Acute Kidney Injury in the Neonate

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KEYWORDS

• Acute kidney injury • Neonate • Critical illness • Biomarkers
• Chronic kidney disease • Acute renal failure

KEY POINTS

- Acute kidney injury (AKI) is common in neonatal intensive care units and seems to affect patient outcomes.
- AKI is a heterogeneous disorder with many mechanisms and management strategies. Current AKI biomarkers are limited and often late indicators that injury has occurred. Development of new, more precise biomarkers is a major focus of current research.
- Care of the neonate with AKI remains supportive. Maintenance of adequate renal perfusion, prevention of fluid overload, avoidance of nephrotoxic medications, and consideration for early initiation of renal supportive therapy are strategies which should improve outcomes.

INTRODUCTION

Neonates who are critically ill are at high risk for acute kidney injury (AKI) as the result of several potential exposures (eg, nephrotoxic medications, sepsis, hypotension, adverse perinatal events such as asphyxia). Recent data suggest an association between AKI and morbidity and mortality in these patients,[1–6] such that AKI can no longer be viewed as an incidental finding; it is an independent risk factor for poor outcomes. Close attention to at-risk patients and early recognition of changes in kidney function are keys to ameliorating this process.

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AKI INCIDENCE AND AT-RISK POPULATIONS IN THE NEONATAL INTENSIVE CARE UNIT

The reported incidence of AKI in the neonatal intensive care unit (NICU) varies widely depending on the patient sample and AKI definition used (see Askenazi and colleagues[7] and Jetton and Askenazi[8] for epidemiology overviews). Groups of newborns recognized as being at increased risk for AKI include infants with perinatal hypoxia;[9–12] premature and very low birth weight (VLBW) infants;[1,4] infants with congenital heart disease, especially those requiring cardiopulmonary bypass;[3,5,13–16] infants requiring extracorporeal membrane oxygenation;[17–23] sick near-term/term infants;[24] and infants with sepsis.[25] In addition, neonates with congenital anomalies of the kidney and urinary tract are at high risk for AKI overlying their underlying chronic kidney disease (CKD). All of these infants should be identified as at risk and undergo close monitoring of kidney function with attention to modifiable risk factors during their NICU stay.

AKI DEFINITIONS AND DIAGNOSIS

AKI is a sudden impairment in kidney function that results in the inability to maintain adequate fluid, electrolyte, and waste product homeostasis. It is a complex and clinically heterogeneous disorder with multiple causes, pathophysiologic pathways, and clinical manifestations. Moreover, there are graded levels of severity that portend different outcomes. To highlight the dynamic and evolving nature of this syndrome, the old description acute renal failure has now been supplanted by the new term AKI. This change in terminology emphasizes the importance of early recognition and intervention at the time of injury rather than waiting until complete organ failure has occurred.[26]

At the bedside, AKI traditionally has been defined as either an increase in serum creatinine (SCr) or decrease in urine output (oliguria; ie, <0.5 mL/kg/h). These traditional biomarkers have several important limitations that are described later. Current focus in AKI research is on the development of more informative and timely biomarkers that will allow earlier detection of AKI, as well as help elucidate the nature of the injury (functional change vs structural damage).[27] Among the most well-studied functional biomarkers are SCr and serum cystatin C, an endogenous proteinase inhibitor that is produced at a constant rate by the body, freely filtered by the glomerulus, and neither secreted nor reabsorbed by the renal tubules.[28] Since 2005, there has been a growing effort to incorporate markers of kidney injury/repair into the definition of AKI. For example, urine neutrophil gelatinase associated lipocalin (NGAL), a small protein that is readily excreted and detectable in the urine following ischemic injury,[29] has been shown to be upregulated hours after renal injury in animal, pediatric, and adult populations (reviewed in Refs.[30–32]). This and other AKI biomarkers show great promise, but are not yet ready for routine use at the bedside.

For now, SCr and urine output remain the standard for identifying AKI events in critically ill infants, although both have limitations. For example, after birth SCr in the newborn reflects maternal creatinine levels. Rather than maintaining a steady state, SCr then declines at varying rates over days to weeks depending on gestational age. Moreover, newborns, especially preterm infants, may have higher SCr levels than their mothers;[33] the creatinine values for these babies may even increase after birth as the result of reabsorption of creatinine in the renal tubules[34–36] and decreased total body fluid. Thus, the natural physiology and immature handling of SCr by the newborn kidney render changes (or lack of change) in SCr difficult to interpret when assessing for AKI. Bruel and colleagues[37] reported critical serum creatinine levels based on gestational age that predicted increased risk of mortality and worse neurodevelopmental outcome at age 2 years: greater than 1.6 mg/dL for preterm infants