นิพนธ์ต้นฉบับ ▪ Original Article

อุบัติการณ์ของภาวะไตเสียหายเฉียบพลันตามเกณฑ์วินิจฉัยสำหรับทารกแรกเกิดในหออภิบาลทารกแรกเกิดวิกฤต

ณภัทร เหล่าอรุณ, ผกาพรรณ เกียรติชูสกุล, สุวรรณี วิษณุโยธิน, อภิชาติ จิระวุฒิพงศ์, จรรยา จิระประดิษฐา, สุนีย์ พนมบัวเลิศ*
ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

Incidence of Acute Kidney Injury by Neonatal RIFLE Criteria in NICU

Napat Laoaroon, Pakaphan Kiatchoosakun, Suwannee Wisanuyotin, Apichat Jiravuttipong, Junya Jirapradittha, Sunee Panombualert*
Department of Pediatrics, Faculty of Medicine, Khon Kaen University

Received: 17 July 2019
Accepted: 14 November 2019

หลักการและวัตถุประสงค์: ภาวะไตเสียหายเฉียบพลันเป็นปัจจัยสำคัญต่ออัตราการตายของทารกแรกเกิดในภาวะวิกฤต แต่ยังไม่มีเกณฑ์การวินิจฉัยที่ชัดเจนสำหรับภาวะไตเสียหายเฉียบพลันในกลุ่มทารกแรกเกิด ในปี พ.ศ. 2556 มีการนำเกณฑ์การวินิจฉัย RIFLE สำหรับเด็กทารกแรกเกิดมาใช้ จึงเป็นที่มาของการศึกษานี้ ในการหาอุบัติการณ์ของการเกิดภาวะไตเสียหายเฉียบพลันในทารกแรกเกิดวิกฤตโดยใช้เกณฑ์วินิจฉัย RIFLE สำหรับเด็กทารก

วิธีการศึกษา: การศึกษานี้เป็นการศึกษาแบบย้อนหลังในเด็กทารกแรกเกิดที่เข้ารับการรักษาตัวในหอผู้อภิบาลทารกแรกเกิดวิกฤตในระยะเวลาจากเดือนมกราคมปี พ.ศ. 2556 ถึงธันวาคมปี พ.ศ. 2557 โดยบันทึกข้อมูลทั่วไปของผู้ป่วย โรคร่วมและผลที่เกิดขึ้น โดยเกณฑ์วินิจฉัย RIFLE สำหรับเด็กทารกแบ่งออกเป็นเกณฑ์การใช้ปริมาณปัสสาวะและการใช้ค่าครีแอทินิน โดยมีวัตถุประสงค์เพื่อ 1. หาอุบัติการณ์ของการเกิดภาวะไตเสียหายเฉียบพลันในทารกแรกเกิดวิกฤต 2. หาปัจจัยที่ทำให้เกิดภาวะไตเสียหายเฉียบพลัน

ผลการศึกษา: จากข้อมูลผู้ป่วยทารก 263 ราย พบว่ามีอุบัติการณ์ของการเกิดภาวะไตเสียหายเฉียบพลันโดยใช้เกณฑ์วินิจฉัย RIFLE สำหรับเด็กทารกถึงร้อยละ 24.3 เปรียบเทียบกับอุบัติการณ์ร้อยละ 8 จากการวินิจฉัยโดยแพทย์ผู้ดูแล ($p<0.01$) ผู้ป่วย 48 ราย (ร้อยละ 75) ได้รับการวินิจฉัยภาวะไตเสียหายเฉียบพลันโดยการใช้เกณฑ์ปริมาณปัสสาวะเพียงอย่างเดียว ปัจจัยที่สำคัญที่ทำให้เกิดภาวะไตเสียหายเฉียบพลันในทารกแรกเกิดในหอผู้อภิบาลทารกแรกเกิดวิกฤตได้แก่ โรคหัวใจพิการแต่กำเนิดและการได้รับยา vancomycin ($p<0.05$) นอกจากนี้พบว่าในเด็กทารกที่มีภาวะไตเสียหายเฉียบพลันนั้นหายโดยสมบูรณ์ถึงร้อยละ 81.3 และอัตราการตายของทารกที่มีภาวะไตเสียหายเฉียบพลันคือร้อยละ 26.5 เทียบกับร้อยละ 4 ของทารกที่ไม่มีภาวะไตเสียหายเฉียบพลัน

Background and objective: Acute kidney injury (AKI) is an important contributing factor to the mortality of critically ill neonates. However, the standardized AKI for this population is still inconclusive until neonatal RIFLE score has been proposed in 2013. This study aimed to identify the incidence of AKI in critically ill neonates by using neonatal RIFLE.

Methods: In this descriptive, retrospective study included all neonates admitted to the tertiary care NICU during January 2013-December 2014. The patient demographics, co-morbidities, and outcomes data were recorded. AKI was classified by neonatal RIFLE into urine output-based criteria and serum creatinine-based criteria. The objectives were 1. To determine the incidence of AKI as defined by neonatal RIFLE score in NICU. 2. To identify factors affecting AKI in critically ill neonates.

Results: A total of 263 neonates were enrolled. The incidence of AKI by neonatal RIFLE was 24.3%, compared with 8% of those diagnosed by attending physicians ($p<0.001$). Forty-eight of 64 patients (75%) with AKI were classified by urine output criteria only, eight patients (12.5%) were diagnosed by eGFR criteria only and eight patients (12.5%) matched both criteria. Congenital heart diseases and administration of vancomycin were found to be significant independent factors of AKI in the NICU ($p<0.05$). Most neonates with AKI (81.3%) had complete renal recovery. The mortality rate of neonates with AKI by neonatal RIFLE was 26.5% compared to 4% of

*Corresponding author : Sunee Panombualert, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Email: sunepa@kku.ac.th

สรุป: พบอุบัติการณ์การเกิดภาวะไตเสียหายเฉียบพลันในเด็กทารกจากการใช้เกณฑ์ประเมินปริมาณปัสสาวะจากการวินิจฉัย neonatal RIFLE ได้สูงถึงร้อยละ 24.3 และตรวจพบได้ตั้งแต่ในระยะแรก จึงเป็นประโยชน์ต่อการรักษา

คำสำคัญ: ภาวะไตเสียหายเฉียงพลัน, เด็กทารก, ทารกแรกเกิด

Conclusion: The incidence of neonatal AKI by using urine output criteria from neonatal RIFLE was high (24%) and useful to detect and early management of neonatal AKI.

Key word: acute kidney injury, neonates, neonatal

ศรีนครินทร์เวชสาร 2563; 35(1): 14-20. ● Srinagarind Med J 2020; 35(1): 1420.

Introduction

Acute kidney injury (AKI) is defined by rapid declining of renal function in hours to days, resulting in impairment of fluid and electrolyte balance and excretion of waste products. AKI is one of major risk factors which contribute to morbidity and mortality in critically ill neonates. However, the consensus criteria for the diagnosis of AKI in the newborn population still have not been established. A cutoff value of serum creatinine more than 1.5 mg/dL or urine output less than 0.5 mL/kg/h had been used in some studies[1].

Incidences of neonatal AKI are varied according to different criteria using to define the condition in each study. The overall incidence of AKI is 8-24% in the newborn population[2]. In critically ill neonates, Koralkar et al.[3] found that the incidence of AKI was 18% in very low birthweight infants and another study by Bezerra et al.[4] showed 20.5% of NICU patients developed AKI. From previous studies in our country, Vachvanichsanong et al.[5] found 6.3% prevalence of AKI in neonates in tertiary care hospital in Thailand.

Many scoring systems have been developed for diagnosis and grading severity of AKI in adult patients, for examples; Risk, Injury, Failure, Loss and End-stage renal disease (RIFLE)[6] and Acute Kidney Injury Network (AKIN)[7]. Similarly, pediatric RIFLE (pRIFLE) was adapted from RIFLE and purposed in 2007 for diagnosis of AKI in pediatric patients[8].

In 2013, pediatric RIFLE was modified for newborn patients as neonatal RIFLE[9] using both estimated GFR and urine output to diagnose AKI but has not frequently been used in current neonatal studies. Our study aimed to find the incidence of AKI in patients in the neonatal intensive care unit (NICU) by neonatal RIFLE as a primary objective. We also evaluated risk factors for AKI, complications, and outcomes of patients.

Methods

This retrospective, cohort study was conducted at Srinagarind hospital, Khon Kaen university, Thailand. Medical records of all infants from birth to 30 days of life who were admitted to NICU from January 2013 to December 2014 were reviewed.

Diagnosis of AKI was made by neonatal RIFLE, which was classified using serum creatinine for estimated GFR (eGFR) criteria and urine output criteria.

For estimated GFR criteria, GFR was calculated by modified Schwartz's Formula[10]. Serum creatinine was measured by a standardized enzymatic method in every patient. For urine output criteria, patient urine volume was measured by either urine catheterization or diaper weight. Urine output on the first day of life was excluded from the record due to normal physiologic oliguria in the first 24 hours of life.

Patients with AKI, either by eGFR or urine output criteria, were classified to five stages of severity according to neonatal RIFLE criteria[9] (Table 1) which differ from pediatric RIFLE especially in urine output criteria. Factors associated with AKI (patient's gestational age, nasal CPAP, endotracheal intubation, congenital KUB anomalies, congenital heart diseases, and drugs administration) and outcome (recovery, need dialysis, death) were collected.

Descriptive statistics (mean, standard deviation and frequency) were performed to analyze the patient's characteristics and outcome. Chi-square and multiple logistic regression analysis were applied to determine the risk factors of AKI. Less than 0.05 of P-value was considered statistically significant.

This study was approved by Khon Kaen University Ethics Committee for Human Research, Khon Kaen University, Thailand. (Reference No. HE581215)

Results

342 neonates were admitted to NICU in 2 years period from January 2013 to December 2014. Forty-three patients were excluded due to incomplete

medical records, and patients who were admitted less than 24 hours were also excluded. Finally, a total of 263 neonates were enrolled in the study. Patient demographic data were shown in Table 2.

The incidence of AKI by neonatal RIFLE in NICU was 24.3% (64 of 263 patients) compared to 8.0% (21 patients) diagnosed AKI by attending physicians (p< 0.001, McNemar test). The number of AKI diagnosed by neonatal RIFLE and classified by severity as shown in Figure 1. By using neonatal RIFLE, forty-eight patients (75%) were diagnosed by urine output-based criteria only, eight patients (12.5%) were diagnosed by eGFR criteria only and eight patients (12.5%) matched both criteria. The mean highest serum creatinine was 1.07±0.75 mg/dL (0.3-4.3) and the mean lowest eGFR was 22.57±10.75 (4.99-64.7).

Factors associated with AKI were patient's gestational age, nasal CPAP, endotracheal intubation, congenital KUB anomalies, congenital heart diseases, and drugs administration (vancomycin, colistin, and inotropic drugs). After these factors were assessed by multivariate analysis to control for possible confounding conditions, congenital heart diseases and vancomycin administration were significant independent risk factors for AKI with adjusted Odds ratio 2.29 (95% CI 1.25-4.19, p = 0.007) and 2.32 (95% CI 1.19-4.51, p = 0.015) respectively.

Most of the neonates with AKI (81.3%) had complete renal recovery after mainly supportive treatment and diuretics. Only two patients were undergone renal replacement therapy. Although there are many acute complications in AKI, our study found that electrolyte imbalances and volume overload occurred in 15.6% and 10.9% of patients, respectively. Mortality in AKI patients from the study

Table 1 Proposed neonatal RIFLE (adapted from Ricci et al.[9])

	Estimated GFR* criteria	Proposed urine output criteria
Risk	eGFR ↓ 25%	< 1.5 mL/kg/h for 24 h
Injury	eGFR ↓ 50%	< 1.0 mL/kg/h for 24 h
Failure	eGFR ↓ 75%	< 0.7 mL/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure > 4 weeks	
End stage	ESRD (persistent failure > 3 months)	

*eGFR was calculated by modified Schwartz's formula[10]

$$eGFR = 0.413 \times \frac{\text{height (cm)}}{\text{serum creatine (mg/dL)}} \text{ mL/min/1.73 m}^2$$

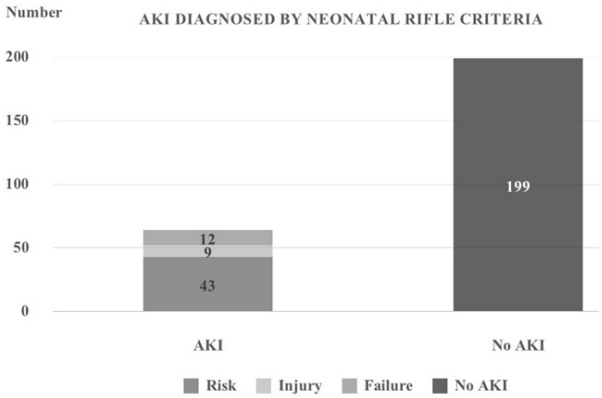

Figure 1 Number of AKI diagnosed by neonatal RIFLE criteria and classified by severity

Table 2 Patient demographic data

Characteristics	Number of patients, N=263 (%)
Male	145 (55)
Female	118 (45)
Inborn patients	192 (73)
Referred patients	71 (27)
Gestational age (mean ± SD)	34.2 ± 3.9 weeks
- Preterm (24-36 weeks)	162 (61.5)
- Term (≥37 weeks)	101 (38.5)
Age on admission (mean ± SD)	0.5 ± 1.8 days
(Median, min-max)	0, 0-15 days
Birthweight (mean ± SD)	2,234 ± 892 g
- Very low birthweight (< 1,500 g)	66 (25.1)
- Low birthweight (1,500-2,499 g)	89 (33.8)
- Normal birthweight (≥ 2,500 g)	108 (41.1)

Table 3 Incidence of acute kidney injury diagnosed by neonatal RIFLE and by attending physicians

	Incidence (%)	95% CI (%)	p-value
By neonatal RIFLE	24.3	19.1 – 29.5	<0.001 (McNemar test)
By attending physicians	8.0	4.7 – 11.2	

was 26.5% (17 of 64 patients).

The overall mortality in this study was 9.5%. Most common causes of death were congenital heart diseases, sepsis, and multiple organ dysfunction syndromes. Low birthweight, respiratory distress, endotracheal intubation, congenital heart diseases and acute kidney injury by neonatal RIFLE were found

to be significant risk factors for mortality in NICU ($p < 0.05$).

Discussion

AKI is an important issue in neonatal intensive care. To our current knowledge, the worldwide incidences of AKI in neonates ranged from 8 to 24 percent [2], the data remained unclear mainly due to lack of consensus criteria for diagnosis. The incidences have been reported higher in high-risk newborns; there were 38% AKI incidence in post cardiac surgery neonates[11] and 62% in perinatal asphyxia patients[12]. Signs of AKI in newborns include oliguria, hypertension, arrhythmia and fluid overload, however early recognition of this condition is still challenging for physicians.

Recently, several studies have focused on classification systems for the diagnosis of AKI. The two most accepted scoring systems are the Risk, Injury, Failure, Loss and End-Stage Renal Disease (RIFLE)[6] and the Acute Kidney Injury Network (AKIN)[7] classification. These classifications had been widely accepted for diagnosis and staging the severity of AKI in adult patients. AKIN criteria had been applied in some studies in neonatal population and showed fair results [3,11,12], this criteria still depends on serum creatinine for diagnosis of AKI. In 2007, Akcan-Arikan et al.[8] had modified the RIFLE criteria for an appliance in critically ill children, known as the Pediatric RIFLE. Urine output measurement had been added to the Pediatric RIFLE to minimize the limitation of using only serum creatinine for diagnosis AKI in pediatric patients, the criteria had been used in many pediatric studies[13-15] and showed good clinical applications. The Pediatric RIFLE's urine output criterion was adapted by Bezerra et al.[4] as Neonatal RIFLE in 2013 by increasing the urine output cut-offs for early detection of abnormal renal function in newborn patients.

From our study, the overall incidence of AKI by neonatal RIFLE criteria in NICU was 24.3% which confirmed that AKI should be concerned as a major problem in newborn patients. Neonatal RIFLE consisted of two criteria which are estimated GFR-based and urine output-based. Most of AKI cases (75%) in our study were diagnosed by urine output-based criterion. The urine output cutoffs in neonatal RIFLE were modified from pediatric RIFLE by increasing urine output threshold to 1.5 mL/kg/h instead of 0.5 mL/kg/h[9], because of normal larger urine volume in newborns from their small capacity to concentrate urine. The results were similar to the previous study by Bezerra et al.[4] which revealed a 21.8% incidence of AKI by the same urine output cutoffs. In most NICUs, urine volume was routinely recorded every 2-8 hours, and this did not harm to patients. Thus urine output measurement can be applied in general practice to help diagnosis AKI, especially in early stages. The main difference between neonatal AKI in this study and the previous studies was that we found higher incidence of neonatal AKI than the previous study using creatinine to determine AKI and we also compared to the previous study in tertiary care NICU in southern Thailand by Vachvanichsanong et al.[5] in 2012, the prevalence of AKI in newborn patients was 6.3% by definition of increased serum creatinine > 2 mg/dL. The lower incidence might be from the definition of AKI using in the study which creatinine cut-off value was quite high so AKI could be underdiagnosed. From our results, only 6 patients (2.3%) had serum creatinine > 2 mg/dL. In the neonatal population, using serum creatinine for diagnosis of AKI has several limitations. Normal distribution of serum creatinine has a wide variation, depends on the degree of prematurity and age, and the level can also be affected by the mother's serum creatinine in the first few days of life. Moreover, serum creatinine may not change until 25% to 50% loss of renal function[1], so the detection of declined renal function may be delayed.

Interestingly, only 21 (8.0%) from 263 patients were diagnosed AKI by attending physicians, without a documented certain method of diagnosis. There was a statistically significant difference ($p < 0.001$) from 24.3% AKI incidence by neonatal RIFLE. We suggested that neonatal RIFLE, especially the urine output-based criterion should be used to make an early diagnosis of acute kidney injury in newborn patients.

Aside from low birthweight, respiratory distress, endotracheal intubation and, congenital heart diseases, we found that AKI by neonatal RIFLE is also one of the major risk factors for mortality in NICU (adjusted OR 11.79, $p < 0.001$). Furthermore, there was a stepwise increment in mortality across all stages of AKI by neonatal RIFLE. This result emphasized the importance of AKI diagnosis in early stages, which could be promptly intervened to avoid complications and preserve residual renal function.

From previous studies, risk factors for AKI in neonates include very low birthweight, low 5-minute Apgar score, maternal drug administration (NSAIDs and antibiotics), endotracheal intubation, respiratory dis-

Table 4 Factors associated with acute kidney injury

	AKI n = 64 (%)	No AKI n = 199 (%)	Odds ratio (95% CI)	p-value
Patient characteristics				
Male sex	109(54.8)	36 (56.3)	1.06 (0.60-1.87)	0.836
Birthweight (g)[a]	2416±897	2176±885	0.62 (0.35-1.09)	0.060
- Low birthweight (<2500 g)	32 (50.0)	76 (38.2)		
Gestational age (weeks)[a]	35.1±4.0	33.9±3.8	0.63 (0.36-1.11)	0.038
- Preterm (<37 weeks)	34 (53.1)	128 (64.3)		0.109
Prenatal history				
Pregnancy complications	24 (37.5)	94 (47.2)	0.67 (0.38-1.19)	0.174
Fetal complications	21 (32.8)	54 (27.1)	1.31 (0.71-2.41)	0.382
Oligohydramnios	5 (7.8)	4 (2.0)	4.20 (1.09-16.20)	0.103
Abnormal prenatal ltrasonography of KUB	2 (3.1)	1 (0.5)	6.39 (0.57-71.64)	0.119
Postnatal history				
Perinatal asphyxia (5-minute Apgar score<3)	1 (1.6)	6 (3.0)	0.51 (0.06-4.32)	0.459
Respiratory distress	50 (78.1)	159 (79.9)	0.90 (0.45-1.78)	0.760
Ventilator support				
- Nasal CPAP	29 (45.3)	120 (60.3)	0.54 (0.31-0.96)	0.035
- Intubation	42 (65.6)	100 (50.3)	1.89 (1.05-3.40)	0.032
Hypovolemia	9 (14.1)	26 (13.1)	1.09 (0.48-2.46)	0.838
Sepsis	31 (48.4)	74 (37.2)	1.59 (0.90-2.80)	0.111
Congenital KUB anomalies	9 (14.1)	11 (5.5)	2.80 (1.10-7.09)	0.030
Congenital heart diseases	33 (51.6)	59 (29.6)	2.53 (1.42-4.50)	0.002
Medications				
- Aminoglycosides	54 (84.4)	188 (95.5)	0.32 (0.13-0.78)	0.013
- Vancomycin	22 (34.4)	34 (17.1)	2.54 (1.35-4.79)	0.004
- Colistin	5 (7.8)	4 (2.0)	4.13 (1.08-15.88)	0.039
- Amphotericin B	3 (4.7)	6 (3.0)	1.58 (0.38-6.51)	0.525
- NSAIDs	12 (18.8)	25 (12.6)	1.61 (0.76-3.42)	0.219
- Inotropes	20 (31.3)	23 (11.6)	3.48 (1.76-6.90)	<0.001

[a]mean ± SD

Table 5 Associating factors of acute kidney injury (AKI) (multivariate analysis)

Factors	AKI n = 64 (%)	Crude OR	Adjusted OR (95% CI)	p-value
Congenital heart disease	33 (51.6)	2.53	2.29 (1.25-4.19)	0.007
Medications				
Aminoglycosides	54 (84.4)	0.32	0.27 (0.1-0.69)	0.007
Vancomycin	22 (34.4)	2.54	2.32 (1.19-4.51)	0.015

Table 6 Outcome of neonatal acute kidney injury (AKI)

Outcome	AKI n = 64 (%)	No AKI N = 199 (%)	p value
Renal replacement therapy			
- Peritoneal dialysis	1 (1.6)		
- Exchange transfusion	1 (1.6)		
Complications			
- Electrolyte imbalance	10 (15.6)		
- Volume overload	7 (10.9)		
Renal failure status			
- Complete recovery	52 (81.3)		
- Not recovery	12 (18.7)		
Mortality	17 (26.5)	8 (4.0)	<0.001 (OR = 8.63)

tress syndrome, patent ductus arteriosus and neonatal medications (NSAIDs, antibiotics, diuretics)[16,17]. In our study, endotracheal intubation, and administrations of vancomycin and inotropes were the risk factors for AKI in NICU with odd ratio 1.89, 2.54, and 3.48 respectively ($p < 0.05$). Otherwise, risk factors which had statistical significance by multivariate analysis were congenital heart diseases (adjusted OR 2.29, $p = 0.007$) and vancomycin administration (adjusted OR 2.54, $p = 0.015$).

Congenital heart disease (CHD) is well known as a risk factor for AKI, especially in patients undergoing cardiac surgery. Tissue hypoxemia, cardiopulmonary bypass, systemic inflammation, low cardiac output states and nephrotoxic drugs are contributing factors to AKI in postoperative patients[11]. Meanwhile, AKI itself also increases mortality rate in CHD patients by worsening volume overload. AKI developed in 35.8% of CHD patients in our study, but the incidence was up to 60% in previous report[11]. Types of CHD and details of treatment that may affect the risk for AKI should be further investigated.

Vancomycin is an antimicrobial agent that is commonly used in critically ill neonates to treat severe infections. Mechanisms of nephrotoxicity relate to renal proximal tubular damage[18]. We found 39.2% of vancomycin-administrated patients had acute kidney injury (adjusted OR 2.54, $p = 0.015$). McKamy et al.[19] had found the relation between nephrotoxicity and the high vancomycin trough level (≥ 15 mg/dL). Therefore, we recommend that serum creatinine and vancomycin level should be monitored closely during treatment.

Aminoglycosides are well-known as a nephrotoxic antibiotic by a mechanism of direct injury to renal tubules. Nevertheless, our study did not show that administration of aminoglycosides was a risk factor for AKI as previously expected. This result was explained by our method of AKI diagnosis which mostly defined by decreasing urine output, while non-oliguric AKI is a character of aminoglycosides nephrotoxicity. For this reason, we recommend that serum creatinine still should be monitored in patients receiving aminoglycosides.

The limitations of our study were a relatively small number of subjects and the difference of urine output measurement methods due to retrospective study design. However, our study provided some helpful data to improve the intensive care of newborns with AKI. Despite many works on the classification system, the ideal marker for renal injury detection before declining of GFR is still needed. Novel biomarkers such as neutrophil gelatinase associated lipocalin, urine interleukin-18, kidney injury marker 1 and others are currently in many studies to identify early injury and improve outcomes in neonates with AKI[1,2]. Still, these biomarkers are under investigation and may not be suitable in resources-limited areas. The urine output criteria from neonatal RIFLE to diagnosis AKI is higher than other criteria for neonates (<1.5 ml/kg/hr for 24 hr VS. <0.5 ml/kg/hr for 6-12 hr[20]) which may cause higher incidence of AKI in this study. However, we strongly suggest that urine output measurement is a simple and useful method for early diagnosis of AKI.

Conclusion

Neonatal RIFLE criteria are practical for diagnosis of AKI in early stage especially the assessment of urine output. The incidence of neonatal AKI by using urine output criteria from neonatal RIFLE was high (24%) in our settings. We suggest performing urine output measurement in every neonatal intensive care unit to early detection of AKI.

References

1. Gleason CA, Devaskar SU. Acute kidney injury and chronic kidney disease. In: Gleason CA, Juul SE, editors. Avery's disease of the newborn. 9th ed. Philadelphia: Elsevier/Saunders; 2014: 1205-21.
2. Vogy BA, Dell KM. The kidney and urinary tract of the neonate. In: Martin RJ, Fanaroff AA, Walsh MC, editors. Fanaroff and Martin's neonatal-perinatal medicine. 10th ed. Philadelphia: Saunders; 2015: 1676-99.
3. Koralkar R, Ambalavanan N, Levitan E, McGwin G, Goldstein S, Askenazi D. Acute kidney injury reduces survival in very low birthweight infants. Pediatr Res 2011; 69: 354-8.
4. Bezerra C, Vaz Cunha L, Liborio A. Defining reduced urine output in neonatal ICU: importance for mortality and acute kidney injury classification. Nephrol Dial Transplant 2013; 28: 901-9.
5. Vachvanichsanong P, McNeil E, Dissaneevate S, Dissaneewate P, Chanvitan P, Janjindamai W. Neonatal acute kidney injury in a tertiary center in a developing country. Nephrol Dial Transplant 2012; 27: 973-7.
6. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Bonventre JV, et al. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8: R204-12.
7. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007; 11: R31.
8. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int 2007; 71: 1028-35.
9. Ricci Z, Ronco C. Neonatal RIFLE. Nephrol Dial Transplant 2013; 28: 2211-14.
10. Schwartz G, Munoz A, Schneider M, Mak R, Kaskel F, Warady B, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol 2009; 20: 629-37.
11. AlAbbas A, Campbell A, Skippen P, Human D, Matsell D, Mammen C. Epidemiology of cardiac surgery-associated acute kidney injury in neonates: a retrospective study. Pediatr Nephrol 2013; 28: 1127-34.
12. Selewski DT, Jordan BK, Askenazi DJ, Dechert RE, Sarkar S. Acute kidney injury in asphyxiated newborns treated with therapeutic hypothermia. J Pediatr 2013; 163: 725-9.
13. Hsu C, Lee C, Su C, Wang Y, Chen H, Chuang J, et al. Incidence, outcomes, and risk factors of community-acquired and hospital-acquired acute kidney injury. Medicine (Baltimore) 2016; 95: e3674.
14. Rustagi R, Arora K, Das R, Pooni P, Singh D. Incidence, risk factors and outcome of acute kidney injury in critically ill children – a developing country perspective. Paediatr Int Child Health 2016: 1-7.
15. Slater M, Gruneir A, Rochon P, Howard A, Koren G, Parshuram C. Risk factors of acute kidney injury in critically ill children. Pediatr Crit Care Med 2016; 17: e391-8.
16. Cataldi L, Leone R, Moretti U, Mitri B, Fanos V, Ruggeri, et al. Potential risk factors for the development of acute renal failure in preterm newborn infants: a case-control study. Arch Dis Child Fetal Neonatal Ed 2005; 90: F514-9.
17. Cuzzolin L, Fanos V, Pinna B, di Marzio M, Perin M, Tramontozzi P, et al. Postnatal renal function in preterm newborns: a role of diseases, drugs and therapeutic interventions. Pediatr Nephrol 2006; 21: 931-8.
18. Zappitelli M, Selewski D, Askenazi D. Nephrotoxic medication exposure and acute kidney injury in neonates. Neoreviews 2012; 13: e420-7.
19. McKamy S, Hernandez E, Jahng M, Moriwaki T, Deveikis A, Le J. Incidence and risk factors influencing the development of vancomycin nephrotoxicity in children. J Pediatr 2011; 158: 422-6.
20. Selewski DT, Charlton JR, Jetton JG, Guillet R, Mhanna MJ, Askenazi DJ, et al. Neonatal acute kidney injury. Pediatrics 2015; 132: e463-73.

SMJ