

**Methods:** Hospital based Prospective observational study. Total 972 patients >1 month of age admitted in PICU were enrolled.

**Results:** The prevalence of AKI in our study was 46.15% and the prevalence of risk, injury and failure in our study was 26.63%, 11.83% and 7.69% respectively. Increasing severity of AKI was associated with an increasing length of PICU and Hospital stay. Significant factors predicting mortality in AKI as compared to non-AKI were failure, sepsis, mechanical ventilation and inotropic support.

**Conclusions:** pRIFLE is not a sensitive predictor of mortality in initial stages of AKI but if AKI is associated with, inotropic and ventilator support it can predict high mortality.

# **KEYWORDS** : AKI, modified pRIFLE criteria

# INTRODUCTION

Studies from our country suggest that 4-6% of pediatric inpatients in general wards and up to 40% in PICUs show Acute Kidney Injury and is important in determining morbidity and mortality<sup>1</sup>.

AKI-associated mortality is decreasing yet remains unacceptably high. Survivors of AKI often have reduced quality of life. Hence early diagnosis and timely management is essential for tackling this situation. Under these circumstances, our knowledge regarding the prevalence of Acute Kidney Injury and risk factors associated with it is highly incomplete, the need for a study to address this problem seems quite essential. Hence, a study was undertaken to estimate the prevalence of Acute Kidney Injury in PICU patients and risk factors associated with it.

### METHODS

A Prospective Observational study was conducted in the Department of Pediatrics, Kamla Nehru Hospital, Gandhi Medical College, Bhopal, after taking the prior approval from institutional Ethical Committee. The study period was from February 2015 to August 2016.

### **INCLUSION CRITERIA-**

1. PICU patients >1 month of age group.

# **EXCLUSION CRITERIA**

- 1. Known cases of Chronic Kidney Disease.
- 2. Patients with stay in PICU <1 day

**SAMPLE SIZE**- Total 972 patients were enrolled during a period of 6 month i.e. August 2015 to January 2016, 338 patients met inclusion criteria out of which 156 were categorized as AKI on the basis of modified RIFLE criteria using estimated creatinine clearance and urine output. Serum creatinine estimation was performed in our Hospital by Jaffe method. Estimated creatinine clearance was calculated using Schwartz equation.

As per the hospital policy, children admitted in PICU if one or more of the following criteria were present: Impaired level of consciousness (Glasgow coma scale < 7), signs suggestive of severe increase in intracranial pressure (e.g., hypertension, bradycardia, papilledema), hypoventilation or respiratory failure (oxygen saturation < 90%), uncontrollable or poorly controlled seizures, hypotension requiring inotropic support and fulminant hepatic failure. Those patients who improved within 1 day are less likely to be in Acute Kidney Injury, were excluded.

Shock was defined as the presence of at least two of the following: Tachycardia (heart rate > 2 SD for age), feeble pulses, cool peripheries

and hypotension (blood pressure <-2SD for age and sex) or capillary filling time >3s. Dagnosis of sepsis was made on the basis of culture reports.

#### RESULTS

In our study prevalence of AKI was 46.15% and prevalence of risk, injury and failure was 26.63%, 11.83% and 7.69% respectively, as identified by pRIFLE.

Mean duration of PICU stay in injury group is 1.556 days more (p value- <0.001) and in failure group is 3.002 days more (p value-<0.001), as compared to risk group, which is statistically significant.



Graph.1-Average Duration of PICU Stay and Hospital Stay

Mean duration of PICU stay in injury group is 1.556 days more (p value- <0.001) and in failure group is 3.002 days more (p value-<0.001), as compared to risk group, which is statistically significant.

Mean duration of PICU stay in failure group is 1.446 days more as compared to injury group (p value- <0.012), which is statistically significant.

Mean duration of Hospital stay in injury group is 3.583 days more (p value- <0.001) and in failure group is 5.779 days more (p value-<0.001) as compared to risk group, which is statistically significant.

### TABLE.1-

Univariate and multivariate multinominal logistic regression of various demographic risk factors as predictors of various stages of AKI as per pRIFLE criteria

	Risk	Unad	justed n regrea	nultino ssion	minal	Adjusted multinominal regression					
		Odds Ratio	95% CI	95% CI	p- value	Odds Ratio	95% CI	95% CI	p- value		
			Lower	Upper			Lower	Upper			
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Gender-Male		.789	0.465		1.328		0.373		0.758		0.457		1.338	0.369
Age <12 months		.25	1.338		3.	3.782		002	2.233		1.295		3.848	0.004
Sepsis		.567	0.	334	0.963		0.	036	0.521		0.294		0.923	0.025
Hypertension		.909	0.	411	2.012		0.	.814	1.167		0.483 2.8		2.819	0.731
Mechanical		.445	0.	641	3.257		0.	.375	2.095		0.784		5.919	0.140
Ventilation		817	0	112	1 623		0	617	0.9	224	0 374 1 81		0 622	
Support		.047	0.442		1.025		0.	.017	0.024 0.3		/4	1.010	0.032	
Injury	Una	adjusted multinominal Adjusted m								nul	tinom	inal		
		regression						regression						
	Odds	95	%	95%	% p-			Odds		9	95% 9		5%	p-
	Ratio	io CI		CI	CI		value		Ratio		CI		CI	value
<u>a 1 1 1 1</u>	1.045	Lov	ver Uppe		er					Lo	Lower		pper	0.044
Gender-Male	1.845	845 0.923		3.68	51	0.8	3	2.274		1.	1.022		.060	0.044
Age <12 months	2.75	.75 1.36		5.52	5.526		)4	5.4	164	2.347		12	2.721	<0.001
Sepsis 2.21		1.0	87	4.515		0.029		1.551		0.674		3	.568	0.302
Hypertension 3.5		1.5	77	7.778		0.00	.002 19		.967 6.		261	63	3.671	< 0.001
Mechanical 1.8		0.6	68	5.0	18	0.24	40	0.5	536	0.	166	1	.729	0.297
ventilation														
Inotropic Support	3.919	.919 1.91		3 8.029		0.0	01	14.	526	5.	114	41	.261	< 0.001
Failure	Una	diusted multinominal					Adjusted multinominal							
T unur e		regressio				011111	regression							
	Od	lds	95	% Cl	[ 9	5%	CI	Od	ds	959	% CI	95	% CI	p-value
	Ra	tio	Lo	ower	1	Upp	er	Rat	tio	Lo	wer	U	pper	
Gender-Male	1.8	360	0.	.809		4.27	2	3.3	53	10	248	9	.011	0.016
Age <12		329	29 0		.330		2.084		07	0.	554	5	5.261	0.352
months		01.5	-	0.5.6	_	224		10.	- 1 -	-			50.1	0.007
Sepsis 2		815	3	.956	$\downarrow$	224	.7	18.	/15	2.	323	1	50.1	0.006
Hypertension	1 9.9	17	4	.046	+	24.3	1	112	2.0	1	256	1	058.5	< 0.00
ventilation	3.8	\$22	1	.396		10.4	6	0.8	29	0.	259	$ ^2$	2.653	0.752
Inotropic Support		374	1	.219		6.7	7	47.	.82	5.	050	4	52.8	< 0.00

we have used multinominal logistic regression analysis to test association between various sociodemographic and clinical factors and stages of AKI. First we have performed univariate multinominal regression to quantify strength of association through odds ratios and its 95 % confidence interval for each individual variable with stages of AKI. Then we have entered all variables in multivariate multi-nominal logistic regression model to calculate adjusted odds ratio. This method helps us in dealing with confounding of association due to multiple variables.

We have used Hosmer-Lemeshow test of goodness of fit for model and model was found to be fit for data. Omnibus test for model coefficients was statistically significant (p<0.001).

On univariate analysis significant factors predicting risk as compared to non-AKI were age <12 months and sepsis. Significant factors predicting injury as compared to non-AKI were age <12 months, sepsis, hypertension and inotropic support. Significant factors predicting failure as compared to non-AKI were sepsis, hypertension, mechanical ventilation and inotropic support.

On multinivariate analysis significant factors predicting risk as compared to non-AKI were age <12 months and sepsis. Significant factors predicting injury as compared to non-AKI were male gender, age <12 months, hypertension, inotropic support. Significant factors predicting failure as compared to non-AKI were male gender, sepsis, hypertension and inotropic support.

# TABLE 2 Univariate and multivariate binary logistic regression of various demographic risk factors as predictors of mortality

Vvariables		Univ	variate		Multivariate (unadjusted)								
	(u	nadjust	ed)Logi	stic	Logistic Regression								
		Regi	ression										
	Odds	95% (	C.I. for	p-	Odds	s 95% C.I. for p-							
	Ratio	Odds	Ratio	value	Ratio	Odds Ratio valu							
		Lower	Upper			Lower	Upper						
Aage <	0.91	0.46	1.80	.789	Excluded								
12 months													
ffemale	0.98	0.49	1.94	.957	Excluded								
Gender													
Ssepsis	2.85	1.33	5.86	.004	.356	.097	1.307	.120					
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#### Volume - 11 | Issue - 01 | January - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Hhypertension	1.23	0.56	2.68	.590	Excluded		luded			
PRIFLE-				< 0.001				.002		
RRisk		I	Ref		Ref					
IInjury	2.31	1.01	5.30	.050	2.176	.641	7.383	.212		
FFailure	8.11	3.09	21.29	< 0.001	18.43	3.650	93.139	< 0.001		
					8					
Iinotropic	8.92	4.08	19.47	< 0.001	5.033	1.778	14.247	.002		
Support										
vventilator	44.84	9.90	202.35	< 0.001	52.49	8.583	321.05	< 0.001		
Support					4		9			

we have used binary logistic regression analysis to test association between various sociodemographic and clinical factors and stages of AKI. First we have performed univariate binary regression to quantify strength of association through odds ratios and its 95 % confidence interval for each individual variable with stages of AKI. Then we have entered all variables in multivariate binary logistic regression model to calculate adjusted odds ratio. This method helps us in dealing with confounding of association due to multiple variables. We have used Hosmer-Lemeshow test of goodness of fit for model and model was found to be fit for data. Omnibus test for model coefficients was statistically significant (p<0.001).

On univariate analysis significant factors predicting mortality in AKI as compared to non-AKI were sepsis, failure, mechanical ventilation and inotropic support.

On multivariate analysis significant factors predicting mortality in AKI as compared to non-AKI were failure, mechanical ventilation and inotropic support.

## DISCUSSION-

Arikan et al  $(2007)^2$  found prevalence of AKI 82%, they included only critically ill patients who received mechanical ventilation. Eric AJ Hoste et al  $(2006)^3$  67%, WF Hui et al  $(2005-2007)^4$  56% also found higher prevalence. Some other studies Krishnamurthy et al  $(2010-2011)^5$ , 25.1%, Omar Alkandari et al  $(2011)^6$ , 17.9% found low prevalence. Present study shows prevalence of AKI was 46.15% and prevalence of risk, injury and failure was 26.63%, 11.83% and 7.69% respectively.

Present study shows that Odds of AKI in children <12 months of age was 1.7946 (Odds Ratio = 1.7946, 95% Confidence interval = 1.0627 to 3.0305, P value = 0.0287) as compared to >12 months, which was statistically significant. Mean age was6.4±5.9 yr for AKI. Akcan-Arikan et al (2007)<sup>2</sup> found the mean age for AKI 6.4±6.4 yr. Omar Alkandari et al (2011)<sup>6</sup> found the mean age for AKI is (5.8±5.7 yr). According to Yadira A. Soler et al(2013)<sup>7</sup>, the mean age of patients of AKI was 7.0 yr.

Our evaluation for potential differences in outcome as a function of attaining AKI by eCCl vs UOP vs both revealed that eCCl demonstrated stronger associations with outcomes. Akcan-Arikan et al (2007)<sup>2</sup> and Kama A Wlodzimirow et al (2009)<sup>8</sup> are in agreement with our study.

In the present study AKI was associated most commonly in CNS patients (27%) followed by renal (glomerulonephritis, UTI, HUS) and GI patients. Sepsis was associated with 51% cases of AKI. Dinna N. Cruz et al (2007)<sup>9</sup> found most common diagnostic grouping for AKI was cardiovascular conditions (20.5%), followed by pulmonary (15%) and sepsis (14.2%). Krishnamurthy et al (2010-2011)<sup>5</sup> found that the common etiologies were infections, PSGN, snake envenomation, hemolytic uremic syndrome (HUS) and congestive cardiac failure. Eric AJ Hoste et al (2006)<sup>3</sup> found most common diagnostic grouping for AKI was cardiovascular followed by CNS conditions.

Present study shows mean duration of PICU and Hospital stay in AKI patients were  $3.7\pm2.03$  and  $8.9\pm4.08$  days, respectively. Akcan-Arikan et al (2007)<sup>2</sup> found mean duration of PICU and Hospital stay in AKI patients were  $16.6\pm22.1$  and  $33.7\pm38.1$  days, respectively.

In present study Mean duration of PICU stay in risk, injury and failure group is 2.8, 4.4 and 5.8 days respectively. Mean duration of Hospital stay in risk, injury and failure group is 7, 10.6 and 12.8 days respectively. Thus increasing severity of acute kidney injury was associated with an increasing length of PICU stay and Hospital stay. The following studies Eric AJ Hoste et al (2006)<sup>3</sup>, Tina Palmieri et al (2006-2008)<sup>10</sup>, are in agreement with present study.

In our study 51.3% patients of AKI had sepsis. Some Indian studies also found high association of sepsis and AKI. Poonam Mehta et al  $(2011)^{11}$  found that sepsis was associated with 60% patients of AKI.

We found sepsis as a predictor of severity of AKI. Sepsis was associated in 96.2% patients with failure stage of AKI. Odds ratio for sepsis in children with failure as compared to risk is 52.586 (Odds Ratio = 52.586, 95% Confidence interval = 6.7 to 407.2, P value = <0.001), which is statistically significant. Tina Palmieri et al (2006-2008)<sup>10</sup> found sepsis in 90% patients of severe AKI.

Present study showed that inotropic support was required in 30% patients of AKI (p value- 0.002). Tina Palmieri et al (2006-2008)<sup>10</sup> also found that inotropic support was required in 35% patients of AKI (p value- <0.05). Present study shows that as the severity of AKI increases requirement of inotropes also increases.

Our study revealed that 15.4% patients of AKI required mechanical ventilation and mortality rate was very high in these patients. However there was no significant difference in mortality between AKI and non AKI group. Akcan-Arikan et al (2007)<sup>2</sup> also found the similar results.

Odds ratio for mortality in children with AKI as compared to non AKI is 1.742 (Odds Ratio = 1.742, 95% Confidence interval = 1.061 to 2.86, P value = 0.014), which is statistically significant.

The mortality in AKI in children has been reported to vary widely from 16% to 43.8%. In our study, it was 30.8%, which is comparable to a study from Italy conducted by Dinna N. Cruz et al  $(2007)^{\circ}$  reporting 36.3% mortality. A retrospective study of 311 children with ARF over a period of 22 years.

In Indian studies Krishnamurthy et al  $(2010-2011)^5$  found 46% mortality in patients of AKI. Poonam Mehta et al $(2011)^{11}$  conducted a study in AIIMS Delhi, found a mortality of 37% in AKI patients.

In our study we found mortality in risk, injury and failure group 18.9%, 35% and 65% respectively. Dinna N. Cruz et al  $(2007)^9$  found 20%, 29.3% and 49.5% mortality in risk, injury and failure group respectively.

In our study, on univariate analysis it was found that significant factors predicting mortality in AKI as compared to non-AKI were sepsis, failure stage of pRIFLE, mechanical ventilation and inotropic support. However, sepsis was eliminated on multivariate logistic regression analysis. Krishnamurthy et al (2010-2011)<sup>5</sup> found requirement of mechanical ventilation as an independent predictor of fatality in children with AKI. Eric AJ Hoste et al (2006)<sup>3</sup> found that the patients with RIFLE class I or F incur a significantly increased risk of inhospital mortality.

#### CONCLUSIONS

Our study revealed that-

Significant factors predicting risk as compared to non-AKI were age <12 months and sepsis. Significant factors predicting injury as compared to non-AKI were age <12 months, sepsis, hypertension and inotropic support. Significant factors predicting failure as compared to non-AKI were hypertension, mechanical ventilation and inotropic support.

Significant factors predicting mortality in AKI as compared to non-AKI were failure stage of pRIFLE, mechanical ventilation and inotropic support.

pRIFLE is not a sensitive predictor of mortality in initial stages of AKI.

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