

# Newborn Critical Care Center (NCCC) Clinical Guidelines

## Acute Kidney Injury

### BACKGROUND

Acute kidney injury (AKI) in the neonate/infant is associated with an increase in morbidity and mortality. Infants who survive AKI are at risk of developing renal dysfunction and chronic kidney disease later in life and, therefore, require long-term follow-up [1-5]. AKI is most common in the first week of life in very low birth weight (VLBW) infants, and the prevalence in infants with associated comorbidities is nearly 40% (see table below) [6].

	Prevalence (%)	Mortality AKI vs. no AKI (%)
	40	14 vs. 4
VLBW <sup>a</sup>	18	55 vs. 5
ELBW <sup>b</sup>	13	70 vs. 22
Sick near term/term	18	22 vs. 0
Sepsis	26	70 vs. 25
Asphyxiated	38	14 vs. 2
ECMO	71	73 vs. 20 <sup>c</sup>

<sup>a</sup>Very low birth weight (VLBW) infants <1500 g.  
<sup>b</sup>Extremely low birth weight (ELBW) infants <1000 g.  
<sup>c</sup>Extracorporeal membrane oxygenation (ECMO).

Risk factors for AKI include neonates born premature, SGA, intrauterine growth restriction [1, 2, 7], hypoxia secondary to respiratory failure or asphyxia [8, 9], hypoperfusion secondary to sepsis, ECMO, necrotizing enterocolitis, abdominal compartment syndrome, patent ductus arteriosus, cardiac disease, high mean airway pressures impairing venous return, decreased fluid intake or increased losses, nephrotoxic medication exposure, and anomalies of the kidney or urinary tract [10-16]. For these infants, it is important to avoid AKI, recognize it promptly if symptoms develop, alter clinical management to prevent disease progression, and appropriately monitor AKI resolution and possible long-term sequelae.

Through this guideline, we aim to maximize the accurate identification of neonates with AKI, utilize a multidisciplinary team approach to the management of neonates/infants with AKI, and standardize outpatient referral for neonates/infants diagnosed with AKI.

## CRITERIA

- AKI is an acute decline in kidney function that results in fluid and electrolyte imbalances/abnormalities and the accumulation of waste products [2]. The diagnosis of AKI depends on a rise in serum creatinine or a decrease in urine output [2].
- AKI is defined by the KDIGO Classification (2013) as outlined in Table 1 (below). These definitions should be used for infants <120 days of age.

**TABLE 1** Neonatal AKI KDIGO Classification

Stage	SCr	Urine Output
0	No change in SCr or rise <0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥ 0.3 mg/dL within 48 h or SCr rise ≥1.5–1.9 × reference SCr <sup>a</sup> within 7 d	<0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0–2.9 × reference SCr <sup>a</sup>	<0.5 mL/kg/h for ≥ 12 h
3	SCr rise ≥3 × reference SCr <sup>a</sup> or SCr ≥2.5 mg/dL <sup>b</sup> or Receipt of dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

Differences between the proposed neonatal AKI definition and KDIGO include the following:

<sup>a</sup> Reference SCr will be defined as the lowest previous SCr value.

<sup>b</sup> SCr value of 2.5 mg/dL represents <10 mL/min/1.73m<sup>2</sup>.

## MANAGEMENT

If the underlying etiology behind the AKI is known, treat the primary condition first while maintaining euvoemia, regularly monitoring renal function (minimum serum creatinine, sodium, potassium, chloride, bicarb, BUN, and urine output every 24 hours), and avoiding nephrotoxic medications to expedite recovery.

### *Physical Examination*

- Assessment of volume status including body weight and vital signs
- Follow strict intake and output (consider foley placement) and monitor daily weights

### *Laboratory Values*

- Obtain serum basic metabolic panel (BMP) and consider urinalysis via bagged specimen
- A single elevated creatinine should be repeated within a minimum of 24 hours

### *Imaging*

- Consider renal ultrasound with doppler to evaluate for congenital renal dysplasia, urinary obstruction, or renal vein thrombosis

### *Fluid Balance*

- A single 10mL/kg normal saline bolus should be considered if prerenal causes are suspected (more IV fluid or blood product (PRBC) may be required if the patient is hypovolemic)

- If the patient remains oliguric after fluid resuscitation, additional IV fluid or blood product should be used with caution due to the risk of anasarca and pulmonary edema
- Restrict fluid intake if there is no response to bolus or if intrinsic renal disease is suspected
- If oliguric with volume overload, consider a one-time dose of furosemide 1mg/kg IV and assess urine output [18]
  - Recheck electrolytes within 6 hours if giving furosemide

### **Limit Risk**

- Identify and treat modifiable risk factors such as infectious etiologies, cardiac dysfunction, or impaired venous return [19]
- Correct hypotension if necessary and obtain blood pressure measurements at a minimum of every 3 hours [20]
- Review with NCCC Pharmacist the need for adjusting medications based on renal clearance
- If possible, avoid nephrotoxic medications and consider other alternatives with NCCC Pharmacist consultation [21]

### **Manage Electrolyte Abnormalities**

- Hyperkalemia
  - For all patients with AKI, evaluate the need for removal of potassium and phosphorous from IV fluids and/or use a formula low in potassium and phosphorus, such as Similac PM 60/40 or plain breast milk
  - Correct hyperkalemia as determined by the [NCCC Hyperkalemia Guidelines](#)
- Metabolic acidosis
  - Consider maximizing acetate in parental nutrition if metabolic acidosis is present
  - If patient develops refractory metabolic acidosis, discuss with the attending physician regarding the use of sodium bicarbonate
- Hyponatremia
  - Consider obtaining plasma and urine osmolality and urine sodium levels to help determine whether hyponatremia is the result of fluid overload or total body sodium depletion
  - Restrict fluid intake rather than increasing sodium supplementation
  - If hyponatremia is severe (<120 mEq/L) or the infant is symptomatic (seizing, lethargic, refractory emesis), consider giving normal saline or 3% sodium chloride [18]

### Replacement of Deficit (mmol Na needed):

$$[\text{Desired Serum Na (mmol/L)} - \text{Actual Serum Na (mmol/L)}] \times \text{Weight (kg)} \times 0.6$$

- Consult nephrology for multidisciplinary management in the setting of severe hyponatremia
- Correction rate should not exceed 0.5-1 mmol/kg/hr (the slower the rate, the better to minimize sudden alterations in serum osmolality)
  - Hypertonic 3% saline (513 mmol/L) infused at a rate of 1.0mL/kg/hr
  - Check serum Na every hour during the first 3 hours of infusion and every 3 hours thereafter

### MONITORING

- Obtain a detailed medical history, including documentation of the presence of risk factors
- If the infant meets any of the above criteria for an AKI, a diagnosis of AKI should be made and “Acute Kidney Failure” should be added to the problem list (ICD 10 code: N17.9)
- If the AKI persists beyond 3 days or if the serum creatinine is  $\geq 2.5$  mg/dL, a Pediatric Nephrology consult should be considered
- Patients with a diagnosed AKI require follow-up by a pediatric nephrologist to evaluate for new onset or worsening chronic kidney disease [23, 24]. The timing of follow-up is dependent on the clinical course.
  - 3-6 months for any infant recovered from AKI requiring dialysis
  - 6-12 months for any preterm or SGA infant with severe AKI (SCr  $\geq 2.5$ mg//dL)
  - 6-12 months for any infant term or preterm with CHD or CLD or ECMO exposure and severe AKI (SCr  $\geq 2.5$ mg//dL).

## References:

1. Koralkar, R., et al., *Acute kidney injury reduces survival in very low birth weight infants*. *Pediatric research*, 2011. 69(4): p. 354-8.
2. Nada, A., E.M. Bonachea, and D.J. Askenazi, *Acute kidney injury in the fetus and neonate*. *Semin Fetal Neonatal Med*, 2016.
3. Mammen, C., et al., *Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: A prospective cohort study*. *American Journal of Kidney Diseases*, 2012. 59(4): p. 523-530.
4. White, S.L., et al., *Is low birth weight an antecedent of CKD in later life? A systematic review of observational studies*. *American Journal of Kidney Diseases*, 2009. 54(2): p. 248-261.
5. Askenazi, D.J., et al., *3-5 year longitudinal follow-up of pediatric patients after acute renal failure*. 2006. 69(1): p. 184-189.
6. Jetton, J.G., et al., *Assessment of worldwide acute kidney injury epidemiology in neonates: Design of a retrospective cohort study*. *Frontiers in Pediatrics* July 2016.
7. Carmody, J.B., et al., *Recognition and reporting of aki in very low birth weight infants*. *Clinical Journal of the American Society of Nephrology*, 2014. 9(12): p. 2036-2043.
8. Yanik, M., D. Askenazi, and N. Ambalavanan, *Acute kidney injury in neonates*. *NeoReviews*, 2015. 16(10): p. e586-e592.
9. Kaur, S., et al., *Evaluation of glomerular and tubular renal function in neonates with birth asphyxia*. *Annals of tropical paediatrics*, 2011. 31(2): p. 129-34.
10. Cuzzolin, L., et al., *Postnatal renal function in preterm newborns: a role of diseases, drugs and therapeutic interventions*. *Pediatric Nephrology : Journal of the International Pediatric Nephrology Association*, 2006. 21(7): p. 931-938.
11. Selewski, D.T., et al., *Neonatal acute kidney injury*. *Pediatrics*, 2015. 136(2): p. e463-73.
12. Selewski, D.T., et al., *Acute kidney injury in asphyxiated newborns treated with therapeutic hypothermia*. *The Journal of pediatrics*, 2013. 162(4): p. 725-729.e1.
13. Patel, D.M. and M.J. Connor Jr, *Intra-abdominal hypertension and abdominal compartment syndrome: An underappreciated cause of acute kidney injury*. *Advances in Chronic Kidney Disease*, 2016. 23(3): p. 160-166.
14. Blinder, J.J., et al., *Congenital heart surgery in infants: effects of acute kidney injury on outcomes*. *The Journal of thoracic and cardiovascular surgery*, 2012. 143(2): p. 368-74.
15. Viswanathan, S., et al., *Risk factors associated with acute kidney injury in extremely low birth weight (ELBW) infants*. *Pediatric Nephrology*, 2012. 27(2): p. 303-311.
16. Rhone, E.T., et al., *Nephrotoxic medication exposure in very low birth weight infants*. *Journal of Maternal-Fetal and Neonatal Medicine*, 2014. 27(14): p. 1485-1490.
17. *Section 2: AKI definition*. *Kidney International Supplements*, 2012. 2(1): p. 19-36.
18. Askenazi, D.J., et al., *Fluid overload and mortality are associated with acute kidney injury in sick near-term/term neonate*. *Pediatric Nephrology : Journal of the International Pediatric Nephrology Association*, 2013. 28(4): p. 661-666.
19. Jetton, J.G. and M. Sorenson, *Pharmacological management of acute kidney injury and chronic kidney disease in neonates*. *Semin Fetal Neonatal Med*, 2017. 22(2): p. 109-115.
20. *Summary of Recommendation Statements*. *Kidney International Supplements*, 2012. 2(1): p. 8-12.
21. Zappitelli, M., D.T. Selewski, and D.J. Askenazi, *Nephrotoxic medication exposure and acute kidney injury in neonates*. *NeoReviews*, 2012. 13(7): p. e420-e427.
22. Hessey, E., et al., *Renal function follow-up and renal recovery after acute kidney injury in critically ill children*. *Pediatric Critical Care Medicine*, 2017. 18(8): p. 733-740.
23. Carmody, J.B. and J.R. Charlton, *Short-term gestation, long-term risk: prematurity and chronic kidney disease*. *Pediatrics*, 2013. 131(6): p. 1168-79.
24. Agras, P.I.M.D., et al. *Acute Renal Failure in the Neonatal Period*. *Renal Failure*, 2004. 26, 305-309.

# Acute Kidney Injury Algorithm

## Diagnosis:

If patient meets Stage 1, 2, or 3 as outlined in the KDIGO Classification below:

**TABLE 1** Neonatal AKI KDIGO Classification

Stage	SCr	Urine Output
0	No change in SCr or rise <0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥ 0.3 mg/dL within 48 h or SCr rise ≥1.5–1.9 × reference SCr <sup>a</sup> within 7 d	<0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0–2.9 × reference SCr <sup>a</sup>	<0.5 mL/kg/h for ≥ 12 h
3	SCr rise ≥3 × reference SCr <sup>a</sup> or SCr ≥2.5 mg/dL <sup>b</sup> or Receipt of dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

Differences between the proposed neonatal AKI definition and KDIGO include the following:

<sup>a</sup> Reference SCr will be defined as the lowest previous SCr value.

<sup>b</sup> SCr value of 2.5 mg/dL represents <10 mL/min/1.73m<sup>2</sup>.

**“Acute Kidney Failure” should be added to the problem list (ICD 10 code: N17)**

## Management:

**Limit Risk:**

- Avoid nephrotoxins
- Correct electrolyte imbalance
- Treat underlying cause

**Monitor:**

- Obtain daily BMP
- Consider renal ultrasound and UA
- If AKI > 3 days or serum creatinine > 2.5 mg/dL, consult Nephrology

**Assess volume status:**

- Strict I/O
- Daily weights
- Consider test bolus vs. fluid restriction

## Follow-up:

**If diagnosed with acute kidney injury while inpatient:**

Schedule follow-up with Pediatric Nephrology in 3-12 months, depending on clinical course (outlined in the monitoring section of the guideline).



Schedule follow-up with SICC within 6 months