ORIGINAL ARTICLE

COMPARISON OF TWO DEFINITIONS (p-RIFLE AND KDIGO) FOR PREVALENCE OF ACUTE KIDNEY INJURY AND IN HOSPITAL MORTALITY IN A PAEDIATRIC INTENSIVE CARE UNIT OF PAKISTAN

Parveen Usman[1], Habib Qaisar[1], Anwar ul Haque[2], Qalab Abbas[1]

[1] Pediatric Critical Care Medicine, Department of Pediatrics and Child Health Aga Khan University, Karachi, [2]Liaquat National Hospital, Karachi-Pakistan

Background: To compare the Paediatric RIFLE (p-RIFLE) and Kidney Disease Improving Global Outcomes (KDIGO) definitions of acute kidney injury (AKI) for frequency of (AKI) and in-hospital mortality in critically ill children. **Methods:** Retrospective review of medical records of all patients (aged 1 month – 16 years) admitted in Paediatric Intensive Care Unit from January 2015–December 2016, with length of stay >48 hours, was done. Patients with chronic kidney disease were excluded. Receiver operating characteristic (ROC) curves were used to evaluate the performance of the p-RIFLE and KDIGO criteria to predict the AKI related mortality. Logistic regression analysis was done to determine the association of different variables with mortality in AKI patient based on p-RIFLE, KDIGO. A *p*-value of <0.05 was considered significant. **Results:** Out of total 823 patients admitted during the study period, 562 patients were included in the study. Median age was 2 years (Interquartile range 8 years). Acute kidney injury frequency according to p-RIFLE and KDIGO were 391 (70%), and 372 (66%) respectively. Overall, 106/823 (12.8%) children died during study period, 78 (19.9%) in AKI by p-RIFLE and 76 (20.4%) in AKI by KDIGO died. The area-under- curve for in-hospital mortality for p-RIFLE and KDIGO criteria were 0.525 (p=0.427), and 0.534 (p=0.276), respectively. **Conclusion:** P-RIFLE is more sensitive compared to KDIGO in diagnosing AKI in critically ill children; identifying a greater number of moderate staged AKI cases. Greater AKI severity is associated with higher mortality in critically ill children.

Keywords: Acute kidney injury, Paediatric intensive care, p-RIFLE, KDIGO

Citation: Usman P, Qaisar H, Haque A, Abbas Q. Comparison of two definitions (p-RIFLE and KDIGO) for prevalence of acute kidney injury and in hospital mortality in a Paediatric intensive care unit of Pakistan. J Ayub Med Coll Abbottabad 2022;34(1):112–7.

INTRODUCTION

Kidney maintains the homeostasis in the body, including fluid and electrolytes balance, acid-base balance, erythropoiesis, and vascular tone regulation.[1,2] Injury to the kidney leads to disruption of all these functions leading to higher morbidity and 4–6 times high mortality compared to patients without acute kidney injury (AKI).[2–5] AKI is a common complication in critically ill children, affecting up to 18–52% of Paediatric intensive care unit (PICU) admissions depending on setting and definitions used.[6,7]

There are approximately more than 30 AKI definitions currently present; three of these are recently developed. In 2004, the Acute Dialysis Quality Initiative group proposed the first evidence-based consensus for adult population, the Risk, Injury, Failure, Loss of Kidney Function, and End-stage kidney disease (RIFLE) classification for AKI. RIFLE was modified in 2007 and evaluated in Paediatric population, termed as p-RIFLE criteria.[2–5,8] Second classification was developed by the Acute Kidney Injury Network (AKIN) which grades AKI severity.[9] The latest definition was published by Kidney disease improving Global Outcomes (KDIGO).[10] This system is combination of RIFLE and AKIN system. KDIGO is new system of definition, its application to AKI and prognostic accuracy compared with p-RIFLE has not been evaluated in detail in critically ill children.[10,11]

Data from single centre study from Netherland has shown incidence of AKI to be 58% based on p-RIFLE criteria.[12] A comparative study done by Sutherland *et al* in 2015 at Cincinnati Children's Hospital, where they compared all three definitions for AKI incidence and outcome in PICU and non PICU Paediatric population, showed difference in AKI incidences across the cohort according to pRIFLE, AKIN, and KDIGO were 51.1%, 37.3%, and 40.3%.[7]

Because of lack of standardized AKI definition in Paediatric population, there is wide variation in epidemiological data of AKI which is hampering the advancement in management and prevention of AKI. Due to high incidence of AKI and its significant contribution to high mortality rates a comparative study of the RIFLE and KDIGO criteria as predictors of mortality in critically ill patients is of

great importance.

We conducted a retrospective study to describe the epidemiology of AKI in PICU based on p-RIFLE and KDIGO definition and compare the both definition (p-RFIEL and KDIGO) for its predictive ability for in hospital mortality. We intend to compare the performance of two commonly used definitions of AKI in critically ill children and determine which definition fares better in diagnosing AKI early and which definition better predicts the severity of AKI. This study will also generate more data to answer the question of agreement between the two definitions. This will contribute to reach an agreement to use one definition or come up with a combination of scores like renal angina index.

MATERIAL AND METHODS

Retrospective review of medical record of all children aged 1 month to 16 years, admitted in four bedded closed multi-disciplinary PICU of Aga Khan University hospital from January 2015 to December 2016, was done after approval from Institutional Ethics Committee (4460-PED-ERC-16). Children with PICU length of stay more than 48 hours, who had at least one measured serum creatinine during PICU stay were included. Initial serum creatinine value (done in emergency room or ward) before the PICU admission was taken as baseline. Children with previous history of chronic kidney disease according to medical records (either deranged serum creatinine before admission, those already on renal replacement therapy and patients with other features of chronic kidney disease) were excluded. Our PICU is an acute unit with ~600 annual admissions, patients are referred to us from the whole city of 20 million as well from other cities. AKI was diagnosed and staged using the p-RIFLE and KDIGO criteria (Table-1). The serum creatinine was measured by Jafe's method on ADVIA 1800 Chemistry System (Siemens Healthliners, Germany), and creatinine clearance has been calculated by modified Schwartz formula.[13] Length of all patients was measured while in PICU and was taken as surrogate for height. Only serum creatinine values were taken for definition purpose similar to Sutherland[7]; because urine output measurement before presentation isn't possible, sometimes urine output can be low because of intravascular volume depletion or shock and not because of AKI, many patients receive diuretics before or during admission; some patient also present in polyuric phase of AKI which can make the diagnosis and staging of AKI biased, so urinary output was not used for AKI diagnosis and staging.[14,15] Serum creatinine was measured on admission in patients who were on ventilatory support, hemodynamically stable or if they were receiving any nephrotoxic agent. There after creatinine is measured daily in patients with AKI or according to the patient status. Data was collected on structured proforma which included -demographic variables like age in years, gender, height in cm and diagnostic categories, clinical variables including inotropic support, mechanical ventilation and renal supportive therapy requirement along with nephrotoxic drug exposure and development of fluid overload. Data collection also included serum creatinine and discharge outcome (survival). Fluid over load was defined as if any one develops positive 48 hours fluid balance (intake and output balance or increase in admission weight of >10%), nephrotoxic exposure was defined as prescription and delivery of a drug which is labelled as nephrotoxic drug by the hospital formulary.[16–18]

The data was analysed using the statistical program SPSS-22. Descriptive statistics were performed for frequency estimates, measures of central tendency and dispersion. Student's t-test was performed to compare means, and the chi-squared test was used to compare proportions. ROC (receiver operating characteristic) curves were used to evaluate the performance of the p-RIFLE and KDIGO criteria to predict the acute kidney injury related mortality. Logistic regression analysis was done to determine the association of different variables with mortality in AKI patient based on p- RIFLE, KDIGO. A *p*-value of <0.05 has been considered significant.

RESULTS

During the study period, 823 patients were admitted, and 562 patients met the inclusion criteria. The characteristics of the whole cohort are shown in (**Table-2**). Median age of the study population was 2 years (interquartile range 8 years); 349 (62%) were males. Major diagnostic categories at admission included sepsis (n=116, 21%), central nervous system diseases (n=100, 18%), respiratory system diseases (n=91, 16%), haematology/oncology diseases (n = 69, 12%), cardiac diseases (n=60, 11%), surgical (n=53, 9%), miscellaneous [road traffic accident and inborn error of metabolism (n = 37, 7%)] and gastrointestinal system diseases (n=36, 6%) (Table-2). 84 (68%) patients required vasopressor support, 351 (63%) patient required mechanical ventilation and 31 (6%) patient required renal replacement therapy. 527 (94%) patients had nephrotoxic drug exposure. 443 (79%) patients develop fluid overload over 48 hours of admissions (**Table-2**).

AKI was diagnosed in 391 (70%) patients by p-RIFLE classification: out of these 391 patients, 90 (23%) were in Risk stage, 158 (40%) in Injury and 143 (37%) were Failure stage. 372 (66%) patients had AKI by KDIGO criteria: 68 (18%) with stage 1, 116 (31%) with stage 2, and 188 (51%) with stage 3. Application of the two definitions did not lead to similar diagnosis or staging of patients. Cohen's κ was run to determine if

there was agreement between two AKI definitions (p-RIFLE and KDIGO) for determining AKI. There was near perfect agreement between the two AKI definition judgments, κ = .906, p<0.05. Additionally, patients with AKI were staged differently on the basis of the definition applied. As for staging of two AKI definition (p-RIFLE and KDIGO), there was near substantial agreement between the staging of two AKI definition judgments, κ = .799, p<0.05. pRIFLE diagnosed more of stage I and II of AKI than KDIGO (90 versus 68 (stage I) and 158 versus 116 (Stage II)) than stage III (143 versus 183 patients). AKI overlap across the two definitions is shown in (

	p-RIFLE			
	No AKI	**Risk**	**Injury**	**Failu**
No AKI	169 (30%)	19 (3%)	2 (0.35%)	0
Stage 1	1 (0.2%)	66 (12%)	0	1 (0.2
Stage 2	1 (0.2%)	5 (0.9%)	106 (19%)	4 (7%
Stage 3	0	0	50 (9 %)	138 (25
Total	171 (30 %)	90 (16 %)	158 (28 %)	143 (25

).

The p-RIFLE criteria was more sensitive than KDIGO (70% versus 66%, p<0.05) for diagnosis of AKI. Fluid overload was present in 329 (84%) patients with AKI diagnosed by p-RIFLE criteria and 314 (84%) AKI diagnosed by KDIGO criteria; each definition has significant p-value of <0.05 (
Table-5).

The p-RIFLE criteria identified 19 more patients with AKI than the KDIGO criteria did: 19 with Risk and 2 with injury (Table-4).

Overall, 106/823 (12.8%) children died during study period, while among those who developed AKI (391 by p-RIFLE and 372 by KDIGO), 78/391 (19.9 %) and 76/372 (20.4%) died respectively. There was significant association of mortality with requirement for vasopressor support, mechanical ventilation and nephrotoxic exposure (p<0.05) (

Table-6).

Predictive ability for mortality (area-under-ROC curves) for in-hospital mortality for p-RIFLE and KDIGO criteria were 0.525 (p=0.427), and 0.534 (p=0.276), respectively (Figure 1).

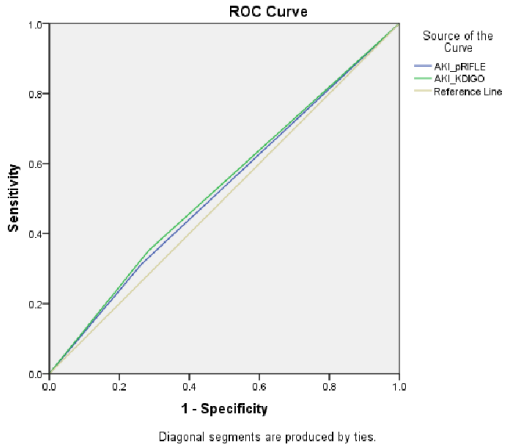

Figure 1: Area under the curves for p-RIFLE and KDIGO classification schemes comparing the predictive ability of p-RIFLE and KDIGO classification for in-hospital mortality.

Area under the Curve 0.528 (95% CI 0.465-0.585, P = 0.427). For KDIGO Area under the Curve 0.534 (95% CI 0.474-0.594, p = 0.276.

Table-1: The p-RIFLE, and KDIGO definitions and classifications for AKI

	p-RIFLE		**KDIGO**	
Staging	Risk	Estimated creatinine clearance decrease by 25%	Stage 1	Increase in serum creatinine 1.5 – 1.9 times from baseline Or Increase creatinine 0.3mg/dl
	Injury	Estimated creatinine clearance decrease by 50%	Stage 2	Increase in serum creatinine 2.0-2.9 times from baseline
	Failure	Estimated creatinine clearance decrease by 75% Or Estimated creatinine clearance < 35 35 mL/min/1.73 m2	Stage 3	Increase in serum creatinine 3 times from baseline Or Serum creatinine 4 mg/dl Or Initiation of renal replacement therapy

Table-2: Demographics and clinical characteristics of study participants

Characteristics		**Frequencies, mean and median (n=562)**
Age, median (IQR)		2 years (8 years)
Gender, n (%)	Male	349 (62%)
	Female	213 (38 %)
Diagnostic categories, n (%)	Gastrointestinal	36 (6%)
	Miscellaneous	37 (7%)
	Surgical	53 (9%)
	Cardiovascular	60 (11%)
	Haematology/oncology	69 (12%)
	Respiratory disease	91 (16 %)
	Neurological	100 (18%)
	Sepsis	116 (21 %)
Vasso-pressor support, n (%)		384 (68%)

Mechanical Ventilation, n (%)	351 (63%)
Renal replacement therapy, n (%)	31 (6%)
Nephrotoxic drug exposures, n (%)	527 (94%)
Fluid overload, n (%)	443 (79%)
Mortality, n (%)	106 (19 %)
AKI based p-RIFLE	391 (70%)
AKI based KDIGO	372 (66%)

Table-3: Agreement between p-RIFLE and KDIGO classification.

Definition		p-RIFLE				
		No AKI	Risk	Injury	Failure	Total
KDIGO	No AKI	169 (30%)	19 (3%)	2 (0.35%)	0	190 (34%)
	Stage 1	1 (0.2%)	66 (12%)	0	1 (0.2%)	68 (12%)
	Stage 2	1 (0.2%)	5 (0.9%)	106 (19%)	4 (7%)	116 (21%)
	Stage 3	0	0	50 (9 %)	138 (25%)	188 (33%)
	Total	171 (30 %)	90 (16 %)	158 (28 %)	143 (25%)	562 (100%)

Kappa value is 0.79, *p*-value <0.05

Table-4: In –hospital mortality according to AKI stratified by KDIGO and p-RIFLE classification schemes

CATEGORY	KDIGO n=372	p-RIFLE n= 391
NONE (%)	30/ 190 (15.7%)	28/ 171 (16.3%)
STAGE 1 / RISK (%)	4/68 (1 %)	7/90 (1.7%)
STAGE 2/ INJURY (%)	19 / 116(5.1 %)	26/158 (6.64 %)
STAGE 3 / FAILURE (%)	53/ 188 (14 %)	45/143 (11.5 %)
ANY CATEGORY (%)	76 / 372 (20.4%)	78/391 (19.9%)

Table-5: Association of different clinical and demographic characteristics with AKI based on p-RIFLE and AKI based on KDIGO by multivariate logistic regression models:

Characteristics	AKI by p-RIFLE (391, 70%)			AKI BY KDIGO (372, 66%)		
	Frequency and percentages	Odds ratio (CI 95%)	*p*- value	Frequency and percentages	Odds ratio (CI 95%)	*p*- value
Gender male, n (%)	237 (61%)	1.220 (0.827 -1.799)	0.310	230 (62%)	1.013 (0.696 – 1.475)	0.946
Vasopressor support, n (%)	281 (72%)	0.867 (0.560– 1.373)	0.524	268 (72%)	0.901 (0.586 – 1.383)	0.632
Mechanical ventilation, n (%)	260 (66%)	0.746 (0.491 -1.133)	0.169	249 (67%)	0.756 (0.503 – 1.137)	0.179
Renal replacement therapy, n (%)	25 (6%)	0.656 (0.259 -1.662)	0.374	25 (7 %)	0.568 (0.225 – 1.438)	0.233
Nephrotoxic drug exposures, n (%)	371 (95%)	0.592 (0.282 – 1.243)	0.592	357 (96%)	0.519 (0.246– 1.092)	0.084
Fluid overload, n (%)	329 (84%)	0.439 (0.277 -0.696)	<0.05	314 (84%)	0.451 (0.286 – 0.713)	<0.05
Mortality, n (%)	78 (13.9 %)	1.077 (0.634 -1.830)	0.784	76 (13.5%)	0.970 (0.578 – 1.628)	0.908

Table-6: Association of different clinical and demographic characteristics, AKI with mortality by multivariate logislitic regression models

Characteristics		Odds ratio (CI95 %)	*p*- value
Gender, Male		1.288 (0.803 – 2.067)	0.294
Vasopressor support		0.133 (0.055 – 0.320)	<0.05
Mechanical Ventilation		0.120 (0.054 – 0.266)	<0.05
Renal replacement therapy		0.584 (0.235 – 1.450)	0.246
Nephrotoxic drug exposures		5.151 (1.635 – 16.225)	<0.05
Fluid overload		1.059 (0.503 – 2.231)	0.880
AKI KDIGO		0.502 (0.132 – 1.911)	0.313
KDIGO	STAGE 1	0.2.105 (0.415 – 10.670)	0.369
	STAGE 2	0.523 (0.071 – 3.854)	0.525
	STAGE 3	0.432 (0.052 – 3.607)	0.438
AKI p-RIFLE		2.22(0.570 – 8.665)	0.250
	RISK	1.509 (0.389- 5.849)	0.552
	INJURY	2.009 (0.257 -15.686)	0.506
	FAILURE	0.974 (0.112 – 8.457)	0.981

DISCUSSION

AKI continues to be associated with increased morbidity and mortality in PICU, which remains a challenge for intensivist and nephrologist. Various studies have compared the KDIGO and RIFLE criteria for AKI in adult population. However, the incidence of AKI varies in paediatric population based on setting and definition used.[19,20] To date only a few previous studies have compared the incidence and mortality of AKI in critically ill children according to these two definitions.[6] This is the first study to compare two different criteria in critically ill children with AKI in Pakistan.

In our study, the incidence of AKI according to the p-RIFLE criteria was higher (70%) than that defined by KDIGO (66%). Overall incidence of AKI in our

study population is higher compared to previous studies.[6,7,21] This could be due to different settings; since our PICU admits very sick patients, and our cohort has varied underlying diagnosis; this is also depicted by the higher number of patients requiring mechanical ventilation (63%) and vasopressor support (68%) as well as the higher overall mortality (12.8%). However, the comparison between AKI incidences based on the p-RIFLE and KDIGO were similar as reported by Sutherland (51.1% and 40.3%), pRIFLE diagnosed more cases of AKI compared to KDIGO.[6,7] pRIFLE also diagnosed more cases in another study by Daneil *et al* in their post cardiac surgery patients.[6] It is also worth mentioning that pRIFLE diagnosed more of stage I and II AKI than KDIGO (90 versus 68 (stage I) and 158 versus 116 (stage II)) than stage III (143 versus 183) AKI which shows that for severity KDIGO performed better than pRIFLE. Another study done in Brazil in adult population showed KDIGO identified more patients with AKI than p-RIFLE, but they included only those individuals who had myocardial infarction.[22] Almost half (45–53%) of patients with AKI had moderate to severe category. Application of the two definitions resulted in different AKI incidences in the same population with difference in their severity too. These staging discrepancies were highlighted by our comparative data, these differences, both in overall incidence and staging are troubling if the literature continues to apply multiple definitions. It may become difficult to compare results of studies that used different definitions, especially from an epidemiologic standpoint. This underscores the need for a single, unified AKI definition. The aim of this definition should be prediction and early recognition of AKI.

Mortality was higher and almost similar in both the definition systems. In our study overall PICU mortality was 106/823 (12.8 %), while among those who developed AKI (391 by p-RIFLE and 372 by KDIGO), 78/391 (19.9%) and 76/372 (20.4%) died respectively. This high mortality is probably due to nature of our PICU patients and severity of underlying disease as 68% and 63% of patients required vasopressor support and mechanical ventilation respectively. In another study by Hui *et al* showed overall PICU mortality of 12% and those with AKI had a mortality of 21%. They used pRIFLE for diagnosing AKI.[23] Sutherland *et al* compared AKI incidence and mortality according to pRIFLE, AKIN and KDIGO and revealed that all three-definition demonstrated there are differences in identification of severity based on staging.[7] Similarly our study showed difference in mortality between two definitions. However, the agreement statistics between the two definition was very good ($\kappa = .906, p<0.05$). This is different to a previous study which reported lesser degree of agreement between the three definitions (AKIN, p-RIFLE, KDIGO) they used.[7] This again could be because of study population as we included only PICU patient which Sutherland et al also included other hospitalized patients. Within the PICU, all two definitions demonstrated higher mortality as severity stage increased. This became apparent in our study when Vasopressor support, nephrotoxic drugs exposure and length of mechanical ventilation data were analysed; greater mortality was associated with longer length of mechanical ventilation, vasopressor support requirement and nephrotoxic drug exposure, this is comparative to a study done in India showed study patient who died has increased rate of mechanical ventilation in 68%.[24]

Identifying critically ill children with appropriate AKI criteria and staged adequately can help develop appropriate interventions to reduce AKI progress. One can start prompt management according to early stage (risk or stage 1) of acute kidney injury in critically ill children; like applying preventive and reno-protective measures such as avoidance of nephrotoxic agents, aggressively maintaining optimal blood pressure, maintaining euvolemia and initiation of organ supportive therapy, may help to decrease burden Of AKI related mortality and morbidity. Addition of renal angina index (RAI) to AKI definition could be one possible solution for prediction and early detection of AKI.[25,7] In the absence of wide availability of AKI biomarkers especially in low resource settings, p-RIFLE or KDIGO along with RAI can help predict AKI and improve outcomes. Our findings should be interpreted in the context of their limitations. Our study is from a single, paediatric institution. We did not apply the urine output AKI criteria. However, the urine output criteria have never correlated with the creatinine criteria or outcomes.[7,15] We also chose to include patients only if they had a baseline creatinine available and at least one follow-up creatinine during the hospitalization, similar to a study done in 2015 by Sutherland *et al*.[7]

CONCLUSION

The p-RIFLE and KDIGO result in different incidences and substantial disparities in staging, but with acceptable overall agreement. Greater AKI severity is associated with higher mortality critically ill children. p-RIFLE is sensitive, identifying a greater number of moderate AKI cases.

Data Availability: Data can be shared by contacting the corresponding author through email.

Conflict of Interests: The authors declare that there is no conflict of interests regarding the publication of

this paper.

Acknowledgments: World federation of Paediatric intensive and critical care societies allow us to participate at the 9th World Federation of Paediatric Intensive and Critical Care Societies Congress (WFPICCS 2018) held in Singapore, June 9-13, 2018.

AUTHORS' CONTRIBUTION

AH and QA came up with idea and protocol. PU and Habib did literature Search, data collection, entry. QA and PU did analysis, all authors contributed in manuscript writing and gave final approval.

REFERENCE

1. Bello-Reuss E, Reuss L. Homeostatic and Excretory Functions of the Kidney. In: Klahr S, editor. The Kidney and Body Fluids in Health and Disease. Boston, MA: Springer US, 1983; p.35–63.
2. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. 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(4):R204–12.
3. Naik S, Sharma J, Yengkom R, Kalrao V, Mulay A. Acute kidney injury in critically ill children: Risk factors and outcomes. Indian J Crit Care Med 2014;18(3):129–33.
4. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, *et al*. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005;294(7):813–8.
5. Elapavaluru S, Kellum JA. Why do patients die of acute kidney injury? Acta Clin Belg 2007;62(Suppl 2):326–31.
6. Lex DJ, Toth R, Cserep Z, Alexander SI, Breuer T, Sapi E, *et al*. A comparison of the systems for the identification of postoperative acute kidney injury in Paediatric cardiac patients. Ann Thorac Surg 2014;97(1):202–10.
7. Sutherland SM, Byrnes JJ, Kothari M, Longhurst CA, Dutta S, Garcia P, *et al*. AKI in hospitalized children: comparing the pRIFLE, AKIN, and KDIGO definitions. Clin J Am Soc Nephrol 2015;10(4):554–61.
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(10):1028–35.
9. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, *et al*. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11(2):R31.
10. Selewski DT, Cornell TT, Heung M, Troost JP, Ehrmann BJ, Lombel RM, *et al*. Validation of the KDIGO acute kidney injury criteria in a Paediatric critical care population. Intensive Care Med 2014;40(10):1481–8.
11. Alkandari O, Eddington KA, Hyder A, Gauvin F, Ducruet T, Gottesman R, *et al*. Acute kidney injury is an independent risk factor for Paediatric intensive care unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: a two-center retrospective cohort study. Crit Care 2011;15(3):R146.
12. Plötz FB, Bouma AB, van Wijk JA, Kneyber MC, Bökenkamp A. Paediatric acute kidney injury in the ICU: an independent evaluation of pRIFLE criteria. Intensive Care Med 2008;34(9):1713–7.
13. Gao A, Cachat F, Faouzi M, Bardy D, Mosig D, Meyrat BJ, *et al*. Comparison of the glomerular filtration rate in children by the new revised Schwartz formula and a new generalized formula. Kidney Int 2013;83(3):524–30.
14. Allen JC, Gardner DS, Skinner H, Harvey D, Sharman A, Devonald MAJ. Definition of hourly urine output influences reported incidence and staging of acute kidney injury. BMC Nephrol 2020;21(1):19.
15. Md Ralib A, Pickering JW, Shaw GM, Endre ZH. The urine output definition of acute kidney injury is too liberal. Crit Care 2013;17(3):R112.
16. Ceneviva G, Paschall JA, Maffei F, Carcillo JA. Hemodynamic support in fluid-refractory Paediatric septic shock. Paediatrics 1998;102(2):e19.
17. Moffett BS, Goldstein SL. Acute kidney injury and increasing nephrotoxic-medication exposure in noncritically-ill children. Clin J Am Soc Nephrol 2011;6(4):856–63.
18. Kaddourah A, Basu RK, Bagshaw SM, Goldstein SL, Investigators A. Epidemiology of Acute Kidney Injury in Critically Ill Children and Young Adults. N Engl J Med 2017;376(1):11–20.
19. Alobaidi R, Morgan C, Goldstein SL, Bagshaw SM. Population-Based Epidemiology and Outcomes of Acute Kidney Injury in Critically Ill Children. Pediatr Crit Care Med 2020;21(1):82–91.
20. Gupta S, Sengar GS, Meti PK, Lahoti A, Beniwal M, Kumawat M. Acute kidney injury in Paediatric Intensive Care Unit: Incidence, risk factors, and outcome. Indian J Crit Care Med 2016;20(9):526–9.
21. Rodrigues FB, Bruetto RG, Torres US, Otaviano AP, Zanetta DM, Burdmann EA. Incidence and mortality of acute kidney injury after myocardial infarction: a comparison between KDIGO and RIFLE criteria. PLoS One 2013;8(7):e69998.
22. Hui WF, Chan WK, Miu TY. Acute kidney injury in the paediatric intensive care unit: identification by modified RIFLE criteria. Hong Kong Med J 2013;19(1):13–9.
23. Gandhi J, Sangareddi S, Varadarajan P, Suresh S. Paediatric index of mortality 2 score as an outcome predictor in Paediatric Intensive Care Unit in India. Indian J Crit Care Med 2013;17(5):288–91.
24. Sethi SK, Raghunathan V, Shah S, Dhaliwal M, Jha P, Kumar M, *et al*. Fluid Overload and Renal Angina Index at Admission Are Associated With Worse Outcomes in Critically Ill Children. Front Pediatr 2018;6:118.
25. Basu RK, Kaddourah A, Goldstein SL, Investigators AS. Assessment of a renal angina index for prediction of severe acute kidney injury in critically ill children: a multicentre, multinational, prospective observational study. Lancet Child Adolesc Health 2018;2(2):112–20.

Submitted: February 9, 2021	*Revised: July 4, 2021*	*Accepted: September 19, 2021*

Address for Correspondence:

Qalab Abbas, Paediatric Intensive Care Unit, Department of Pediatrics and Child Health, Aga Khan University, Karachi-Pakistan

Email: qalab.abbas@aku.edu