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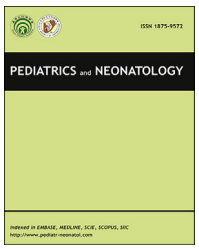

ORIGINAL ARTICLE

Diagnosis and Risk Factors of Acute Kidney Injury in Very Low Birth Weight Infants

Ankana Daga, Fredrick Dapaah-Siakwan*, Sharina Rajbhandari, Cassandra Arevalo, Agnes Salvador

Department of Pediatrics and Adolescent Medicine, Einstein Medical Center, Philadelphia, PA, USA

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Key Words
acute kidney injury;
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Background: Acute kidney injury (AKI) is common in critically ill premature infants. There is a lack of consensus on the diagnostic definition of AKI in very low birth weight (VLBW) infants. The primary aim of this study was to determine the incidence and risk factors for AKI in VLBW infants using the AKI network (AKIN) and pRIFLE (pediatric Risk, Injury, Failure, Loss, End-Stage) criteria and to evaluate whether Clinical Risk Index for Babies (CRIB II) score is a predictor of AKI. The secondary objective was to determine the extent of agreement between the AKIN and pRIFLE criteria in the diagnosis of AKI in VLBW infants.
Methods: This was a retrospective chart review of 115 VLBW (< 1500 g) infants born in an academic center with a Level 3B neonatal intensive care unit. Multiple congenital anomalies, transfer to other centers, or death within the first 2 weeks were the exclusion criteria. Relevant data were collected and analyzed in the first 2 weeks postnatally.
Results: AKI incidence, according to AKIN and pRIFLE criteria, was 20.1% and 22.6%, respectively. As per the interrater reliability analysis, there was a fair agreement between the two criteria (kappa = 0.217). AKI was nonoliguric. The length of stay was significantly longer in the AKI group. Prenatal nonsteroidal anti-inflammatory drug exposure, lower gestational age, lower birth weight, respiratory distress syndrome, mechanical ventilation, patent ductus arteriosus, hypotension, late onset sepsis, and higher CRIB II scores were significantly associated with AKI. Our regression analysis found CRIB II scores to be an independent risk factor for AKI (odds ratio = 1.621; 95% confidence interval, 1.230–2.167; $p = 0.001$).
Conclusion: The determination of AKI using the pRIFLE and AKIN criteria yielded different results. pRIFLE appears to be more sensitive in VLBW infants. A high CRIB II score was recorded for AKI. Future studies are necessary to develop a uniform definition and identify the risk factors to improve the outcomes in this population.

* Corresponding author. Einstein Medical Center, 5501 Old York Road, Philadelphia, PA 19141, USA.
E-mail address: fdapaahsiakwan@gmail.com (F. Dapaah-Siakwan).

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1. Introduction

Acute kidney injury (AKI) has replaced acute renal failure as a term used for the sudden decline in kidney function. AKI has been shown to be an independent risk factor for morbidity and mortality in neonates.[1,2] However, there is a lack of consensus as to which AKI diagnostic definition should be used in very low birth weight (VLBW) infants. In 2004, the Acute Dialysis Quality Initiative group proposed the RIFLE (Risk, Injury, Failure, Loss, End-Stage) criteria for AKI diagnosis.[3] These criteria have been modified to pediatric RIFLE (pRIFLE) for use in children[4] and the AKI network (AKIN) criteria. The AKIN definition of AKI includes patients who experience a 0.3-mg/dL increase in serum creatinine within a 48-hour period.[5] More recently, neonatal RIFLE (nRIFLE) was proposed with a new cutoff value for oliguria defined as UO $<$ 1.5 mL/kg/h in neonates.[6]

The incidence and risk factors for neonatal AKI in VLBW infants vary depending on the hospital and population studied.[1,7] This may be attributable to the varied pattern of care delivered at different neonatal intensive care units (NICUs) and the differences in birth weight (BW) of preterm infants. To overcome this and allow for comparison, several neonatal illness severity scores have been developed to predict mortality and morbidity in preterm infants. The Clinical Risk Index for Babies (CRIB) II[8] is a validated 5-item scoring system used worldwide to determine the illness severity in addition to predicting morbidity and mortality[9,10] in preterm infants $<$ 32 weeks. CRIB II is determined within 1 hour, and the 5-item components include BW, gestational age (GA), body temperature, base excess, and the sex of the infant. Scores range from 0 to 27 and are inversely related to outcomes. Limited data exist on the incidence and risk factors for AKI in VLBW infants when compared to other patient populations,[11] and the utility of CRIB II scores as a predictor of AKI in VLBW infants has not been extensively studied.

Despite multiple modifications for each unique population, there is no unifying AKI diagnostic definition. Although AKIN and pRIFLE have been compared in pediatric intensive care unit patients,[12] there have been no studies comparing these criteria in VLBW infants. The primary aim of the study was to determine the incidence and risk factors for AKI in VLBW infants using the AKIN and pRIFLE criteria, and evaluate whether CRIB II score is a predictor of AKI. The secondary objective was to determine the extent of agreement between the AKIN and pRIFLE criteria in the diagnosis of AKI in VLBW infants.

2. Methods

2.1. Study population

We retrospectively reviewed all VLBW infants admitted to a level 3B NICU of an academic center serving an inner city population. All infants who were born between January 2012 and December 2013 and whose BW was $\leq$ 1500 g were included in the study. Patients born with any major congenital anomalies involving the kidneys were excluded. We also excluded infants who died within the first few days of life, those who had an insufficient number of serum creatinine values prior to death or transfer to another center as well, as periviable infants who were not resuscitated and provided with only comfort care. The Institutional Review Board at the center approved the study protocol and waived the need for consent.

2.2. Data collection

Data were collected from the electronic medical records of all patients. The data included maternal and infant demographics, GA, BW, APGAR (Appearance, Pulse, Grimace, Activity, Respiration) scores, admission temperature and base excess, medications, laboratory results, respiratory support, and morbidities. Illness severity on admission was assessed using the updated CRIB II score.[8] AKI was classified using all three definitions: pRIFLE, AKIN, and nRIFLE (Table 1). For each definition, the creatinine criterion and/or urine output criterion was used. An AKI diagnosis was made only after the first 48 hours of life, which avoided calling the expected low urine output during the first 2 days of life of an infant as AKI. Additionally, because neonatal serum creatinine may reflect maternal creatinine in the first 2 days of life, serum creatinine measurements were recorded only after the first 48 hours of life. For patients with multiple episodes of AKI, the highest stage reached for any episode was used for the analysis. Serum creatinine was measured using an alkaline picrate (Jaffe) method traceable to isotope dilution mass spectrometry. As the pRIFLE criterion uses the estimated glomerular filtration rate (eGFR) in its definition (Table 1), we used the modified Schwartz and Work[13] method to best calculate the eGFR, which has been used in prior studies for pediatric patients aged between 0 years and 18 years.[4,14–16]

2.3. Definitions

Respiratory distress syndrome was defined as respiratory distress accompanied by hypoxemia, Fio_2 requirement $>$ 35%, and ground glass appearance on chest X-ray. Small for gestational age was defined as BW $<$ 10^{th} percentile for the GA. Presumed early-onset clinical sepsis was defined as the onset of signs of sepsis within the first 72 hours of life without a positive blood or cerebrospinal fluid culture and receipt of antibiotics for at least 5 days.[17] Late-onset sepsis was defined as occurring after 72 hours of life.[18]

2.4. Statistical analysis

All statistical analyses were performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA). Medians for continuous variables were compared using with Mann–Whitney *U* test because the assumptions of normality could not always be satisfied. Proportions for categorical variables were compared using Pearson's Chi-square or Fisher's exact tests as appropriate. Continuous variables with normal distribution were compared using means and Student *t* test. Odds ratios and 95% confidence intervals were calculated to determine the odds of developing AKI among infants with or without it. Because of the high possibility of multicollinearity, forward stepwise binary logistic regression was performed to determine the variables that were considered to be independent risk factors for AKI within the first 2 weeks

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