremia, hemodynamic stability, and risk in increasing intracranial pressure.

Machines and circuits for KRT

- CKRT machines may be able to modify blood and dialysate flow rates according to the child’s weight.
- In neonates, the total extracorporeal blood volume may exceed 10% (unlike pediatrics) with the use of crystalloids, colloids, or packed RBCs to prime the circuit.
- High flux dialyzers can be applied if administering hemofiltration and should account for the body weight and surface area of the patient.

Vascular Access

- The right internal jugular vein is the ideal catheter insertion site for children <20 kg or if the catheter is <10 F.
- Large diameter catheters should be utilized for safe and efficient with reduced risk of complications.
- Ultrasound guided insertion is suggested for efficiency.

Dialysis/Replacement Solution

- Lactate free dialysate solution may be utilized in the pediatric population with ALF.
- Increased concentration of calcium and sodium can support hemodynamic stability.

Blood and Dialysate Flow Rate and Dialysis Dose

- The panel suggests using high-volume CKRT between 60 and 120 mL/kg/h, depending on ammonia clearance as well as the clinical and biochemical response.

Initiation, Duration, and Monitoring

- Early initiation of KRT is suggested, especially as a bridge to liver transplantation in critically ill pediatric patients with ALF.
- A combination of CKRT, MARS, and TPE may be used for treatment in AKI with ALF
 - High-volume CKRT is suggested for treating ALF, maintaining fluid balance, recovering metabolic function, and removing water soluble toxins.
 - MARS is suggested for hepatic encephalopathy
 - TPE is suggested for coagulopathy

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