Introduction

AKI affects a significant proportion of critically ill children. Although the reported incidence is variable due to its various definitions – a recent study using the KDIGO AKI definition reported that around 25% of all children admitted to a pediatric intensive care unit (PICU) had some form of AKI and of them 6% needed some form of RRT. The mode of RRT available includes the para-corporeal mode i.e. peritoneal dialysis (PD) and the blood based extracorporeal modes which includes HD and HF with or without dialysis (CVVHD/CVVHDF/CVVH). Along with these standard modes is the hybrid mode such as SLED which can be combined with hemofiltration (SLED-F). Pediatric population with AKI presents with challenges quite different from adult population. Among these one of the most important challenge is the wide range of sizes we encounter in pediatric practice- from newborn (term/preterm babies) with weight as low as 1 kg or even below to right up to obese adolescent. As “one size never fits all”, we need to often adapt the RRT prescription on a case by case basis.

We recommend that a unit delivering pediatric RRT should be able to provide full range of RRT, i.e., PD and all modes of blood-based RRT.

We suggest that this should be done in a child-friendly environment through health personnel who have been trained in pediatric RRT. The unit should preferably have access to a multi-disciplinary pediatric team with experience in other pediatric subspecialties.

Indications for initiation of renal replacement therapy in pediatric acute kidney injury

We recommend initiating RRT in AKI when any of the conditions below are present [Table 1].

Among these indications fluid overload has emerged as a new established indication over the last decade with studies repeatedly showing it to be an independent marker of mortality in paediatric AKI. Most of the PICU will initiate fluid removal once the fluid overload in the child exceeds 15%. If diuretic fails or is not feasible (such as intravascular depletion despite overall fluid overload, as often seen in nephrotic syndrome, liver cirrhosis or congestive cardiac failure) RRT is indicated for fluid removal.

Recommendations for initial choice of type of renal replacement therapy in pediatric acute kidney injury

We suggest that any of the following modes of RRT may be used in the critically ill child with AKI, and that treatment may need to be individualized.

Technically all modes of dialysis as mentioned above can be used in pediatric AKI. Concomitant hypotension/shock often present in children with AKI in PICU makes IHD difficult as they are not able to tolerate the sudden intravascular volume changes which this mode entails. Table 2 summarizes a detailed account of the pros and cons of the various modalities. Extracorporeal RRT is also challenging in small children particularly in infants because of the difficulty in getting appropriate vascular access as well as size appropriate dialyzers and dialysis tubing.

- We suggest that neonates and infants less than 10 kg should be managed with PD except where expertise and infrastructure is available for CVVH/SLED.
- We recommend that hemodynamically unstable children with AKI such as those with sepsis should be managed by PD or CVVH or SLED as they are unlikely to tolerate IHD.
- We suggest that if CVVH/SLED are not available, PD may be used as a mode of RRT even among sick in children in PICU.
- CVVH and SLED have some advantages over standard PD such as better clearance and more control over UF but are significantly more expensive than PD and require sophisticated infrastructure and expertise.
- Till date there are no evidence suggesting one mode of RRT to be superior to another in pediatric AKI.
- We suggest that there are very few relative contraindication to PD such as surgical abdomen, gastroschisis and diaphragmatic hernia
- We suggest that hemodynamically stable children with AKI can be managed with IHD provided size appropriate dialyzers and dialysis circuit is available.
- We suggest that the form of CRRT either CVVH, CVVHD, or a CVVHDF, should be chosen according to available clinician expertise.
- We suggest that in presence of appropriate expertise and infrastructure SLED can be tried as a cheaper alternative to CVVH.
- We recommend that all therapies should be veno-venous

Table 1: Indications for initiation of renal replacement therapy in pediatric acute kidney injury

| Condition                                      |
|------------------------------------------------|
| Refractory electrolyte imbalance               |
| Refractory fluid overload (>15% weight gain refractory to diuretics) |
| Refractory acidosis                            |
| Uremic organ involvement (pericarditis, encephalopathy, neuropathy, myopathy) |
| Progressive severe dysnatremia (Na⁺ >160 or <115 mEq/L) |
| Non-obstructive oliguria (<200 ml/12 h) or anuria (<50 ml/12 h) |
| Malignant Hyperthermia                         |
| To create space for nutrition in oliguric/anuric children |
| Removal of endogenous toxins (e.g., ammonia)/exogenous toxins (i.e., poisons) |
| Neonatal hyperammonemia and other inborn errors of metabolism. |
and pump driven using dedicated machines with safety devices including blood leaks, transmembrane pressure and air detection alarms.

- We do not recommend use of AV techniques as efficacy & safety monitoring may be inadequate.
- We suggest that patients with concomitant AKI and hepatic failure or traumatic brain injury be treated with peritoneal dialysis, CRRT or SLEDD Sustained low efficiency daily dialysis, rather than IHD. Advanced liver disease with AKI and traumatic brain injury are associated with raised intracranial pressure, which is worsened by IHD. By contrast ICP intracranial pressure is unaffected or slightly lowered by CRRT, while a single study suggests that SLEDD is similar to CRRT with respect to ICP.

### Vascular Access for Pediatric Blood-based Renal Replacement Therapy

Acute blood-based RRT is usually done though vascular catheters acting as temporary vascular access.

We recommend that:
- Catheters should be of biocompatible material
- Wide range of blood lines should be available as in pediatric one has to deal from small babies to large adolescents [Table 3]
- We suggest that stiff temporary catheters (vascath) use for vascular access be restricted to acute HD for a period of less than 3 weeks
- All temporary lines carries a high risk of catheter acquired infection and should be converted to cuffed permanent line if HD is continued beyond 3–4 weeks.
- Dedicated dual-lumen temporary catheter should be preferred
- Largest possible lumen size should be used. We recommend that the diameter of the vascular access catheter should not exceed 50% of the vein it is being inserted into. Ultrasonographic measurements and real time imaging at the bedside should be used to ensure this.
- We suggest that the vascular access may be inserted in either the femoral or IJVs.
- IJV access is superior to subclavian vein because it preserves the future AVF implantation on the arm of the child if he / she evolve into ESRD.
- Femoral access should be used only in emergency, and should not be in place for longer than 7–10 days because of higher risks of infection as well as thrombosis.
- We suggest that a vein should be dedicated for the dialysis access to prevent interference with antibiotics, nutrition, and inotropes which are being continuously infused. Thus, if an IJV has been chosen by the ICU team for infusions, we suggest siting the dialysis access in the femoral vein at least in the initial stage when a patient is on maximum pressors.

### Table 2: Modes of renal replacement therapy

| Procedure                  | PD | IHD   | CVVHD | SLEDD |
|----------------------------|----|-------|-------|-------|
| Continuous therapy         | Yes| No    | Yes   | Intermediate |
| Hemodynamic stability      | Yes| No    | Yes   | Yes   |
| Ease of achieving required fluid balance | May not be possible | Difficult if unstable | Yes | Yes |
| User friendly              | Yes| Yes   | Yes   | Yes   |
| Solute removal             | Low| Yes   | Yes   | Yes   |
| Control over ultrafiltration | Variable | Yes   | Yes   | Yes   |
| Anticoagulation free       | Yes| Possible | Difficult* | Possible |
| Removal of toxins in poisoning cases | Not very effective | Yes | Variable | Yes |
| Nursing requirement        | Low| Moderate | High | Moderate |
| Patient mobility           | No | Yes   | No    | Yes   |
| Cost                       | Low| Moderate | High | Moderate |
| Need for vascular access   | No | Yes   | Yes   | Yes   |
| Infection risk             | Yes| Yes   | Yes   | Yes   |
| Utility in inborn errors of metabolism | No^ | Yes | Yes | Yes |

*Regional citrate anticoagulation may be required. PD: Peritoneal dialysis, IHD: Intermittent hemodialysis, SLEDD: Sustained low-efficiency dialysis, CVVHD: Continuous venovenous hemodialysis

### Table 3: Catheter sizes and insertion sites

| Patient size          | Catheter size                          | Site of insertion                  |
|-----------------------|----------------------------------------|------------------------------------|
| Neonates/small infants| Umbilical venous Catheter/umbilical artery Catheter - 3.5/5 F or two single-lumen 5 F or double-lumen 6.5, 7 F | Umbilicus |
| Weight up to 20 kg    | Double-lumen 8F                         | Femoral/jugular vein               |
| Weight 20 to 30 kg    | Double-lumen 10F                        | Femoral/jugular vein               |
| Weight over 30 kg     | Double lumen 11.5F                      | Femoral/jugular veins (NB: rarely, inferior vena cava can be accessed through translumbar or trans hepatic access. Subclavian should be avoided and used only in emergency and where other access attempts have failed) |
Selections of Machines for Undertaking Blood-Based Renal Replacement Therapy

Recommendations

**Intermittent hemodialysis**

We suggest that standard HD machines used for MHD can be used for IHD for AKI.

**Sustained low-efficiency dialysis**

We suggest that a machine be chosen for SLED, which can deliver the lowest possible dialysate flow, at least as low as 300 mL/min.

In adults most often standard HD machine can be used for SLED. Unfortunately, most of the available HD machines are unable to reduce the dialysate flow below 200 mL/min – 300 mL/min [most machines deliver minimal dialysate flows rate of 300 mL/min, ArrT plus delivers flows of 200 mL/min – Table 4]. Ideally, in SLED, the dialysate flow rate should not exceed twice the BFR lower dialysate flow rate is often required in smaller children. (Currently, Fresenius 5008 is able to provide a dialysate flow rate as low as 100 mL/min). This machine has an optional pediatric module with dedicated software.

### Table 4: Machines for SLEDD

| Parameter                                      | Fresenius 5008 | Fresenius ArrT plus | DBB-07 Nikissho | Artis (Gambro) | Diamax | Dialog Plus (B Braun) |
|------------------------------------------------|----------------|---------------------|-----------------|----------------|--------|-----------------------|
| Water requirement                              | 1.5-6 bar      | 1.5-6 bar           | 1-7 bar         | 1-6 bar        | 1-4 bar | 0.5-6 bar             |
| Electricity requirements                       | 100-240 V AC, 47-63 Hz | 100-240 V AC, 47-63 Hz | 220-240 V AC, 50/60 Hz | 220-240 V AC, 50/60 Hz | 120-230 V AC, 50/60 Hz |
| Blood Flow                                     | 30-600 mL/min | 5-500 mL/min        | 40-600 mL/min   | 0-580 mL/min   | 300-700 mL/min in increments of 100 | 30-560 mL/min |
| Dialysate flow                                 | 0-1000 mL/min in increments of 100 | 200-800 mL/min | 300-700 mL/min in increments of 100 | 300-800 mL/min in increments of 100 | 300-700 mL/min in increments of 100 | 30-560 mL/min |
| Heparin pump                                   | Syringe 0.5 to 10 mL/h | Syringe 0.5 to 10 mL/h | Syringe 0-9.9 mL/h | Syringe         | Syringe | Syringe               |
| Ultrafiltration                                | 0-4000 mL/h (in steps of 10 mL) | 0-4000 mL/h (in steps of 10 mL) | 0.1-4000 mL/h | 0-4000 mL/h | 100-5000 mL/h | 0-5500 mL/h |
| Maximum treatment time (h)                     | 24             | 10                  | 12              | 24             | 6       | 10                    |
| Compatibility with multiple dialyzer and tubing sets | Yes        | Yes                | Yes             | Yes            | Yes     | Yes                   |
| Sodium and ultrafiltration profiling           | Custom         | Custom             | Also bicarbonate profiling | Also bicarbonate | Flexible | Flexible              |
| Dialysate sodium/ conductivity range           | 125-151 mmol/L, (12.8-15.7 mS/cm) | 125-151 mmol/L, (12.8-15.7 mS/cm) | 12.5-15.5 mS/cm | 130-160 mmol/L | 10-17 mS/cm | 12.5-16 mS/cm |
| Dialysate temperature range                    | 34°C-39°C      | 34°C-39°C           | 34°C-40°C       | 30°C-39°C      | 30-40°C | 33°C-40°C            |
| Dry powder concentrate use*                    | Bibag (650 or 900 g) | Bibag (650 or 900 g) | No              | Yes (Bicart) Acetate-free citrate bicarb sterile concentrate available | No | Yes Solucart or Bicart |
| Online replacement fluid preparation           | Yes            | Yes                | Yes             | Yes            | No      | Yes                   |
| Heated citrate                                 | 85°C           | 85°C               | 85°C            | 85°C           | 65°C    | 85°C                  |
| Peracetic acid/sodium hypochlorite             | 37°C           | 37°C               | 37°C            | 37°C           | Not specified | 37°C                  |
| System self-test                               | Yes            | Yes                | Yes             | Yes            | Yes     | Yes                   |
| Additional features                            | OCM, BTM, and BPM | OCM, BTM, and BPM | DDM, BVM and BPM | Diascan and Hemoscan monitors | Not specified | Online Kt/V available |

OCM: Online clearance monitor, BTM: Body temperature monitor, BPM: blood pressure monitor, TMP: transmembrane pressure
Fresenius Medical Care has recently (July 2017) recommended that the 5008 machine not be used in children <17 kg following reports of balancing system errors. This has led to concern that excessive UF can occur in smaller children, a potential hazard.

**Sustained low-efficiency dialysis hemofiltration (sustained low-efficiency dialysis -F)**

We suggest that machines capable of generating online fluid may be used for HDF and SLED-f. These should be equipped with at least 2 and preferably a 3rd ultrafilter in the replacement fluid delivery circuit. All machines should be of a “fail safe” design.

**Continuous veno-venous hemofiltration /continuous venovenous hemodiafiltration**

We suggest that machines used for CRRT have the following specifications.

All machines used for CRRT should be dedicated, with their own disposables. The machines should have a minimum of 3 and preferably 4 or more pumps to make all forms of treatment possible. The machines should have an error of <2.5% in measurement of UF volumes. Gravimetric balancing scales are preferable to flow measurements. Table 5 summarizes the key features of the available CRRT machines.

**Dialysis Fluid and Replacement Fluid**

**Recommendations**

- For IHD and SLED, we recommend that bicarbonate based dialysate should be used.
  - We suggest that Bicarbonate based dialysate be used in CRRT.
  - The dialysis fluid sodium is normally kept between 135 and 140 mmol/L with the gap between serum sodium and dialysis sodium not exceeding 10 mmol/L.
  - We suggest not using a zero potassium in pediatric HD because of risks of arrhythmia and normally potassium is kept at 2 mmol/L. Higher potassium may be used in cases of hypokalemia.
  - We recommend that calcium concentration in the dialysis fluid is normally kept around 1.5 mmol/L.
  - We suggest that dry powder citrate bicarbonate dialysate be used for SLED in the ICU. The final dialysate contains a citrate concentration of 2–3 mmol/L and this decreases the chance of extracorporeal circuit clotting. Ahmed et al. have shown remarkable success in performing SLED without any anticoagulation using dry citrate bicarbonate concentrates even in AKI patients with acute hepatic failure.
  - We suggest using high dialysis fluid calcium and sodium and low dialysis fluid temperature to improve tolerance among hemodynamically unstable children in PICU.
  - Whenever online HDF or SLEDD-f is carried out it is mandatory to ensure that the water used for dialysis is of ultrapure standard.
  - We recommend that isotonic bicarbonate based fluid be preferred as replacement fluid in CRRT.
  - We recommend that calcium-free dialysate and replacement fluid (Biphozyl) should be used in patients receiving regional citrate anticoagulation.

| Machine parameter       | Prismaflex (Baxter/Gambro) | Multifiltrate (Fresenius) | Multifiltrate (pediatric option) | Diapact (B. Braun) |
|-------------------------|---------------------------|---------------------------|---------------------------------|-------------------|
| Electrical requirement  | 100-240 V, AC, 50/60 Hz   | 100-240 V, 3.2 A, AC 50/60Hz | 100-240 V, 3.2 A, AC 50/60Hz   | 110-240 V, 3.5 A, AC 50/60Hz |
| Roller pumps            | 5                         | 6                         | 6                               | 3                 |
| Scales                  | 4                         | 4                         | 4                               | 3                 |
| Principle               | Gravimetric               | Gravimetric               | Gravimetric                     | Gravimetric       |
| Range of load cell      | 0-11 kg                   | Up to 24 kg               | Up to 24 kg                     | 0-27 kg           |
| Filter sets             | Dedicated                  | Dedicated cartridges, but any filter/dialyzer usable Individual tubing lines can be changed | Dedicated cartridges, but any filter/dialyzer usable Individual tubing lines can be changed | Dedicated but filter change possible with luer lock and Hansen connector system Individual tubing lines can be changed |
| Blood flow rate         | 10-450 ml/min             | 10-500 ml/min             | 10-100 ml/min                   | 10-500 ml/min     |
| Dialysate flow rates    | 0-8000 ml/h               | 100-4800 ml/h             | 100-1500 ml/h                   | 0-300 ml/min      |
| PBP rate                | 0-8000 ml/h               | -                         | -                               | -                 |
| Replacement fluid       | 0-8000 ml/h               | 100-9600 ml/h             | 100-3000 ml/h                   | 0-250 ml/min      |
| Effluent                | 0-8000 ml/h               | 12 L                      | -                               | 0-400 mL/min      |
| UF rate                 | 0-2000 ml/h               | 0-1800 ml/h               | 0-500 ml/h                      | 0-2000 ml/h       |
| Heparin                 | 50-ml syringe             | 50-ml syringe             | 50-ml syringe                   | 50-ml syringe     |
| Regional citrate        | Possible one external pump | Possible integrated       |                                 | Not specified     |
| anticoagulation required|                           |                           |                                 |                   |

UF: Ultrafiltration, PBP: Pre blood pump
• The PBP bag should be Regiocit for this treatment.

Table 6 shows the available fluids with their composition for use in CRRT.

**Recommendations for dialyzers and hemofilters**

Similar to mode of dialysis; strong evidences in favor of any particular type of dialyzer resulting in lower mortality or better long term kidney survival is lacking.

We recommend that

• Synthetic dialyzers (polysulfone [PS], polyacrylonitrile [PAN] and polycarbonate) should be preferred because of their lower immunogenicity and better solute removal.

• Bio-incompatible cuprophane dialyzers should be avoided in ICU since they carry increased risk of mortality compared to bio-compatible membranes.

• High flux dialyzer with bigger pore size does guarantee better solute / fluid clearance but should only be used with ultrapure water as otherwise there is a chance of backfiltration of endotoxins into the blood stream.

• The size of the dialyzer is calculated by its surface area and is available in a wide range (0.2 m² to 1.7 m²). The surface area should be as large as possible to optimize clearances but should not exceed that of the child.

However for the first HD session dialyzer surface area should not exceed 75% of body surface area to avoid disequilibrium syndrome.

• Standard IHD and SLED may be carried out with low-flux dialyzers.

• SLED-f requires high-flux, ultra-flux or special high-porosity dialyzer

• CRRT requires special hemofilter sets, usually as part of a complete set, each of which is compatible with specific machines only.

Table 7 contains a list of pediatric dialyzers with their specifications while Table 8 contains those of CRRT sets currently available in India.

### Extracorporeal Circuit Recommendation

We recommend that

• The total extracorporeal blood volume (tubing and dialyzer) should preferably be less than 10% of the child’s total blood volume.

Formula for calculating total blood volume (TBV):
- Infant or < 20 kg: 80 mL/kg
- Children or 20–50 kg: 70 mL/kg
- Adult or > 50 kg: 60 mL/kg

---

**Table 6: Dedicated fluid bags for continuous renal replacement therapy**

| Composition (mmol/L) | MultiBic (Fresenius) | Multiplus (Fresenius) | Prismasol (Gambro) | Regiocit (Baxter) | Biphozyl (Baxter) |
|----------------------|----------------------|----------------------|--------------------|------------------|------------------|
| Sodium               | 140                  | 140                  | 140                | 140              | 140              |
| Potassium            | 0-4                  | 2                    | 0                  | 0                | 4                |
| Calcium              | 1.5                  | 1.5                  | 1.75               | 0                | 0                |
| Magnesium            | 0.5                  | 0.75                 | 1                  | 0                | 0.75             |
| Chloride             | 110                  | 110                  | 110                | 86               | 122              |
| Bicarbonate          | 35                   | 35                   | 32                 | 0                | 22               |
| Phosphate            | -                    | 1                    | -                  | -                | 1-2              |
| Glucose              | 5.55                 | 5.55                 | 0                  | 0                | 0                |
| Citrate              | -                    | -                    | -                  | 18               | -                |
| Osmolality (mOs/L)   | 290-300              | 300                  | 287                | 244              | 290              |

**Table 7: Dialyzers/hemofilters for sustained low-efficiency dialysis**

| Parameter                  | Sureflux 5N (Nipro) | FX40 (Fresenius) | FX ped (Fresenius) | Polyflux 6H (Gambro) |
|----------------------------|---------------------|------------------|-------------------|---------------------|
| Surface area (m²)          | 0.5                 | 0.6              | 0.2               | 0.6                 |
| Priming volume (mL)        | 34                  | 53               | 18                | 52                  |
| UF coefficient             | 2.7                 | 20               | 7                 | 33                  |
| Urea clearance             | 130*                | 170*             | 76*               | 50*                 |
| Creatinine clearance       | 109*                | 144*             | 64*               | 50*                 |
| Phosphate clearance        | 62*                 | 138*             | 57*               | 49*                 |
| Material                   | Cellulose triacetate| Helixone         | Helixone          | Polyflux^            |
| Fiber inner diameter (micron) | 200             | 185             | 220              | 215                 |
| Thickness                  | 15                  | 35               | 35                | 50                  |
| Blood flow (mL/min)        | 50-200              | 30-100           | 50-200            |                     |
| Sterilization              | Gamma ray           | Inline steam     | Inline steam      | Inline steam        |

*At Qb=200 ml/min, ^At Qb=50 ml/min, Polyflux is a blend of polyarylethersulfone, polyvinylpyrrolidone, polyamide, UF: Ultrafiltration
• Blood tubing are available in three sizes that vary in their priming volume:
  (a) Neonatal – 25 mL
  (b) Pediatric – 75 mL
  (c) Adult – 127 mL.

Dialyzer volume is usually given in the product information package
N.B. Dialyzer’s volume should be added to the tubing volume to estimate the total extracorporeal blood volume
• We suggest that an effort should be made to ensure availability of appropriate size tubing. In its absence and if the blood circuit volume exceeds 10% of blood volume, one can try priming of blood circuit, i.e., filling up the blood circuit with blood or 5% albumin prior to start of dialysis to avoid hypovolemia.

**Recommendations for blood and dialysate flow rate**

We suggest that even in hemodynamically stable children BFR should not exceed 10 mL/kg/min.

Higher BFR equates to better clearance but as it also entails rapid blood volume shift it is often not tolerated in hemodynamically unstable children. In such scenarios the BFR needs to be reduced and to compensate for this, one needs to increase the duration of dialysis.

High dialysis fluid flow rate (DFR) also improves clearance which plateaus around 500 mL/min. In SLED, reduced DFR ensures lower clearance rates with maintenance of plasma osmolality as well as better hemodynamic stability.

We recommend that

For intermittent hemodialysis
• BFR = Initially at lower limit of 2–3 mL/kg/min and as tolerated increased to an upper limit of 5–7 mL/kg/min,
  \( \text{DFR} = 500 \text{ mL/min} \)

For sustained low-efficiency dialysis
• BFR should be \( \leq 5 \text{ mL/kg/min} \) (up to a maximum of 200 mL/min) and DFR should be \( \leq \) twice of BFR

---

**Table 8: Filter sets for continuous renal replacement therapy**

| Filter specifications | M100 | M60 | HF20 | Ultraflux AV Paed |
|-----------------------|------|-----|------|-------------------|
| Membrane              | AN-69| Polysulfone | Polysulfone |
| Housing and headers   | Polycarbonate | Polycarbonate | Polycarbonate |
| Surface area (m²)     | 1.0  | 0.6 | 0.2  | 0.2              |
| Appropriate patient weight (kg) | 30 | 11-29 | <8 | <10 kg |
| Blood flow (mL/min) minimum to maximum | 75 and above | 50 and above | 20-100 | No data |
| Set blood volume (mL) | 152 | 93  | 60   | 54 mL           |
| Priming volume (mL)   | 66   | 42  | 24   | 18              |
| Maximum TMP (mmHg)    | 450  | 450 | 500  | 500             |
| Clearance in CVVHD mode with UF=0 at Qb=150 mL/min and effluent 2.5 L/h | at Qb=100 mL/min and effluent 1 L/h | at Qb=50 mL/min and effluent 0.5 L/h | No data |
| Urea (mL/min)         | 41   | 17  | 8.3  | No data |
| Inulin (mL/min)       | 23   | 12  | 6.9  | No data |

UF: Ultrafiltration, TMP: Transmembrane pressure, CVVHD: Continuous venovenous hemodialysis

---

**For sustained low-efficiency dialysis-F**

• The BFR should be 5–7 mL/kg/min up to a maximum of 200 mL/min.

• The total UF rate (desired hourly UF and replacement fluid rate) should be predetermined by the patient’s requirement and the blood flow set thereafter so that the filtration fraction is <25% of the blood flow (specially applicable to HF and HDF). The machine automatically calculates fluid removal from the set UF and replacement fluid volumes, but the filtration fraction has to be calculated by the operator when writing the prescription.

**For continuous renal replacement therapy**

We recommend a BFR of 2–4 mL/kg/min up to a maximum of 150 mL/min.

We recommend that the total effluent volume should be 2 L/h/1.73 m² or 30 mL/kg/h. This dose has been used in three observational pediatric studies, but unlike in adults no randomized controlled studies on dose comparison have been performed.

The machine calculates and displays the effluent rate and dose in ml/kg/hour from the input values of PBP, dialysate, replacement fluid and patient fluid removal rates. Based on the anthropometric data of weight, hematocrit and choice of pre or post replacement fluid the machine also displays the filtration fraction.

**Recommendation for duration of renal replacement therapy**

Duration of the RRT session depends on multiple factors including:
(a) Degree of uremia and whether it is the first session or whether the child already has had previous sessions of RRT.
(b) Extent of fluid overload and the fluid removal target for the specific session.
(c) Type of RRT, i.e., whether IHD or SLED or CVVH
(d) Manpower and machine availability.
• Classical IHD is for 3–4 h and SLED is defined as session of 6 h or longer
• We recommend that the duration for first HD is kept to a minimum particularly in cases with severe azotemia, to avoid dialysis disequilibrium. Initial target is to reduce urea by 30% and hence first IHD session is usually for less than an hour
• We suggest that formal urea kinetic modeling can be used to calculate the first session length from the dialyzer specifications, blood flow and initial blood urea level
• Mannitol at 1 g/kg can be given at the starting of the initial RRT session in order to maintain vascular volume / prevent fluid shift into cells, even in the face of sudden drop in osmoles which can happen as the urea is reduced by dialysis. Addition of mannitol does increase the risk of intravascular fluid overload/ pulmonary edema and potential spike in BP but with mannitol one can aim a higher initial urea reduction up to 50%
• We recommend that the frequency of acute HD is decided as per the clinical requirement of the child depending on biochemical parameters and fluid overload. Usually in AKI daily RRT is needed at least initially
• We recommend that CRRT be performed as a continuous therapy and out of unit procedures be kept to a minimum during this time
• We recommend that effluent volumes be temporarily increased to compensate for down time during out of unit procedures.

Recommendation for ultrafiltration goal

We recommend that the UF goal be chosen based on degree of fluid overload and the hemodynamic status of the child.
• The initial rate of UF during conventional HD should be about 10 mL/kg/h and should not exceed 0.2 mL/kg/ min or 5% of body weight in one session.
• In critically ill children with hemodynamic instability, rate of UF has to be much lower and these children benefit from CVVH or SLED where in significant UF is possible without hemodynamic compromise as small volumes are removed hourly but over a prolonged period resulting in significant cumulative fluid removal.
• We suggest that patient net fluid removal in CRRT be set at 2–4 mL/kg/h
• We recommend that UF in CRRT or SLEDD-f is the total of desired UF, and replacement fluid and should not exceed 25% of the blood flow.

Recommendation for anticoagulation

As blood comes in contact with blood circuit it tends to clot and hence anticoagulation is required. Anticoagulation becomes a concern if clotting is altered such as in children with sepsis and disseminated intravascular coagulation (DIC) or liver failure. Standard anticoagulation protocol is usually heparin at specified dose.

We recommend that
• If not contraindicated unfractionated, heparin should be the anticoagulant of choice during IHD/SLED and CRRT. Doses according to body weight are shown in Table 10.
• After an initial loading dose of heparin, infusion may be initiated and adjusted according to the aPTT reports [Table 7]. In patients receiving LMWH, the same can be continued with the doses given just before a session of IHD or SLED. Bedside monitoring is not possible and the risk of bleeding is increased with the use of LMWH in AKI
• IHD can be conducted without heparin by using regular saline flushes. As usually children with altered coagulation in PICU are septic, hypotensive and on multiple inotrope standard IHD is difficult
• SLED is often more feasible in such critically ill children and recent publications have proven that heparin-free dialysis is possible in them
• For conducting heparin-free session the most commonly used process is regular flushes with saline equal to the circuit volume. One has to incorporate these volumes when estimating the net UF
• CRRT almost always requires anticoagulation and in patients with DIC, regional anticoagulation with citrate and calcium may be used
• We recommend that regional citrate anticoagulation be used for patients undergoing CRRT in whom systemic anticoagulation is contraindicated
• We recommend monitoring the blood and circuit levels of ionic calcium 2 hourly and the infusion rates adjusted in regional citrate anticoagulation. We suggest that the rates of citrate and calcium infusions be adjusted according to Table 9
• We suggest not using the option “Citrate anticoagulation with External Pump” in children or if used decreasing the blood flow to 2 to 2.5 mL/kg/h
Rationale – When the regional citrate anticoagulation with an external pump is used the PBP rate is automatically set at ten times the BFR by an inbuilt program to obtain a citrate concentration of 3 mmol/L. If the blood pump is set at 4 mL/kg/min, the PBP will automatically run at 40 ml/kg/h, which exceeds the prescribed effluent rate. Thus very little Biphozyl is delivered and the patient receives an overdose of citrate often leading to metabolic acidosis and excessive anticoagulation
• We suggest that regional anticoagulation with Regiocit and Biphozyl may be performed as follows: Set desired BFR. Start Regiocit (mL/hour) on the PBP line at 6 to 7.5 times the BFR (e.g., 600–750 mL/h for a blood flow of 100 mL/min). Prepare calcium gluconate solution of 250 mL of 10% calcium
Monitoring

As during extra corporeal RRT a significant percentage of TBV is outside the body it always has the potentiality of causing medical catastrophes. This is particularly so for hemodynamically unstable children. Monitoring of patient’s clinical condition is hence essential.

We recommend that the following clinical and laboratory parameters be monitored
- Vitals such as respiratory rate, pulse rate/pulse volume, BP, and oxygen saturation in critically ill children
- Input (IV fluids + oral fluids + IV medications and other infusions) and output (ultrafiltrate + urine output + extra renal loss) charting
- Hemoglobin, platelets, and bleeding parameters (prothrombin time and aPTT)
- Renal parameters including electrolytes
- Blood born virus screen (HBsAg, HCV, and HIV) should be done prior to HD.

N.B. SLED as it is done over a prolonged period has the potential of causing low electrolytes/phosphate and hence in children undergoing SLED they need to be monitored and sometime even may need to be supplemented.

Table 9: Dosing in regional citrate anticoagulation

| Circuit ionic calcium | Citrate dose adjustment |
|-----------------------|-------------------------|
| Patient weight        |                         |
| >20 kg                | Decrease by 40 mL/h      |
| <20 kg                | Decrease by 20 mL/h      |
| <0.35                 | No change               |
| 0.35-0.5              | No change               |
| 0.5-0.6               | Increase by 40 (mL/h)    |
| >0.6                  | Increase by 20 mL/h      |

Table 10: Heparin dose

| Weight (kg) | Heparin dose (IU/kg) | Total initial dose (IU) |
|-------------|----------------------|-------------------------|
| 5-15        | 10-16                | 50-250                  |
| >15-25      | 16-20                | 250-500                 |
| >25         | 20                   | 500-1000                |

Heparin rates per hour: 10-20 unit/kg/h aiming for ACT 150% or aPTT in 120-160 s, ACT: Activated clotting time, aPTT: Activated partial thromboplastin time

Glucose with 750 mL 0.9% normal saline. Start calcium gluconate infusion (mL/hour) through a separate central line and infusion pump at 0.5 times the blood flow (e.g., 50 mL/h for a blood flow of 100 mL/h) Adjust the rate of dialysate and replacement fluid with Biphozyl, desired UF and calcium gluconate infusion to obtain a total effluent volume of 2 L/h/1.73 m² or 30 mL/kg/h
- Monitor ionic calcium, potassium, and pH from the blood and ionic calcium from the circuit every 2-4 h and adjust infusion rates as per Table 9
- In heparin protamine regional anticoagulation, the aPTT of both the patient and the extracorporeal circuit between the sampling ports should be monitored. For an infusion of 500 units/h of heparin a neutralizing infusion of 5 mg/h of protamine will be required.

Recommendations for goals of renal replacement therapy
- Steady level in CRRT and predialysis level in IHD or SLED of BUN of ≤ 60 mg/dL should be achieved within 48 h after initiating dialysis
- Volume status as close to euvoelemia as possible
- Correction of acidosis to maintain pH ≥7.2
- Maintain serum electrolyte levels within reasonably normal limits (sodium: 130–148 mmol/L, potassium: 3.5–5.5).