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Research Paper

Renal Angina Index for Predicting Acute Kidney Injury in Critically Ill Children: A Prospective Follow-up Study

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ABSTRACT

Background and Aim: Renal Angina Index (RAI), which combines risk strata and clinical injury signs of acute kidney injury (AKI) helps identify sick paediatrics at risk of developing severe AKI. This study aimed to estimate the proportion of critically ill children with a positive RAI score at admission who develop severe AKI on day 3 of paediatric intensive care unit (PICU) admission.

Methods: This prospective follow-up study was done among 100 children without preexisting kidney disease and with at least 3 days of stay in the pediatric intensive care unit of a tertiary care teaching hospital in South India. The RAI score was calculated at admission. The KDIGO score was applied on day 3 of admission. The proportion of children with a positive RAI score (8 or more) who developed severe AKI (the kidney disease: Improving global outcomes [KDIGO] stages 2 and 3) was calculated. Short-term outcomes in terms of duration of hospital stay and mortality were also studied.

Results: A total of 100 children aged 29 days to 12 years were included in the study. Fifty-one percent of them were found to be RAI-positive at admission. Also, 41.2% of RAI-positive children developed severe AKI on day 3 of admission. Among the 31% of children who were diagnosed with severe AKI by day 3 of admission, 67.7% had a positive RAI score at the time of admission (P<0.05). AKI was found to be associated with increased median duration of hospital stay.

Conclusion: The RAI score can predict AKI in critically ill children.

Keywords: Acute kidney injury (AKI), Child, Renal angina index (RAI), Creatinine, Biomarkers

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Introduction

Acute kidney injury (AKI) is defined by a reversible rise in serum creatinine and nitrogenous waste products, and by the kidney's inability to regulate electrolyte and fluid homeostasis properly [1]. A prospective observational investigation conducted at a tertiary care hospital in southern India declared an AKI incidence of 25.1% among critically ill children [2]. The kidney disease: Improving global outcomes (KDIGO) instruction introduces AKI based on urine output and serum creatinine values. Serum creatinine alone is an imperfect marker for predicting severe AKI; hence, there is a need for novel AKI biomarkers. The Renal Angina Index (RAI) score has been proposed to risk-stratify critically ill children at high risk of developing severe AKI. The RAI is the product of risk strata and clinical injury signs of AKI, which can identify sick paediatrics at risk of developing severe AKI (KDIGO stages 2–3) and is superior to many illness-severity scores in such anticipation [3, 4]. Our main aim was to determine the proportion of critically ill children with a positive RAI score developing severe AKI (KDIGO stages 2-3) on day 3 of intensive care unit admission. Short-term outcomes in terms of the need for renal replacement therapy, duration of hospital stay, and mortality were also studied.

Materials and Methods

After approval by the Institutional Human Ethics Committee of the institution, a prospective follow-up study until discharge was conducted from July 2021 to August 2022 among the children admitted to the paediatric intensive care unit (PICU).

In a study conducted by Gawadia et al., conducted in Chacha Nehru Bal Chikilsalaya, Delhi, on 160 children [5], the proportion of RAI-positive children was 53%, which was utilized to calculate the sample size. With a permissible error of 20%, the final sample size was calculated as 100.

A consecutive sampling of all children aged 29 days to 12 years admitted to the PICU was done. Children with pre-existing kidney disease and children who stayed in PICU for less than 3 days were excluded. Socio-demographic data, anthropometry, and vital signs at admission were collected. Baseline creatinine value and fluid overload percentage were noted. The RAI (ranging from 1 to 40) was computed by multiplying the risk score by the higher of the two assigned injury scores. An RAI score of ≥8 was assigned a positive RAI score [6] (Table 1).

All children included in the study were followed up, and on day 3 of PICU admission KDIGO staging was performed to classify AKI. Stage 2 or higher was considered severe AKI. All the children were followed up until discharge and the duration of hospital stay was recorded. The proportion of children with a positive RAI score who developed severe AKI on day 3 was estimated. The proportion of children with a positive RAI score who required renal replacement therapy was also estimated.

Statistical analysis

Data were analysed using SPSS software, version 23. Continuous variables are expressed as median (IQR) and categorical variables are reported as proportions. The chi-square test was used to assess associations between categorical variables.

Results

A total of 100 children in the age group of 29 days to 12 years were included in the study. The median age was 2 years (0.6-7). Fifty-three percent were female and 47% were male. Fifty-one (51%) children were found to be RAI-positive (RAI score ≥8) at admission. The demographic and clinical features are summarised in Table 1.

Thirty-six children (36%) developed severe AKI during the course of PICU stay. Among these, 86% (n=31) developed severe AKI on day 3 of admission. Also, 41.2% (n=21) of RAI-positive children developed severe AKI on day 3 of admission. Table 2 summarises the association of a positive RAI score with the occurrence of AKI on day 3 and the need for renal replacement therapy. Out of the 31 children who progressed to severe AKI by day 3 of admission, 67.7% (n=21) had a positive RAI score at admission($P<0.05$). A positive RAI score demonstrated a positive predictive value of 41.1% and a negative predictive value of 79.5% for predicting the development of severe AKI by day 3 of admission.

Of the 51 RAI-positive children, 27.5% (n=14) required renal replacement therapy. Eight of the RAI-negative children also required RRT. Of the 22 children who required RRT, 63.6% (n=14) were found to be RAI-positive at admission. However, this association was not statistically significant. Also, 61.1% (n=22) of cases of severe AKI required renal replacement therapy. Five of them required haemodialysis and 17 patients underwent peritoneal dialysis.

Table 1. Calculation of the RAI score [6]

Risk Level		
Type of Patient	**Level of Risk**	**Score**
Intensive care unit admission	Moderate	1
Solid organ or stem-cell transplant	High	3
Ventilation or inotropic support	Very high	5
Injury Level		
Serum Creatinine Relative to Baseline	**Fluid Overload (%)**	**Score**
No change	<5	1
>1–1.49x	5–10	2
1.5–1.99x	11–5	4
≥2x	>15	8

The association between the occurrence of severe AKI and the outcome and duration of PICU stay and total hospital stay is depicted in Table 3. Among the study population where mortality occurred, 48.1% had severe AKI. This association was not statistically significant. The median duration of total hospital stay in the surviving study population was found to be higher in children with severe AKI (median value: 17) when compared to those without severe AKI (median value: 14). This association was statistically significant (Table 4).

Discussion

A considerable proportion of children admitted the PICU develop AKI. Many drugs used in the ICU may contribute to the development of AKI. In the present study, a positive RAI score at PICU admission showed a significant association with the occurrence of severe AKI on day 3 of admission. Although mortality was higher among children with AKI, it was not statistically significant. AKI was found to be associated with an increased median duration of hospital stay.

Basu et al. conducted a large, multi-center prospective observational study on critically ill children and showed that assessment of the RAI early during ICU stay offered a distinct predictive advantage compared to increased serum creatinine levels for clinically significant AKI [6]. A positive RAI score demonstrated higher positive and negative predictive value and a higher Youden's index for severe subsequent AKI than KDIGO stage 1 [7]. Kaur et al. reported that this index can serve as a bedside tool to predict severe AKI occurrence after PICU admission and is superior to both KDIGO stage 1 renal injury and PRISM-II scores [8]. Our study, though limited by a smaller sample size, is consistent with these results and proves that RAI offers a bedside approach to anticipate severe AKI and is superior to serum creatinine levels alone.

Severe AKI alone is not an independent risk factor for predicting mortality. According to Mehta et al., although crude mortality is higher in AKI patients compared to those without, AKI is not an independent predictor of death in multivariate analysis [9]. Progression of AKI, according to the KDIGO staging criteria, is independently linked to higher mortality in the PICU, whereas improvement in AKI stage is associated with a stepwise reduction in mortality [10]. In our study population where mortality occurred, 48.1% had severe AKI, but this was not statistically significant.

The study conducted by Sharma et al. added that total days of PICU and hospital stay were higher in patients with AKI, compared to non-AKI patients ($P<0.001$ and $P=0.009$, respectively) [11]. Our study also shows that severe AKI is associated with a significant increase in the duration of hospital stay. Severe AKI was further associated with greater duration of mechanical ventilation, duration of vasoactive support, and lengths of PICU and hospital stay [12].

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Table 2. Demographic data of the participants

Demographic Variables	Category	No. (%)
Age	1 month–1 year	45(45)
	1-5 years	27(27)
	5-12 years	28(28)
Gender	Male	47(47)
	Female	53(53)
Blood pressure	Normal	70(70)
	Hypotension	26(26)
	Hypertension	4(4)
Oxygen saturation	Normal	51(51)
	Hypoxia	49(49)
Coagulation parameters	Normal	84(84)
	Coagulopathy	16(16)
Hydration status	Normal	87(87)
	Dehydration	13(13)
Nephrotoxic drug use	Nephrotoxic drugs immediately prior to admission	14(14)
	Nephrotoxic drugs during the current admission	19(19)
Premorbid conditions	Heart disease	12(12)
	Neurological diseases	21(21)
	Respiratory disease	2(2)
	Gastrointestinal diseases	3(3)
Diagnosis at admission	Congestive cardiac failure	4(4)
	Pneumonia, asthma, and other respiratory diseases	35(35)
	Liver failure	4(4)
	Sepsis and septic shock	13(13)
	Shock (other than septic shock)	8(8)
	Renal disease	6(6)
	Meningitis, AES, and status epilepticus	11(11)
	IEM	4(4)
	Snake bite	3(3)
	DKA	1(1)
	MIS-C	3(3)
	Postoperative	6(6)
	ADD	2(2)
Ejection fraction on day 0	<45	16(16)
Mechanical ventilation	Needed	69(69)

Demographic Variables	Category	No. (%)
Inotropes during days 0-3	1	21(21)
	2	16(16)
	3	10(10)
	>3	2(2)
RAI score on day 0	RAI-positive (≥8)	51(51)
	RAI-negative (<8)	49(49)
KDIGO score on day 3	0	53(53)
	1	16(16)
	2	13(13)
	3	18(18)
Severe AKI (KDIGO ≥2)	Day 3	31(31)
	During hospital stay	36(36)
Renal replacement therapy	Needed	22(22)

Abbreviations: AES: Acute encephalitis syndrome; IEM: Inborn error of metabolism; DKA: Diabetic ketoacidosis; MIS-C: Multisystem inflammatory syndrome in children; ADD: Autosomal dominant disorders; RAI: Renal angina index; KDIGO: The kidney disease: Improving global outcomes; AKI: Acute kidney injury.

Table 3. Association of positive RAI score and severe AKI on day 3 and the need for RRT

RAI	AKI on Day 3		Need for RRT	
	Yes	No	Yes	No
Positive	21	30	14	37
Negative	10	39	8	41
	Chi-square value: 5.03 P=0.025; RR: 2.018 (95% CI, 1.061%, 3.838%)		Chi-square value: 1.80 P=0.179;RR: 1.6814 (95% CI, 0.774%, 3.650%)	

Abbreviations: AKI: Acute kidney injury; RRT: Renal replacement therapy; RAI: Renal angina index.

Table 4. Association between severe AKI and outcome and median duration of PICU and hospital stay

AKI	Outcome		Median Duration of PICU Stay	Median Duration of Total Hospital Stay
	Discharged	Mortality		
Severe	23	13	5	17
No severe	50	14	4	14
	Chi-square value: 2.36 P=0.124; RR: 1.6508 (95% CI, 0.8749 to 3.115)		P=0.16	P=0.008

Abbreviations: AKI: Acute kidney injury; RRT: Renal replacement therapy; PICU: Paediatric intensive care unit.

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The RAI score takes into account additional risk factors, like mechanical ventilation and inotropic support, in addition to serum creatinine values. Even though novel AKI biomarkers superior to serum creatinine have emerged, considering cost-effectiveness, the RAI is a better bedside tool to predict AKI in resource-limited settings. Moreover, calculating the RAI at admission may encourage the cautious use of nephrotoxic agents, which may further improve patient outcomes.

Conclusion

A positive RAI score yielded a positive predictive value of 41.1% and a negative predictive value of 79.5% for predicting severe AKI by the third day of admission.

The RAI can serve as a bedside method to predict severe AKI and is superior to serum creatinine levels alone.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Institutional Human Ethics Committee (Code: 06/06/2021/MCT).

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Authors' contributions

Conceptualization and Supervision: Geetha Saradakutty, Methodology: Nithindas Thandayan; Data collection: Nithindas Thandayan, Bindusha Sasidharan; Data analysis: Nithindas Thandayan; Funding acquisition and Resources: Geetha Saradakutty; Investigation, Writing original draft, and Writing review & editing: All authors.

Conflict of interest

The authors declared no conflict of interests.

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