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Original Research Article

A COMPARATIVE STUDY ON RENAL ANGINAL INDEX VS SERUM CREATININE AS A PREDICTOR OF ACUTE KIDNEY INJURY IN A PEDIATRIC INTENSIVE CARE UNIT

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Abstract

Background: To determine the percentage of children in paediatric intensive care with a positive Day 0 (8–12 hours after admission) RAI who develop severe acute kidney injury on Day 3. To evaluate the predictive power of RAI with that of S.Creatinine for the development of severe acute kidney injury (72 to 96 hours of admission). **Materials and Methods:** From March 2020 to October 2020, 147 kids who were admitted to the PICU for longer than 8 hours were prospectively evaluated. Basic investigations performed upon admission, such as Renal Angina Index and Serum Creatinine (RAI).RAI Positive subjects were those whose RAI score on Day 0 was less than 8.The proportion of PICU patients with a Day 0 RAI score of 8 or below who develop severe AKI on Day 3 of admission were considered as significant. The secondary outcome included a comparison of Day 0 RAI's predictive power to that of serum creatinine as well as the correlation between various risk factors and the onset of severe AKI on Day 3 and Day 0 RAI. **Result:** This study showed that a positive Renal Anginal Index (>8) is a strong predictor of Acute Kidney Injury. In this study more than 80 percent of patients with RAI positivity on Day 1 of admission developed AKI on day 3 of admission. **Conclusion:** Children who have a positive Renal Angina Index developed poor renal function and had bad outcomes. Traditional Serum Creatinine-based renal damage measures cannot compare to the discriminative accuracy of the Renal Anginal Index.

INTRODUCTION

Independent of the severity of the illness, acute kidney damage raises mortality rates overall. Acute kidney injury increases hospital stay, cost, and days spent on a ventilator independently and is a risk factor for mortality with an odds ratio as high as 4.8.[1,2] With multi-organ failure, hematopoietic stem cell or solid organ transplant, and extracorporeal membrane oxygenation for acute respiratory distress syndrome, Acute Kidney damage raises mortality rates in adults and children by 10% to 57%. Although a slight initial elevation in serum creatinine increases the likelihood of later developing Acute Renal damage, a rise in creatinine of more than 25% in children undergoing cardiopulmonary bypass is a substantial risk factor for lengthening stay and requiring mechanical ventilation in hospital. On follow-up, 40 to 50 percent of kids with acute renal injury exhibited symptoms of chronic kidney disease. Therefore, Acute Renal Injury poses a significant burden on the juvenile patient group as well as the overall health care system. There are no proven treatments for Acute Renal damage. Treatment of oxidative and inflammatory injury, prevention or reduction of fluid overload, and optimization of renal perfusion pressure through preload or vasopressor medication are all parts of managing Acute Kidney Injury.[3,4] The Acute Renal Injury has not been lessened by any of the aforementioned measures. It has not been demonstrated that increasing renal perfusion through volume adjustment and vasopressor support decreases death rates in patients with Acute Kidney Injury. The effectiveness of treatment for oxidative and inflammatory kidney injury remains mainly unproven. There is no widespread consensus for the use of renal replacement therapy for inflammatory mediators in Acute Kidney Damage. When children begin receiving continuous renal replacement therapy, more fluid is administered and mortality rate are independently linked. Preventive approaches aiming at maintaining enough renal perfusion pressure, avoiding nephrotoxic drugs to treat sepsis, reducing hypoxia, and ensuring adequate nutrition are the state of the art for Acute Kidney injury treatment. Delayed recognition likely contributes to

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poor outcome. When Acute Kidney injury is diagnosed, it has frequently proceeded to a point of damage where immediate intervention may not be possible. This paradigm was developed since early diagnosis is limited by the obsolete detection mortality, which is dependent on creatinine and urine output. Creatinine is unquestionably a late marker of acute renal injury, and even slight increase in serum creatinine are indicative of serious kidney damage.

Aims

The purpose of this study was to evaluate the predictive value of RAI to that of the individual Renal Injury Markers (S. Creatinine) for the emergence of severe Acute Kidney Injury in paediatric critical care patients who have a positive Day 0 (8–12 hours after admission) RAI and who experience severe acute renal damage on Day 3 (72 to 96 hours of admission). Analyze the RAI's ability to foresee the emergence of severe AKI on the third day after intensive care unit admission.

MATERIALS AND METHODS

Study Design: Prospective observational study

Location: The Coimbatore Medical College Hospital's paediatric intensive care unit (PICU).The Coimbatore Medical College Hospital's institutional ethics committee granted their clearance.

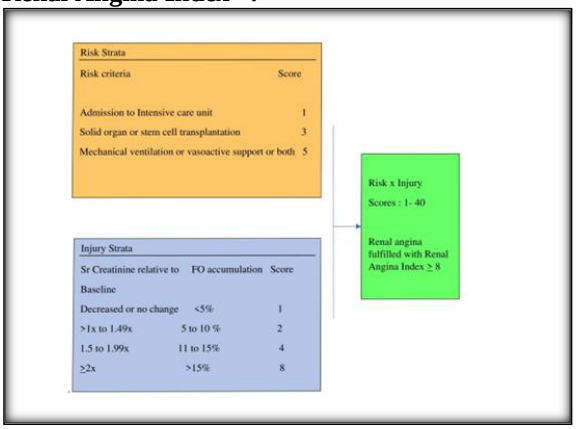
Time: March 2020 to October 2020

Study Subjects: All consecutive children between the ages of 1 month and 12 years old who were admitted to the PICU, who stayed there for at least 8 hours, and who had recorded body weight and intake-output data during this time were included in the study. Children with known chronic renal disease, those with AKI at stages 2 or 3, and those on dialysis were excluded.

Sample Size: A sample size of 140 was obtained using the following parameters: 10% annual incidence of severe AKI (stages 2 and 3) in PICU, precision of 5%, and alpha error of 0.05. Our ultimate sample size was 147, and we calculated a protocol deviation attrition rate of 5%.

Methodology: Subjects who satisfied the eligibility requirements were enrolled after giving their informed consent, and pertinent data, such as anthropometry, demographic factors, the admission diagnosis, co-morbidities, vital signs, and other clinical and laboratory parameters, were recorded. Those who spent less than three days in the PICU were not included in the study. On day zero, fundamental tests were performed, including a full hemogram, urea, creatinine, total protein, albumin, sodium, and potassium. Upto Day 3, serum creatinine was determined daily; beyond that, it was done in accordance with clinical needs. All enrolled individuals' RAIs were calculated between 8 and 12 hours after their admission to the PICU on Day 0.Risk Group Score and Renal Injury Score were combined to create the Renal Angina Index. RAI Positive subjects were those whose RAI score on Day 0 was more than 8.Day 0 was specified as the first day of the PICU admission, which was taken into account at least eight hours after PICU admission. The time frame between 72 and 96 hours following PICU admission was referred to as Day 3.The KDIGO AKI classification stage 2, which is defined as Serum Creatinine of at least 200% above baseline or nadir value or 0.5 mL/kg/h of urine output for at least 12 hours, is used to identify Severe Acute Kidney damage. Fluid overload on Day 0 was calculated as a percentage of bodyweight by deducting urine output or any other significant additional renal losses throughout the course of 8–12 hours of arrival in PICU from the total amount of fluid consumed during this time. If baseline serum creatinine was not available, baseline GFR was determined using reference Creatinine Clearance in accordance with age guidelines. The proportion of kids in PICU with a Day 0 RAI score of 8 or more who develop severe AKI on Day 3 of admission was the main result. The secondary outcome included a comparison of Day 0 RAI predictive power to that of serum creatinine, as well as the relationship between various risk variables and the onset of severe AKI on Day 3.

Renal Angina Index[5]:



The index calculation for the fulfillment of renal angina is assessed 8 – 12 h after a patient is admitted to an intensive care unit and used for prediction of severe acute kidney injury 72 h (3 days) later. Risk factors are determined as described above and assigned a point value (1, 3, and 5, where 1 denotes the lowest risk and 5 denotes the highest risk).[5]

Mechanical ventilation and vasoactive support should be used within 8 -12-h timepoint but are not required to be simultaneous for a patient to be scored 5 points. Injury strata are described and assigned to a patient as appropriate.

The index is a multiplication of the risk and injury scores assigned. Fluid Overload=percentage of fluid overload.

Analysis using statistics: Sensitivity, specificity, positive predictive value, and negative predictive value calculations were used to evaluate the statistical strength of the Day 0 RAI score.For predicting severe AKI on Day 3, Receiver Operating Characteristic

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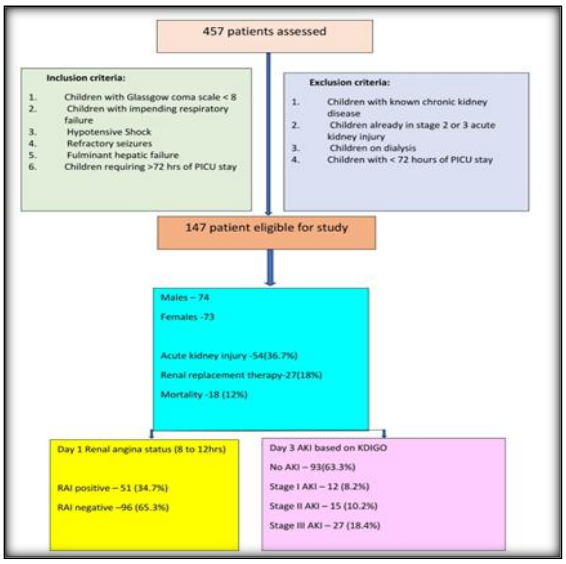
(ROC) curves for Day 0 RAI levels and Day 0 serum creatinine were built. SPSS version 23 was used to analyse the data. At P< 0.05, each and every result was deemed significant.

RESULTS

147 children in all were enrolled in the study.54 children (36.7%) out of the 147 total children had AKI. Among the 147 children that participated in the study, 74 (50.3%) were boys and 73 (49.7%) were girls. AKI was diagnosed in 24 males (32.4%) and 30 females (41.1%) of the study's young participants. Gender and the onset of AKI are not significantly related.



Among 147 children enrolled, 59 (36.7%) developed shock. Of these children, 49 required early support with medications like adrenaline to boost their heart function. Notably, 40 children with shock developed acute kidney injury (AKI). This link between shock and AKI was statistically significant, with a p-value less than 0.001, indicating a strong association. This finding suggests that abnormal blood flow likely plays a major role in the development of AKI.[6] A staggering 81.60% of the 49 children who required early inotrope support, such as adrenaline and nor adrenaline infusion, developed acute kidney injury (AKI). This alarmingly high rate further emphasizes the significant role that abnormal blood flow plays an important part in the development of AKI.[7,8]

Within 8 to 12 hours of admission, 37 (25.2%) of the 147 children needed early mechanical ventilation.34 of the 37 children who needed mechanical ventilation within 8 to 12 hours of arrival and were therefore statistically significant (p value 0.001) for developing Acute Kidney Injury. Acute Kidney Injury is more likely to occur in children who need early intubation and mechanical breathing.[9,10]

According to KDIGO recommendations, 54 (36.4%) of the 147 children were found to have Acute Kidney damage on day 3 of hospitalisation. According to KDIGO,[11] recommendations, out of 54 children with AKI, 12 (8.2%) had Stage I Acute Kidney Injury, 15 (10.2%) had Stage II Acute Kidney Injury, and 27 (18.4%) had Stage III Acute Kidney Injury. Twenty-six of the twenty-seven children with Stage III acute kidney injury received peritoneal dialysis, while one received hemodialysis.[12]

18 (12.2%) of the 147 children who participated in the study died as a result of the disease, while 129 others were discharged. Sepsis with multiorgan dysfunction was the most frequent cause of mortality in this research group (6.1%). AKI is a significant factor in these children's poor outcomes.[13]

In comparison to the RAI negative group, which had a mean hospital stay of 10.54 days, the RAI positive group's stay was on average 15.74 days. When compared to patients without renal impairment, those who had acute kidney injury stayed in the hospital longer overall, and this difference was statistically significant (p value 0.001 based on unpaired T test).

According to this unpaired T test, a rise in serum creatinine from the day 1 baseline does not statistically significantly predict the onset of acute kidney injury. Compared to a single value of Serum creatinine, serial monitoring of Creatinine from day 1 to day 3 can predict acute kidney injury with significance. [Table 2]

Early Renal Anginal index positivity within 8 to 12 hours of admission can reliably predict Acute kidney Injury in children and it has statistical significance with p value of <0.001. [Table 3]

Factors like fluid overload,[14] thrombocytopenia, hypoalbuminemia and altered coagulation profile are individually associated with increased risk of Acute Kidney Injury. [Table 4]

Change in serum creatinine levels from baseline on day 1 could not reliably predict occurrence of Acute Kidney Injury in children.

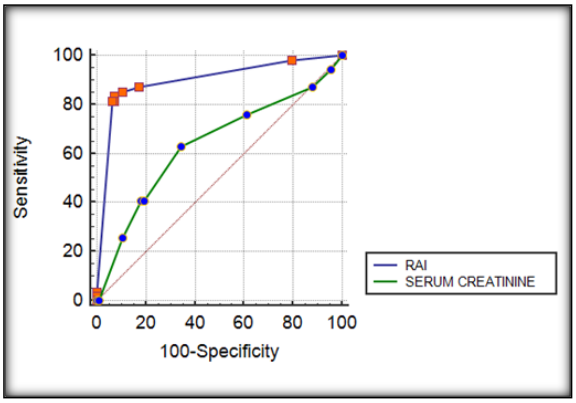


Figure 1: ROC curve Analysis:

Table 1: Clinical Profile of Children included in the study

Diagnosis	Frequency	Percentage
Dengue Fever	45	30.6

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Bronchopneumonia	11	7.5
Sepsis	9	6.1
Status Epilepticus	9	6.1
MISC	8	5.4
Viral Hemorrhagic Fever	7	4.8
Snake Bite	6	4.1
Congenital heart disease	5	3.4
MODS with Sepsis	5	3.4
Acute Severe Asthma	4	2.7
Diabetic Ketoacidosis	4	2.7
Acute diarrheal diseases	3	2.0
Acute Pancreatitis	2	1.4
Acute gastro enteritis	2	1.4
Primary immunodeficiency with Sepsis	2	1.4
Acute disseminated encephalomyelitis	1	.7
Acute encephalitic syndrome	1	.7
Acute fulminant hepatic failure with hepato renal syndrome	1	.7
Acute respiratory distress syndrome	1	.7
Congenital adrenal hyperplasia with intra cerebral bleed	1	.7
Chediak higasi syndrome	1	.7
Communicaing hydrocephalus with TB meningitis	1	.7
Ewings Sarcoma	1	.7
Fever with thrombocytopenia	1	.7
SAM/Pneumonia	1	.7
GDD with sepsis	1	.7
Gullian barre syndrome	1	.7
HLH with acute hepatic failure	1	.7
ITP with intracerebral bleed	1	.7
Kawasaki disease	1	.7
Viral meningitis	1	.7
Neonatal cholestasis with sepsis	1	.7
Paracetamal poisoining	1	.7
TB pleural effusion	1	.7
Rat killer piosoining	1	.7
Right cervical lymphnode abscess	1	.7
RTA with spleenic rupture	1	.7
Severe PAHType2 respiratory failure	1	.7
Late haemorrhagic disease of new born	1	.7
Wiskot aldrich syndrome	1	.7

Table 2: Serum Creatinine and AKI

Serum Creatinine	**AKI**				**Unpaired t test p value**
	Present		**Absent**		
	Mean	**SD**	**Mean**	**SD**	
Baseline	.35	.11	.40	.09	0.004
DAY 1	.51	.18	.59	.16	0.008
DAY 3	1.06	.55	.45	.10	<0.001

Table 3: Renal Anginal Index and AKI

Renal anginal index	**AKI**				**TOTAL**		**CHISQUARE TEST P VALUE**
	Present		**Absent**				
	N	**%**	**N**	**%**	**N**	**%**	
POSITIVE	45	88.2%	6	11.8%	51	100.0%	<0.001
NEGATIVE	9	9.4%	87	90.6%	96	100.0%	
TOTAL	54	36.7%	93	63.3%	147	100.0%	
MEAN+/-SD	9.44+/-5.34		2.61+/-2.26				<0.001*

Table 4: RISK FACTORS

Blood parameters	**AKI**				**Unpaired t test P value**
	Present		**Absent**		
	Mean	**SD**	**Mean**	**SD**	
Fluid overload(8)	5.64	4.35	2.73	1.13	<0.001
Total count	13795.19	7947.88	6972.24	4889.30	<0.001
Hemoglobin	11.00	2.54	11.60	2.47	0.159
Platelets	277105.56	200657.43	138193.32	125176.90	<0.001
Neutrophil	66.98	16.97	57.94	16.54	0.002
Lymphocyte	24.29	15.92	29.18	14.86	0.063
Serum proteins	5.26	1.16	5.83	.98	0.002
Albumin	3.12	.86	3.65	.59	<0.001
Globulin	2.14	.66	2.18	.90	0.767
PT	21.86	8.53	17.22	6.50	<0.001

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APTT	39.19	17.46	30.28	10.62	<0.001
INR	1.33	.43	.96	.27	<0.001

Table 5: RenalAnginal Index Verus Serum Creatinine

Serum creatinine	Renal anginal index				Unpaired t test P value
	Positive		Negative		
	MEAN	SD	MEAN	SD	
BASELINE	0.35	0.11	0.41	0.095	0.002
DAY 1	0.50	0.17	0.59	0.16	0.003
DAY 3	1.03	0.58	0.49	0.19	<0.001

Table 6: Serum Creatinine Change Over 3 Days Vs AKI

Serum creatinine changes From baseline to day 3	AKI			Chisquare test P value
	Present	Absent	Total	
Increased	22	46	68	0.307
	32.4%	67.6%	100.0%	
Decreased or no change	32	47	79	
	40.5%	59.5%	100.0%	
Total	54	93	147	
	36.7%	63.3%	100.0%	

Table 7: Serum Creatinine Change Over 3 Days Vs RAI

Serum creatinine changes From baseline to day 3	Renal anginal index			Chisquare test P value
	Positive	Negative	Total	
Increased	19	49	68	0.111
	27.9%	72.1%	100.0%	
Decreased or no change	32	47	79	
	40.5%	59.5%	100.0%	
Total	51	96	147	
	34.7%	65.3%	100.0%	

Table 8: ROC ANALYSIS

Rai vs serum creatinine day 1	
Difference between areas	0.263
Standard error	0.0550
95% confidence interval	0.155 to 0.371
Z statistic	4.779
Significance level	P < 0.001

Variable	Cut off	AUC	SE	95% CI	P value
RAI	>8	0.899	0.0281	0.838 TO 0.942	<0.001
SERUM CREATININE DAY 1	</=0.5	0.636	0.0493	0.553 TO 0.714	0.006

RAI and AKI

Renal anginal index	AKI			Chisquare test P value
	Present	Absent	Total	
>8	45	7	52	<0.001
	86.5%	13.5%	100.0%	
<8	9	86	95	
	9.5%	90.5%	100.0%	
Total	54	93	147	
	36.7%	63.3%	100.0%	

RAI and AKI

Statistic	VALUE	95% CI
Sensitivity	83.33%	70.71% TO 92.08%
Specificity	92.47%	85.10% TO 96.92%
Positive likelihood ratio	11.07	5.38 TO 22.80
Negative likelihood ratio	0.18	0.10 TO 0.33
Disease prevalence	36.73%	28.94% TO 45.07%
Positive predictive value	86.54%	75.74% TO 92.98%
Negative predictive value	90.53%	84.00% TO 94.56%
Accuracy	89.12%	82.93% TO 93.65%

Serum Creatinine and AKI

Serum creatinine Day 1	AKI			Chisquare test p value
	Present	Absent	Total	
</=0.5	34	32	66	0.001
	51.5%	48.5%	100.0%	

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>0.5	20	61	81	
	24.7%	75.3%	100.0%	
Total	54	93	147	
	36.7%	63.3%	100.0%	

Serum Creatinine and AKI

Statistic	Value	95% CI
Sensitivity	62.96%	48.74% to 75.71%
Specificity	65.59%	55.02% to 75.14%
Positive likelihood ratio	1.83	1.29 to 2.59
Negative likelihood ratio	0.56	0.39 to 0.82
Disease prevalence	36.73%	28.94% to 45.07%
Positive predictive value	51.52%	42.88% to 60.06%
Negative predictive value	75.31%	67.65% to 81.65%
Accuracy	64.63%	56.32% to 72.33%

The sensitivity, specificity, positive predictive value, and negative predictive value for a positive day 1 RAI were determined to be 83.33%, 92.47%, 86.54%, and 90.53%, respectively.

A Receiver Operating Curve was created with an Area Under the Curve (AUC) of 0.899 (95% CI 0.838 TO 0.942) for evaluating individual values of day 1 RAI for predicting AKI on day 3.

AUC for serum creatinine at enrollment was 0.636, significantly lower than that for RAI.

DISCUSSION

There is a pressing need to diagnose Acute Kidney Injury so that timely intervention can be made. AKI biomarkers can assist in early diagnosis but they are costly to perform and their predictive performance lacks when used in wrong clinical context. In this study out of 457 children admitted in PICU, 147 children were enrolled in the study population. 54 children (36.7%) developed Acute kidney injury.

In this study Acute Kidney Injury showed a strong association with poor outcomes in children, which is similar to AWARE study.[15]

By day 3 after admission, 27 out of the 147 children had significant Acute Renal injuries. In the current study, Renal Anginal Index was more accurate at predicting Acute Kidney injury in critically ill children than Serum Creatinine. This study demonstrated a high correlation between Acute Renal Injury and a positive Renal Anginal Index (>8) on the first day of admission. Early identification and diagnosis of AKI susceptibility may result in earlier AKI treatment initiation or care adjustments, minimising the negative effects of AKI and lowering mortality. One of the frequent end damage of shock is AKI.

The immediate cause of Acute Kidney Injury is hypoperfusion. Hypoperfusion-related disturbances in other organ systems, such as coagulopathy, can result in Acute Kidney Injury. AKI patients in the study had shock in a significant proportion compared to non-AKI patients. The fact that many AKI patients exhibited prolonged APTT, PT, and INR values shows that coagulopathy is a significant risk factor for the development of Acute Kidney injury. The current study's finding that more than 80% of patients who tested positive for RAI on Day 1 of admission also experienced acute kidney injury (AKI) on Day 3 of admission is consistent with research by Basu et al,[16] and Gawadia et al.[17] Treatments like mechanical breathing and ionotrope support were statistically significantly more common in the AKI group than in the non-AKI group.

In these patients, AKI is independently linked to worse outcomes. The most popular and practical ways to monitor renal function are Creatinine rise and urine output. In critically ill patients, an early diagnosis of Acute Kidney injury can improve prognosis. The Renal Anginal Index aids in the early diagnosis of AKI. Renal anginal index is a concept that combines risk variables with early indicators of damage. In our study, the early RAI +ve group had a greater incidence of AKI than the RAI -ve group. Fluid overload is a factor in the renal anginal index and a key sign of the severity of the illness. Fluid balance, which in turn reflects fluid intake, perfusion, and renal function, is represented by fluid overload. Renal failure risk was found to be elevated by persistent fluid excess.

Early fluid overload was independently linked, with a p value of 0.001, to an elevated risk of renal failure. Therefore, the goal of hemodynamic treatment strategies in AKI should be to minimise fluid excess. Acute kidney damage has been linked to elements such as anaemia, thrombocytopenia, hypoalbuminemia, and altered coagulation profiles. This research showed a link between sepsis and multiorgan dysfunction syndrome and severe acute renal injury. It was found that patients in the RAI +ve group needed more mechanical ventilation, ionotrope support, and renal replacement therapy than other patients. According to this study, the renal anginal index has a high AUC of 0.899 at RAI -8 for predicting acute kidney injury. So according Basu et al,[16] and Gawadia et al,[19] the negative predictive value for the renal anginal index under 8 is higher at 90.53%.[17]

In this study, 3 of the 6 snakebites patients were diagnosed with acute renal damage on day 3 after admission. Within 8 to 12 hours of hospitalisation, their Renal Anginal Index was less than 8. On the first day of admission, Renal Anginal Index was unable to consistently detect Acute Kidney impairment in

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snakebite patients. When a patient has acute kidney injury from a snake bite, their serum creatinine level is not elevated at the time of admission, and it doesn't rise until serious renal damage has already taken place. In individuals with snake bites, renal biomarkers can be used to predict acute kidney impairment in advance.

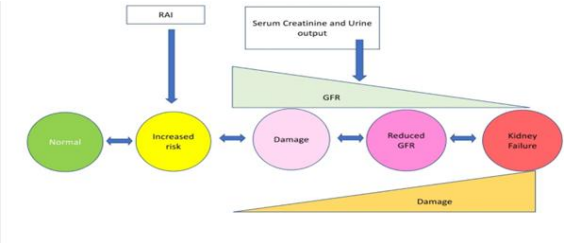

Figure 2: Renal Anginal Index Vs Serum Creatinine

CONCLUSION

When the Renal Angina Index is positive, children's overall outcomes and renal function are both negatively impacted. According to this study, children who are critically unwell and at a high risk of developing AKI are accurately identified by a Renal Anginal Index > 8. Renal anginal index has more discriminative accuracy than conventional renal damage measures based on Serum Creatinine. The Renal Anginal Index is more accurate than Serum Creatinine and provides a medical professional with an early chance to identify the possibility of developing severe acute kidney injury. Renal anginal index can be used to identify patients at risk for AKI in resource-constrained settings when renal biomarkers cannot be afforded.

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