Incidence and Risk Factors of Acute Kidney Injury in Congenital Heart Disease Children Post Cardiac Surgery Applying Akin and Rai Criteria and Biomarker Cystatin C Levels – A Cross Sectional Study for A Period of One Year

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INTRODUCTION

The survival of patients with congenital heart disease has increased dramatically due to recent advances in cardiac surgery,yet morbidity rates remain high .
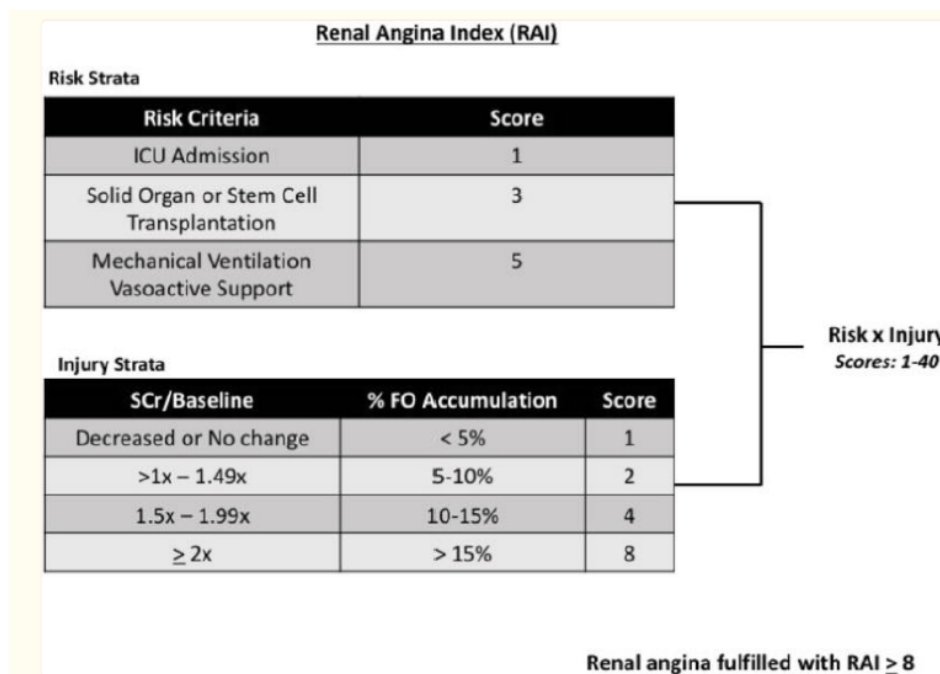
Acute kidney injury (AKI),defined as abrupt decline in renal function,is a common complication in critically ill patients admitted to paediatric cardiac intensive care unit .studies show wide range of AKI prevalence ranging between 15 and 64% with mortality rate of 10-89% among those requiring dialysis in devoloping countries .

Significant continous risk factors for AKI include younger age ,high pre op estimated glomerular filtration rate(eGFR) ,longer surgery time ,longer cardio pulmonary bypass time ,longer aortic cross clamp time .

Cystatin C has also been used by researchers to evaluate AKI after contrast agent use and pediatric cardiac surgery. Zappitelli *et al*. proposed the use of cystatin C instead of creatinine to diagnose AKI. They concurred that cystatin C, like creatinine, is also filtered through glomerulus.The serum concentrations of cystatin C are not affected by muscle mass or gender, although corticosteroids, and thyroid disease may affect its levels. They replaced creatinine in AKIN criteria by cystatin C and found that the incidence of AKI as defined by creatinine was more than double of AKI defined by cystatin C. There was an agreement between Stage 2

(and 3) AKI, between creatinine and cystatin AKI. There was a significant difference in the incidence of Stage 1 AKI between creatinine and cystatin groups because the increase in cystatin C was late. The time to the first diagnosis of AKI was 2 days versus 1 day for creatinine AKI and cystatin AKI, respectively. The cystatin AKI was more strongly associated with kidney injury molecule 1 (KIM 1) and interleukin 18 (IL-18) compared with creatinine AKI. In spite of all observations and studies of alternative biomarkers serum creatinine prevails as the most commonly used molecule to diagnose and stage AKI.

Risk stratification for AKI may be possible using the concept of *renal angina ,* which combines risk factors and early signs of loss of function (increases in serum creatinine or degrees of fluid accumulation) to stratify patients for risk subsequent severe AKI (Stage 2 or 3 AKI by the KDIGO criteria3) . The time point of three days was chosen because of the poor patient outcome associated with severe AKI occurring 48 hours after ICU admission and as a point to signify clinically significant AKI (termed "persistent AKI").The RAI was highly sensitive as a screening tool for severe AKI risk; absence of renal angina, defined as an index value below the validated cut-off of 8, demonstrated high negative predictive (92–99%) value for severe AKI on day three. Furthermore, confirmatory biomarkers integrated into the RAI of patients with a RAI $\geq$ 8 improved positive prediction for AKI (i.e., higher pre-test probability increasing post-test probability).

Renal Angina Index (RAI)

Risk Strata

Risk Criteria	Score
ICU Admission	1
Solid Organ or Stem Cell Transplantation	3
Mechanical Ventilation Vasoactive Support	5

Injury Strata

SCr/Baseline	% FO Accumulation	Score
Decreased or No change	< 5%	1
>1x – 1.49x	5-10%	2
1.5x – 1.99x	10-15%	4
≥ 2x	> 15%	8

Risk x Injury
Scores: 1-40

Renal angina fulfilled with RAI ≥ 8

BACKGROUND

The incidence of acute kidney injury in post cardiac surgery varies between 15 and 64% with mortality rate of 10-89% among those requiring dialysis. The purpose of this study is to present our experience with AKI post cardiac surgery with emphasis on predisposing or aggravating factors.

OBJECTIVE

To ascertain the risk factors of acute kidney injury in congenital heart disease children post cardiac surgery comparing with AKIN criteria and RENAL ANGINA INDEX along with Biomarker Cystatin c.

METHODOLOGY

It is cross sectional study conducted in Department of CVTS ,KLESDr.Prabhakar Kore Hospital and Medical Research Centre Belagavi.Children aged 1month to 12years post cardiac surgery have been evaluated using AKIN criteria which includes pre and post Sr.Creatinine levels within 72hours ,Cardiopulmonary bypass time, Aortic cross clamp time ,mechanical ventilation duration of inotropic support, Nephrotoxic drug exposure. RAI within 72hours which include risk and injury scores .Cystatin c done within 24hours of surgery is early predictor of AKI.

RESULTS AND STATISTICAL ANALYSIS

| CHARACTERISTIC	AKI		Mean diff.	p value by 't' test
	Yes	No		
Age (years)	5.17 (± 5.18)	2.36 (± 2.35)	2.802	0.360
Pre-op Urea (mg/dl)	24.25 (± 10.44)	22.41 (± 8.5)	1.839	0.689
Pre-op Creatinine (mg/dl)	0.3 (± 0.08)	0.35 (± 0.12)	0.051	0.412
eGFR	83.6 (± 61.65)	97.44 (± 31.32)	13.839	0.686
Intra -op Bypass time	77.73 (± 34.49)	65 (± 21.12)	12.730	0.477

Aortic cross clamp time	50.03 (± 28.88)	42.5 (± 22.71)	7.527	0.618
24hrs Urine output (ml/kg/hr)	2.25 (± 0.66)	3.24 (± 1.34)	0.985	0.159
48hrs Urine output (ml/kg/hr)	2.65 (± 0.93)	3.48 (± 1.41)	0.828	0.262
72hrs Urine output (ml/kg/hr)	2.45 (± 1.35)	3.69 (± 1.57)	1.245	0.136
Ventilation (days)	2.5 (± 1.29)	1.81 (± 0.94)	0.689	0.185

CHARACTERISTIC	AKI		Mean diff.	p value by 't' test
	Yes	No		
RA index	14 (± 6.27)	8.92 (± 1.32)	5.081	0.001
Cystatin C	1.35 (± 0.7)	0.66 (± 0.15)	0.685	0.001

Test Result Variable(s)	Area under the curve	95% Confidence Interval		p value
		Lower Bound	Upper Bound	
RA index	0.807	0.577	1.000	0.046

ROC Curve - RA index
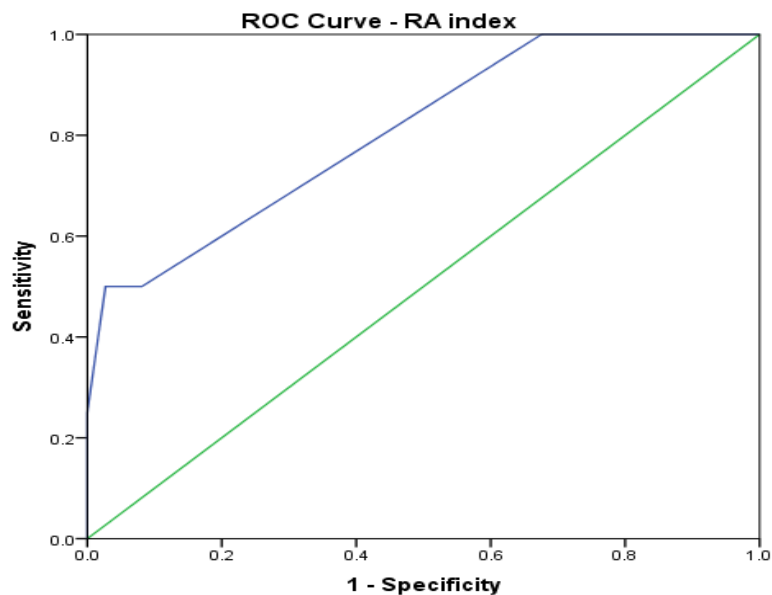
Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
9.50	50.00%	91.89%	40.00%	94.44%	87.80%
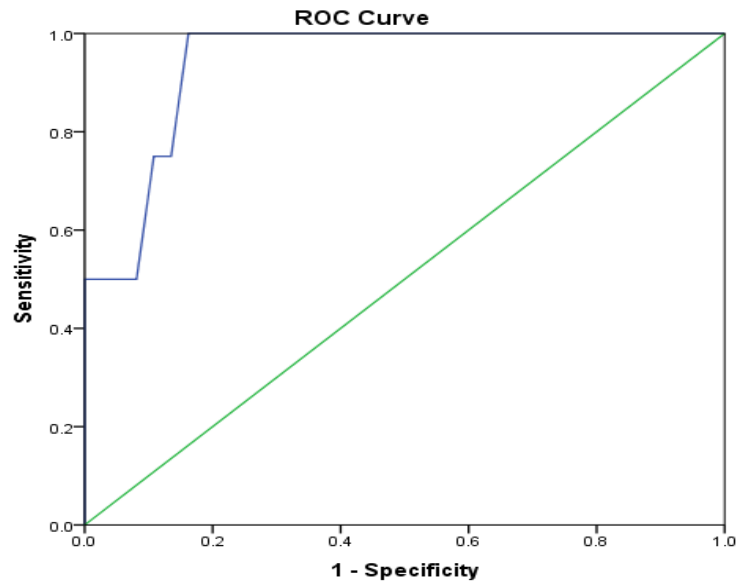
RESULTS

41 patients were enrolled in this study between 1month to 12years of age .This study had an average age of 2 .8 yrs with 48% of females.AKI occured in 10 % (4 patients)within 3 days post cardiac surgery of which 1 required dialysis .Longer cardiopulmonary bypass time and Aortic cross clamp time was linearly and independently associated with acute kidney injury .Renal Angina index positive is associated with AKI with specificity of 91.8% and sensitivity -50% and NPV-94.4%.High Serum cystatin C levels is associated with AKI with specificity -100%, sensitivity -50%,PPV-100%.Devolopement of AKI was associated with prolonged ventilation and increased length of hospital stay .

CONCLUSION

Acute Kidney Injury (AKI) occurring in post cardiac surgery patients needs to be recognised. Combination of Renal Angina Index (RAI) and serum cystatin C levels can be used for early prediction of Acute kidney injury .Cardiopulmonary Bypass time may be marker for case complexity . Adequate sample size is required for prediction of AKI by RA index and serum cystatin C levels .

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