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Original Article

Comparative Study of Akin Staging and Pediatric - Risk, Injury, Failure, Loss, End-stage Kidney Classification in Identifying Acute Kidney Injury in Critically Ill Children

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Abstract

Introduction: Acute kidney injury (AKI) is a common comorbidity in critically ill children, associated with an increased risk of morbidity and mortality. Modern definitions of AKI based on changes in serum creatinine (Cr) and urine output (UO) are the risk, injury, failure, loss, end-stage kidney (RIFLE) classification, and AKI network (AKIN) staging.

Aims and Objectives: The aim of this study was to compare AKIN staging and pediatric RIFLE (p-RIFLE) classification of AKI in critically ill children admitted to Paediatric Intensive Care Unit (PICU) at Institute of Child Health and Research Centre (ICH and RC), Madurai.

Materials and Methods: A prospective observational study done in children 1 month – 12 years of age, admitted to PICU at ICH and RC, Madurai, over a period of 1 year. Demographic information, comorbidities, and serial serum Cr values were collected. UO was measured 6th hourly. AKI was defined by AKIN staging and p-RIFLE classification. Results analyzed using SPSS version 19.

Results: In our study, total of 342 children were enrolled. 106 children had AKI by AKIN staging and 103 had AKI by p-RIFLE criteria, incidence being 31% and 30.1%, respectively. According to AKIN staging, Stage 1 included 43 (40.6%), Stage 2 included 28 (26.4%), Stage 3 included 35 (33%) cases. According to p-RIFLE classification, risk category included 35 (34%), injury category included 31 (30.1%), and failure category included 37 (35.9%) cases. The mortality rate was 42.5% (AKIN staging) and 43.6% (p-RIFLE classification). Mortality among the stages was 34.9%, 39.3%, and 54.3% in AKIN Stage 1, 2, and 3, respectively, with odds ratio of 0.59, 0.84, and 2.06, respectively. According to p-RIFLE, mortality was 37.1%, 38.7%, 54% in risk, injury, and failure class, respectively. There was no difference between AKIN staging and p-RIFLE classification in identifying AKI cases and predicting mortality.

Conclusion: Both criteria correlate highly with outcome and demonstrate excellent inter-stage discrimination. Both were good predictors of mortality.

Key words: Acute kidney injury, Acute kidney injury network, Pediatric-risk; injury; failure; loss; end-stage kidney

INTRODUCTION

The reported incidence of acute kidney injury (AKI) admitted to intensive care unit (ICU) varies widely in critically ill children from 10% to 80%. The wide variations in the reported incidence of AKI are due to the presence of more than 30 definitions for AKI in previous literary texts. Therefore, it necessitated the need to establish a precise definition for AKI.

A uniform definition for AKI has existed only since 2004, when the acute dialysis quality initiative (ADQI) proposed the risk, injury, failure, loss, end-stage kidney disease (RIFLE) criteria[1] for AKI in adults. Later, in 2007, a modified pediatric RIFLE (p-RIFLE)[2] emerged. Since then, two modifications of the RIFLE: AKI network (AKIN)

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(2007)[3] and kidney disease: Improving global outcomes (KDIGO) (2012)[4] have emerged. All of the three modern definitions are based on changes in serum or plasma creatinine (Cr) and urine output (UO).

There are studies comparing RIFLE and AKIN criteria, have shown little difference between them.[5-7] However, these studies are limited to comparison of criteria's in adults and not in pediatric population.

The ADQI convened an international consensus panel in 2002 and proposed the RIFLE criteria for use in critically ill adults in 2004.[5] The RIFLE classification[1] is based on serum creatinine (SCr) and UO determinants and considers three severity classes of AKI (risk, injury and failure), according to the variations in SCr and/or UO and two outcome classes (loss of kidney function and end-stage kidney disease).

A modification of the RIFLE (known as the p-RIFLE) has been suggested for use in pediatric populations in 2007.[2] The changes are minor and include a focus on the estimated Cr clearance (eCCl), calculated using the Schwartz formula[8] as the measure of glomerular filtration rate (GFR). SCr in children is dependent on body mass, which is directly related to height and age of a child. Schwartz formula is, therefore, appropriate for use in children (eCCl = K × length in cm/plasma Cr in mg/dL).

AKIN proposed a new classification of AKI which came into practice in March 2007.[3] It is regarded as the later version of the RIFLE classification with some modifications. The diagnosis of AKI is only considered after achieving an adequate status of hydration and after excluding urinary obstruction. The AKIN classification only relies on SCr and not on GFR changes; baseline SCr is not necessary in the AKIN classification, and it requires at least two values of SCr obtained within a period of 48 h. These modifications were based on the cumulative evidence that even small increases in SCr are associated with a poor outcome (Table 1).[9]

Aims and Objectives

The aim of this study was to compare AKIN staging and p-RIFLE classification of AKI in critically ill children admitted to paediatric ICU (PICU) at Institute of Child Health and Research Centre, Madurai.

MATERIALS AND METHODS

The design is a prospective observational study of critically ill children admitted to PICU at Institute of Child Health and Research Centre, Govt. Rajaji Hospital, Madurai.

All children within the age group of 1 month to 12 years with the length of stay for at least 48 hours in PICU over a period of 1 year (July 2015-June 2016) were included in the study after getting consent from parents. Patients with known chronic kidney disease and bilirubin level >5 mg/dl were excluded from the study. The Institutional Ethical Committee approval obtained.

Sample size was calculated using the formula $4pq/d^2$ (P – incidence of AKI, Q – (1-P), D – absolute precision). The incidence of AKI in critically ill children was estimated to be around 30% based on current literature and assuming a variation of 5% (absolute precision d = 0.05), the sample size was estimated to be around 335.

The study subjects were enrolled consecutively until the sample size was achieved. A detailed clinical history and a thorough physical examination were conducted as soon as the patient was stabilized and weight, height, temperature, blood pressure, pulse, respiratory rates, capillary refill, oxygen saturation, presence of dehydration, presence of anemia, presence of edema were noted. Systemic examination also was done. Height was measured for those children who were 2 years and above and were able to stand using a stadiometer. Those younger than 2 years or those too sick to stand had their length taken using a stadiometer placed flat on a table.

The diagnosis of AKI was based on the AKIN staging; p-RIFLE classification was also used to diagnose AKI for the purpose of comparing AKIN staging and p-RIFLE classification. SCr or UO was used to diagnose and stage AKI, using a criterion that led to a higher stage classification.

Data collected includes demographic information, admission diagnoses/final diagnosis and comorbidities, SCr at the time of admission, other hematological and metabolic parameters. A total of 4 ml of intravenous blood was withdrawn (2 ml for complete blood count and 2 ml for renal and liver function tests) and centrifuged. SCr estimation was performed by modified Jaffe method[10] using the autoanalyzer. This measured value was considered as "initial" SCr. Estimation of SCr was repeated daily for 3 consecutive days and daily thereafter until discharge from hospital. UO was measured 6th hourly in PICU.

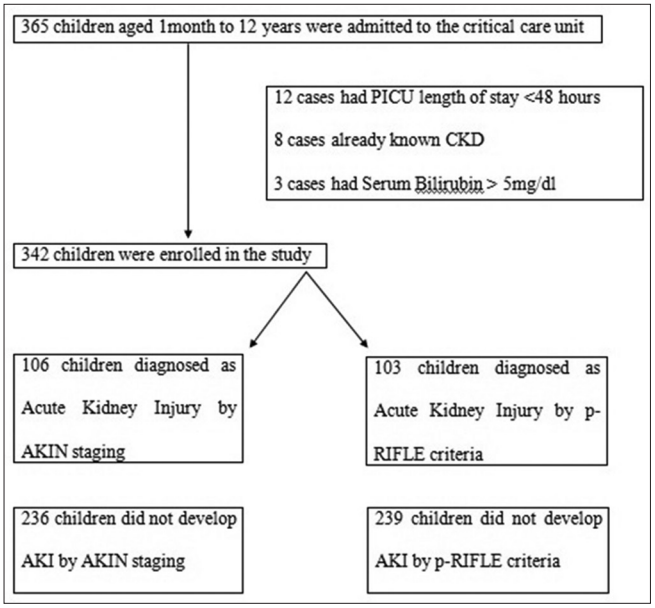
eCCl was calculated as percent change of daily Cr from baseline Cr (using Schwartz formula), Baseline Cr used is lowest consistent SCr 90 days or more before admission. For patients without a prior baseline, an assumed Cr clearance of 75 ml/min/1.73 m^2 is used.[1,11]

Statistical Analysis

Results were analyzed using the SPSS version 19 (IBM corporation, New York, U.S.A).

RESULTS

Our study enrolled 342 children in the period of 12 months and observed for the development of AKI.



On the whole, 342 critically ill children admitted to PICU were screened for AKI. 106 children developed AKI giving an incidence of 31% (by AKIN staging). 103 children developed AKI using p-RIFLE classification giving an incidence of 30.1%. Both AKIN staging and p-RIFLE classification were statistically significant in detecting the number of AKI cases.

The severity of AKI was given by the staging of AKI. According to AKIN staging, Stage 1 included 43 (40.6%) cases, Stage 2 included 28 (26.4%) cases, Stage 3 included 35 (33%) cases. According to p-RIFLE classification, 35 (34%) children were included in risk category, 31 (30.1%) were included in the injury category, and 37 (35.9%) were included in the failure category. Three cases of risk category progressed to injury category and 3 cases to failure category while 1 case from injury category progressed to failure category (Tables 2 and 3).

Mortality rate in children with AKI (as described by AKIN stage) was found to be 42.5% in our study. 45 out of 106 expired during the study. All these 45 cases were identified as AKI by p-RIFLE criteria also and mortality rate according to p-RIFLE classification was 43.7% (45/103). Among the AKIN Stage 1 cases, 15/43 (34.9%) died, in Stage 2 cases, 11/28 (39.3%) died, and in Stage 3 cases, 19/35 (54.3%) died (differences were not statistically significant). Among p-RIFLE class, in risk class, 13/35 (37.1%) died; in injury class, 12/31 (38.7%) died; and in failure class, 20/37 (54%) died (Tables 4-8).

DISCUSSION

From our observational study, the incidence of AKI in critically ill children admitted to PICU in our institute

Table 1: Definition of acute kidney injury

Classification	Stage	Creatinine criteria	Urine output criteria
RIFLE (Bellomo *et al*., 2004)	Risk	Increased creatinine×l. 5 or GFR decrease>25%	<0.5 ml/kg/h×6 h
	Injury	Increased creatinine×2 or GFR decrease>50%	<0.5 ml/kg/h×12 h
	Failure	Increased creatinine×3 or GFR decrease>75% or creatinine≥4 mg/100 ml (acute rise of≥0.5 mg/100 ml/dl)	<0.3 ml/kg/h×24 h or anuria×12 h
	Loss	Persistent ARF=Complete loss of renal function>4 weeks (defined as the need for RRT for>4 weeks)	
	End-stage	End-stage renal disease (defined as the need for dialysis for>3 months)	
Pediatric RIFLE (Akcan-Arikan *et al*., 2007)	Risk	eCCl decrease by 25%	<0.5 ml/kg/h×8 h
	Injury	eCCl decrease by 50%	<0.5 ml/kg/h×16 h
	Failure	eCCl decrease by 75% or eCCl<35 ml/min/1.73 m^2	<0.3 ml/kg/h×24 h or anuria×12 h
	Loss	Persistent failure>4 weeks	
	End-stage	End-stage renal disease (persistent failure>3 months)	
AKIN (Mehta *et al*., 2007)	1	Increased creatinine×1.5-2 or creatinine increase>0.3 mg dl	<0.5 ml/kg/h×6 h
	2	Increased creatinine×2-3	<0.5 ml/kg/h×12 h
	3	Increased creatinine×>3 or creatinine>4.0 mg/dl with an acute increase of 0.5 mg/dl	<0.3 ml/kg/h×24 h or anuria×12 h
KDIGO acute kidney injury working group, 2012)	1	Increased creatinine×1.5-1.9 or>0.3 mg/dl increase	<0.5 ml/kg/h×6-12 h
	2	Increased creatinine×2.0-2.9	<0.5 ml/kg/h×>12 h
	3	Increased creatinine×3 or creatinine>4.0 mg/dl or initiation of RRT or eGFR<35 ml/min per 1.73 m^2 (<18 years)	<0.3 ml/kg/h×>24 h or anuria×>12h

AKIN: Acute kidney injury network, GFR: Glomerular' filtration rate, eCCl: Estimated creatinine clearance, eGFR: Estimated glomerular filtration rate, KDIGO: Kidney disease, improving global outcomes, RRT: Renal replacement therapy, RIFLE: Risk, injury, failure, loss, end-stage kidney

Table 2: Case distribution by AKIN staging

Staging	Cases (%)
Stage 1	43 (40.6)
Stage 2	28 (26.4)
Stage 3	35 (33)
Total	106 (100)
	(*P*<0.0001)

AKIN: Acute kidney injury network

Table 3: Case distribution by p-RIFLE criteria

RIFLE classification	Cases (%)
Risk	35 (34)
Injury	31 (30.1)
Failure	37 (35.9)
Total	103 (100)
	(*P*<0.0001)

p-RIFLE: Pediatric-risk, injury, failure, loss, end-stage kidney

Table 4: Case mortality in AKIN stage

AKIN stage	Survivors (%)	Death (%)	Total (%)
Stage 1	28 (65.1)	15 (34.9)	43 (100)
Stage 2	17 (60.7)	11 (39.3)	28 (100)
Stage 3	16 (45.7)	19 (54.3)	35 (100)
Total	61 (57.5)	45 (42.5)	106 (100)

AKIN: Acute kidney injury network

Table 5: Case mortality in p-RIFLE class

RIFLE class	Survivors (%)	Death (%)	Total (%)
Risk	22 (62.9)	13 (37.1)	35 (100)
Injury	19 (61.3)	12 (38.7)	31 (100)
Failure	17 (46)	20 (54)	37 (100)
Total	58 (56.3)	45 (43.7)	103 (100)

p-RIFLE: Pediatric-risk, injury, failure, loss, end-stage kidney

Table 6: Demographic parameters of critically ill child with AKI

Parameter	Baseline characteristics (*n*=106)
Age (months) (median [range])	36 (2-144)
Sex (%)	Male - 58 (54.7) Female - 48 (45.3)
PRISM III score (mean±SD)	26.4±8.3
Duration of stay (days) (mean±SD)	
Survivors	11.1±4.1
Non-survivors	7.1±4.0
Overall	9.4±4.5
Mortality *n* (%)	45 (42.5)
Mechanical ventilation *n* (%)	59 (55.7)
Shock *n* (%)	77 (72.6)
Encephalopathy *n* (%)	33 (31.1)
Renal replacement therapy *n* (%)	28 (26.4)

AKI: Acute kidney injury, SD: Standard deviation

was found to be 31% using AKIN staging. The incidence in this study was comparable with a study done by Krishnamurthy *et al.* at JIPMER,[12] where the incidence was reported to be 25.1% in PICU and by Mehta *et al.* at AIIMS,[13] where the incidence was 36.1%. This study used SCr and UO that has been used in several similar studies in children.

The incidence of AKI in critically ill children admitted to PICU of our institute using p-RIFLE classification was found to be 30.1%. This was comparable with the incidence of a study done by Srinivasa *et al.* at KIMS, Bangalore, using p-RIFLE classification which showed an incidence of 26.1%.[14] Another study by Naik *et al.*[15] using p-RIFLE classification showed an incidence of 40.9%. This study used SCr and eCCl/estimated glomerular filtration rate (eGFR) using Schwartz formula that has been used in several studies in children. This study, however, reports a slightly lower incidence of AKI using p-RIFLE classification similar to a study by Winnie *et al.* done at mulago because of the use of GFR, which takes into account a child's age, height, and weight. This study has the benefit of having calculated the GFR, a better index of kidney function than SCr. However, there occurs an overestimation of the GFR, another measures such as UO is recommended to improve the sensitivity of the p-RIFLE criteria. When using both, either the UO criteria or the Cr criteria that shows the worst possible outcome should be considered. comparable with the incidence of a study done by Srinivasa *et al.* at KIMS, Bangalore, using p-RIFLE classification which showed an incidence of 26.1%.[14]

Another study by Naik *et al.*[15] using p-RIFLE classification showed an incidence of 40.9%. This study used SCr and eCCl/eGFR using Schwartz formula that has been used in several studies in children. This study, however, reports a slightly lower incidence of AKI using p-RIFLE classification similar to a study by Winnie *et al.* done at mulago because of the use of GFR, which takes into account a child's age, height, and weight. This study has the benefit of having calculated the GFR, a better index of kidney function than SCr. However, there occurs an overestimation of the GFR, another measures such as UO is recommended to improve the sensitivity of the p-RIFLE criteria. When using both, either UO criteria or Cr criteria that shows the worst possible outcome should be considered. Thus, p-RIFLE is useful in determining severity, and thus predicting the mortality, and for monitoring the progress of AKI.[16]

By p-RIFLE Classification

In our study, maximum RIFLE score was achieved in almost all children within 72 h of admission to PICU which was again comparable to study by Naik *et al.* Schneider *et al.* reported that almost 50% patients developed their maximum RIFLE

Table 7: Staging

Staging	Present study (%)	Krishnamurthy *et al.*[12] (%)	Srinivasa *et al.*[14] (%)	Mehta *et al.*[13] (%)
Stage 1	43 (40.6)	19 (35.2)	93 (37.5)	48 (65.8)
Stage 2	28 (26.4)	14 (25.9)	88 (35.5)	13 (17.8)
Stage 3	35 (33)	21 (38.9)	67 (27)	12 (16.4)
Total	106 (100)	54 (100)	248 (100)	73 (100)

Table 8: Classification

Classification	Present study (%)	Srinivsa *et al.*[14] (%)	Naik *et al.*[15] (%)
Risk	35 (34)	108 (60.7)	39 (37.9)
Injury	31 (30.1)	51 (28.7)	37 (35.9)
Failure	37 (35.9)	19 (10.6)	27 (26.2)
Total	103 (100)	178 (100)	103 (100)

Table 9: AKIN stage

AKIN stage	Survivors (%)	Death (%)	Total (%)	Odds ratio	95% CI	*P* value
Stage 1	28 (65.1)	15 (34.9)	43 (100)			
Stage 2	17 (60.7)	11 (39.3)	28 (100)	0.84	0.32-2.20	0.692
Stage 3	16 (45.7)	19 (54.3)	35 (100)	2.06	0.84-5.08	0.083
Total	61 (57.5)	45 (42.5)	106 (100)			

CI: Confidence interval, AKIN: Acute kidney injury network

Table 10: RIFLE class

RIFLE class	Survivors (%)	Death (%)	Total (%)	Odds ratio	95% CI	*P* value
Risk	22 (62.9)	13 (37.1)	35 (100)			
Injury	19 (61.3)	12 (38.7)	31 (100)	0.502	0.19-1.28	0.152
Failure	17 (46)	20 (54)	37 (100)	1.863	0.70-4.91	0.209
Total	58 (56.3)	45 (43.7)	103 (100)			

CI: Confidence interval, RIFLE: Risk, injury, failure, loss, end-stage kidney

score within 24 h of admission and about 75% achieved it by 7th day of PICU stay. Due to the decreasing sensitivity and increasing specificity as one moves through the categories from risk, to injury, to failure,[16] it is possible that many more patients were categorized as p-RIFLE-risk, while some were missed as we consider the p-RIFLE-failure category.

The mortality in AKI in children also has been reported to vary widely from 16% to 43.8%.[2,17-20] In our study, it was 42.5% (by AKIN staging) and 43.7% (by p-RIFLE classification), which is comparable to a recent study from Kuwait reporting 43.8% mortality.[20] The mortality rate in a study by Krishnamurthy *et al.*[12] was found to be 46.3%. In the study by Naik *et al.*,[15] mortality was found to be 15.5% in AKI group. In a study by Mehta *et al.*,[13] the mortality was 37% in AKI group. In a study by Miklaszewka *et al.*,[21] 2014 the mortality was found to be 40%. In a study by Martin *et al.*,[22] 2013 the mortality was 44%. Studies by Miklaszewka and Martin used p-RIFLE class to define AKI.

From the Tables 9 and 10 which compare the mortality in each stage of the disease classifications, it is evident that there was no statistical significance between AKIN staging and RIFLE classification. Similar observation was made in a study by Srinivasa *et al.* In a study by Sutherland *et al.*,[23] they found that p-RIFLE, AKIN, and KDIGO result in different incidences and substantial disparities in staging. All three definitions correlate highly with outcomes and demonstrate excellent interstage discrimination. In a study by Levi *et al.*, they found that the RIFLE, AKIN, and KDIGO scores were all good predictors of mortality in critically ill patients, and there were no differences among them in terms of predicting death. These scores are good predictors of death.

CONCLUSION

There is no difference between AKIN staging and p-RIFLE classification in identifying AKI cases. Both the criteria were good predictors of mortality.

Limitations of the Study

In our study, the estimation of a normal baseline GFR for age was used since all patients did not have a prior GFR

recorded. UO measurement was difficult in most cases and only eCCl or SCr was used to stage AKI.

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