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Prediction Of Acute Kidney Injury Using Renal Angina Index In Pediatric Intensive Care Unit

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Abstract

Prediction of AKI or risk stratification of patients in danger of kidney damage is crucial for initiating preventive measures for AKI. Thus, an appropriate risk assessment for AKI is required in every patient admitted to the intensive care unit (ICU). the renal angina index (RAI), which is determined based on changes in renal function, was proposed to risk stratify critically ill children at high risk of AKI. determine the ability of renal angina index to predict acute kidney injury in children in pediatric intensive care unit and comparing its abilility with that of serum creatinine. This study is a prospective obsevational study was carried on 162 children admitted in pediatric intensive care unit, All studied patients have been subjected to full history taking, complete clinical examination and Measurement of Complete blood count, Serum creatinine, Liver function tests (ALT, AST, PT, PTT, INR) and electrolytes. Calculation 0f renal angina index and Detection of patients developed AKI at D3 according to KDIGO criteria. This study included 100 children. 54% of the studied patients were males and 46% were females, their mean age was 6.3 years, Seventy percent of the studied sample had AKI, there were no statistically significant differences between patients with and without AKI regarding sex, age, or weight, ROC curve analysis showed that RAI, and creatinine (each alone) can significantly predict AKI at the shown cutoff values. RAI is more sensitive and specific (79.6% & 64.8% respectively) than creatinine (61.4% & 63.3%).

Keywords: Acute Kidney Injury; Renal Angina Index; PICU

1. Introduction

Acute kidney injury (AKI), formerly known as acute renal failure (ARF) denotes a sudden and often reversible reduction in the kidney function, as measured by glomerular filtration rate (GFR) [1].

There is no clear definition of AKI. Several different criteria have been used in research studies such as RIFLE, AKIN (Acute Kidney Injury Network) or KDIGO (Kidney Disease: Improving Global Outcomes) criteria. However, KDIGO is the most recent and most commonly used. According to KDIGO, AKI is the presence of any of the following:

- Increase in serum creatinine by 0.3 mg/dL or more (26.5 micromoles/L or more) within 48 hours.
- Increase in serum creatinine to 1.5 times or more baseline, within the prior 7 days.
- Urine volume less than 0.5 mL/kg/h for at least6 hours. [2]**.**

AKI is a very common condition especially among hospitalized patients. It can be seen in up to 7% of hospital admissions and 30% ICU admissions. [3]

AKI is often an important factor that contributes to decision to hospitalize for other conditions, if not being the sole reason for hospitalization. Most drugs or procedures that use contrast media may need to delay due to co-existent AKI. Most of the drugs are renally excreted, and dosages might need to be adjusted to account for the reduced renal function. [4]

Prediction of AKI or risk stratification of patients in danger of kidney damage is crucial for initiating preventive measures for AKI. Thus, an appropriate risk assessment for AKI is required in every patient admitted to the intensive care unit (ICU). Although the Kidney Disease Improving Global Outcomes (KDIGO) guideline defines AKI according to serum creatinine and urine output, serum creatinine is an imperfect marker for detecting severe AKI, and novel AKI biomarkers are emerging. AKI biomarkers, such as cell cycle arrest markers (tissue inhibitor of metalloproteinases 2 and insulin-like growth factor binding protein 7), 3,5 neutrophil gelatinase-associated lipocalin, and L-type fatty acid–binding protein (L-FABP) were reported to predict AKI. However, it is necessary that these biomarkers be used in an appropriate setting, because they may be affected by co_morbidities, and their performance may decrease in a different setting. [5]

Recently, the renal angina index (RAI), which is determined based on changes in renal function, was proposed to risk stratify critically ill children at high risk of AKI. The concept of renal angina has come into use to highlight the characteristics of renal injury as an analogy to the concept of angina pectoris, which is used to increase the suspicion of acute coronary syndrome in cardiology. The RAI is assumed to serve as a potential tool for detecting early signs of persistent AKI. [6]

The aim of this study was to determine the ability of renal angina index to predict acute kidney injury in children in pediatric intensive

care unit and comparing its abilility with that of serum creatinine.

2. Patients and methods

This study is a prospective obsevational study was carried on 162 children admitted in pediatric intensive care unit at Benha University Hospitals from October 2019 to March 2020 . This study was approved by the ethical committee of the Faculty of Medicine, Benha University. Informed written consents were taken from parents of the included patients.

Inclusion criteria: All enrolled patients were:

- All children, 1 month to 12 years, admitted in pediatric intensive care unit, for at least 8 hours and remaining for more than 3 days and having documented body-weight and intake-output records over this duration.

Exclusion Criteria:

- Known cases of chronic kidney disease.
- Children already on dialysis.

There were 387 hospitalizations during the recruitment period and, of these 121 patients were eligible for the study. Parental consent was not granted in sixteen cases and two children died before the start of the examination. Of the 103 cases who had RAI done and creatinine measured , three children were excluded after they discharged from PICU before 3 days of stay . 162 children aged from 1 month to 12 years with mean age (6,3±5,4 year). They were 88male (54%) and 74 females (46%).

All studied patients have been subjected to full history taking, complete clinical examination and Measurement of Complete blood count, Serum creatinine. (On day of entry (D0), 24h (D1), 48h (D2)and 72h (D3)), Liver function tests (ALT, AST, PT, PTT, INR) and electrolytes.

Calculation 0f renal angina index; [7]**.** Detection of patients developed AKI at D3 according to KDIGO criteria [2]**.**

2.1. Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 software (SpssInc, Chicago, ILL Company). Categorical data were presented as number and percentages, Chi Square (χ^2) was used to analyze them. Quantitative data were tested for normality using Shapiro-Wilks test assuming normality at P>0.05. Normally distributed variables were expressed as mean ±standard deviation, median and inter-quartile range (IQR) were added when non-parametric, and analyzed by Mann Whitney U test (ZMWU) for 2 independent groups. ROC curves were constructed to assess validity and predictivity of the studied variables in prediction of AKI.

3. Results

This study included 162 children. 54% of the studied patients were males and 46% were females, their mean age was 6.3 years, the median is 5 years ranging from 2 months to 12 years. The weight of the studied sample ranged between 3 to 59 kg with mean and median values of 19.1 and 15.5 kg. Table 1

Table (1) Basic characters of the studied sample

Variable		**No. (N=162)**	**% (100%)**
Sex	**Male**	88	54.0
	Female	74	46.0
	Mean ±SD	**Median**	**Range**
Age (years)	6.3±**5,4**	5.0	2 months- 12 ys
Weight (kg)	19.1±**14.0**	15.5	3-59

Seventy percent of the studied sample had AKI, there were no statistically significant differences between patients with and without AKI regarding sex, age, or weight (P>0.05 for all). Table 2

Table 2: Comparing patients with and without AKI according to basic characters

Variable		**AKI (n=113)**		**No AKI (n=49)**		**X^2**	**P**
		No.	**%**	**No.**	**%**		
Sex	**Male**	71	62.9	23	46.7	**2.26**	**0.13 (NS)**
	Female	42	37.1	26	53.3		
Age (ys)	**Mean±SD**	5.7±4.4		4.4±4.6		**Z_{MWU}= 1.52**	**0.13 (NS)**
	Median (Range)	5 (2m-12 ys)		1 (2m-12 ys)			
Weight (kg)	**Mean±SD**	16 (20.2±14.5)		10 (16.3±12.6)		**Z_{MWU}= 1.35**	**0.17 (NS)**
	Median (Range)	3-59		4-45			

Z_{MWU}=Z value of Mann Whitney U test

Table 3 shows that 79.1% of patients with positive RAI suffered from AKI compared to 21% of those with negative RAI. This difference was statistically highly significant (P<0.001).

Table (3) Comparing patients with and without AKI according to RAI

			AKI at D3		X^2	P
			Positive	**Negative**		
RAI	Positive	Count	89	16	31.8	<0.001
		% within RAI	79.1%	30.9%		(HS)
	Negative	Count	24	33		
		% within RAI	21%	68%		
Total		Count	113	49		
		% within RAI	67%	33%		

Table 4 shows that 79.6% of patients with positive creatinine suffered from AKI compared to 58.7% of those with negative creatinine. This difference was statistically significant (P<0.05).

Table (4) Comparing patients with and without AKI according to serum creatinine

Serum creat		AKI at D3		X^2	P
		Positive	Negative		
Positive	Count	77	15	5.18	
	% within Setum creatinine	68,7%	31,3%		
Negative	Count	36	34		0.023 (S)
	% within Setum creatinine	52,8 %	47,2%		
Total	Count	113	49		
	% within Setum creatinine	67.0%	33.0%		

The mean values of risk , injury , and RAI scores were significantly higher among patients with AKI (5.04, 4.78, and 22.7 respectively) than those without (3.93, 3.16, and 12.47 respectively). All P values are <0.05. Table 5

Table (5) Comparing patients with and without AKI according to the studied scores

Variable	**AKI (n=70)**			**No AKI (n=30)**			Z_{MWU}	**P**
	Mean	**± SD**	**Range**	**Mean**	**± SD**	**Range**		
Risk score	5.04	1.95	1-6	3.93	2.44	1-6	2.51	0.012 (S)
Injury score	4.78	2.44	1-8	3.16	2.05	1-8	3.14	0.002 (S)
RAI score D0	22.7	15.4	2-48	12.33	12.47	2-48	3.48	=0.001 (HS)

ROC curve analysis showed that RAI, and creatinine (each alone) can significantly predict AKI at the shown cutoff values. RAI is more sensitive and specific (79.6% & 64.8% respectively) than creatinine (59.4% & 61.2%). Fig 1& 2

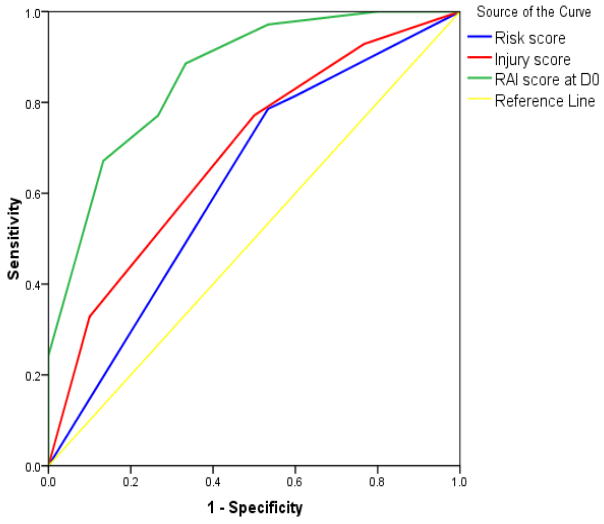

Fig 1: ROC curve for the performance of RAI in early diagnosis (prediction) of AKI

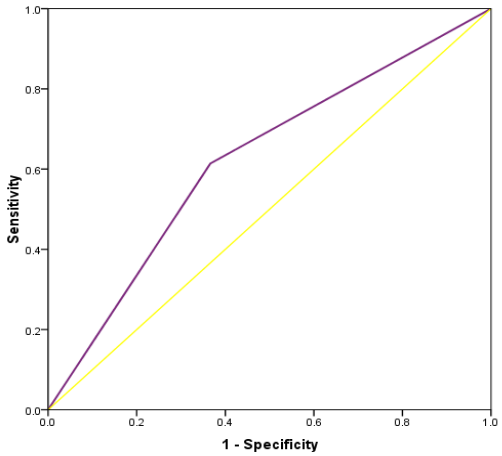

Fig 2: ROC curve of creatinine

4. Discussion

This study included 162 children, 54% male and 46% females. The patients mean age was 6.3±5.4 years (2 months: 12 years) and their mean weight was 19.1±14.0 years (3-59 kg).

The predominanace of male sex (54%) was similar to previous studies [8], Of the 433 patients admitted to PICU, 237 (54.73%) were male. And in another study [9], Among the 688 patients enrolled in the study, 55.6% were male. Also in [10] study, From 400 patients, F:M ratio was 1:1.2. Moreover, [11] have identified male sex as a risk factor for PICU admission.

In this study, the mean Risk score was 4.8±2.06, the mean injury score was 4.2±2.5, RAI was calculated from product of the renal risk and renal injury score. Renal angina positivity was defined as RAI ≥ 8. The RAI score was positive in 74% and negative in 26% and its mean value at day 0 was 20±14.7. While serum creatinine was positive in only 48% of cases and negative in 52%. AKI at day 3 was positive in 69,7% and negative in 30,3% of cases.

This was in agree with [12]–[15], who reported that RAI performed better than baseline serum creatinine and percentage fall in eCr/Cl from baseline in predicting AKI. As in [15] study, Thirty-eight children had RAI > 8 at admission (37.2%). Thirty-three children had AKI on day 3 of admission (32.3%).

Various studies of AKI in the PICU have reported incidence ranging widely between studies; Menta et al.[16] reported a 36.1% incidence of AKI in the critically ill children included in their study. Naik et al. [17] reported 40.9% of patients developed AKI as defined by modified RIFLE criteria. Gupta et al. [18] reported 42.9% out of 536 patients developed AKI, as defined by modified pRIFLE criteria. Plotz et al. [19] reported incidence of 58% of AKI in PICU. While Akcan et al. [20] showed a high incidence of 82%. The reported difference in incidence of AKI in different studies could be due to different study population, PICU environment and/or according to definition of AKI.

In this study, there was no statistical difference between patients with positive AKI and patients with negative AKI regarding their age, sex or weight.

In Naik et al. [17] study, The mean (SD) age of the entire cohort was 3.30 (3.80) years (range 1 month to 16 years). Mean (SD) age of children in the AKI group was 2.35 (3.24) years, whereas in the non-AKI group was 3.95 (4.02) yrs (P = 0.002). There was no significance difference between AKI group and non-AKI group regarding their sex. On the comparison of admission diagnosis in AKI and non-AKI patients; Sepsis, gastroenteritis, status epilepticus, bronchopneumonia and central nervous system infections were significantly more common in patients with AKI.

In De-zan et al**.** [21] study, The most common PICU admission diagnosis in AKI cases were heart disease (38.6%), respiratory failure (16.8%) and postsurgical non-cardiac patients (11%). While in Rustagi et al. [22] study, The most common diagnosis underlying AKI were acute lower respiratory tract infection, CNS illness and severe dehydration. This difference between studies in admission diagnosis is due to different study population.

In this study, there was a statistical difference between patients with AKI and patients without AKI regarding RAI score in D 0 (the mean RAI score was 22.7±15.4 in AKI and 12.33±12.47 in non- AKI, p=0.001).

In Kaur et al. [14] study, RAI positivity was seen in 16.7% cases, of which 36.2% developed AKI at 4 days vs. 2.3% in RAI-negative cases ($p < 0.001$).

In Gawadia et al. [12] study, on Day 0, 86/162 (53%) children had a RAI ≥8. The lowest RAI of 1 was seen in 32 (19.8%) children, while 15 (9.3%) had the highest RAI of 40. Of the 86 children who were RAI positive on Day 0, 62 (72.1%; 95% CI 62.6 %-81.4%) developed severe AKI on Day 3 in contrast to 2/76 (2.6%) children who were RAI negative (RR 95.5; 95% CI 21.7, 420.4; P <0.001).

In this study, ROC curve analysis showed that positive RAI score and positive creatinine can significantly predict AKI at the cutoff values. With AUC (RAI score=0.730 and positive creatinine =0.629). RAI was more sensitive and specific than creatinine.

This was in agree with Sethi et al. [15] study, RAI score could predict D3 AKI with AUC= 0.73 (CI: 0.61-0.82), with sensitivity 81.8 and specificity 69.6 , PPV to predict D3 AKI was 56.3 and NPV to predict D3 AKI was 88.9.

In Gawadia et al. [12] study, A positive Day 0 RAI was found to have a sensitivity of 96.9%, a specificity of 75.5%, a positive predictive value of 72% and a negative predictive value of 97.4%. A Receiver operating characteristic (ROC) curve was constructed for assessing individual values of Day 0 RAI for predicting severe AKI on Day 3, with an AUC (Area Under the Curve) of 0.90 (95% CI 0.85, 0.95). Serum creatinine at enrolment and Percentage fall in eCrCl from baseline showed AUC (0.68 and 0.73, respectively) much inferior to that of RAI.

In Sundararaju et al. [13] study, Receiver operator characteristic curves to examine the diagnostic accuracy of RAI score in discriminating patients with severe AKI showed AUC of 0.82 (95% CI: 0.73–0.90) for severe AKI on day 3 and AUC of 0.73 (95% CI: 0.62–0.84) for severe AKI on day 7 , An RAI score of ≥12 or ≥20 had higher diagnostic utility than RAI ≥8 in predicting severe AKI on day 3 and day 7. RAI thresholds of 8 as well as 12 or 20 had satisfactory sensitivity (82.8% and 79.3%, respectively) and high NPV (96.5% and 97%, respectively) for the development of severe AKI on day 3.

5. Conclusion

The RAI is easy to perform and can be done at bedside in the PICU. Identification of patients at a higher AKI risk using RAI stratification could theoretically guide the enrollment for a novel AKI biomarker or therapy trial, which could ultimately guide treatment strategy. Moreover, this can help physicians in judicious fluid and drug management in these patients. We feel that RAI should also be done in all critically ill children along with illness severity scores at the time of admission.

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