

Acute Kidney Injury in Infants and Neonates

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Abstract: Context: AKI in neonates and infants is associated with significant morbidity and mortality. Aims: To evaluate epidemiology, clinical profile and outcomes of acute kidney injury in neonates and infants. Settings and Design: Prospective observational study from over 1 year period. Methods and Material: Neonates and infants with clinical symptoms or abnormal laboratory parameters suggesting acute kidney injury were included in the study. Demographic characteristics, clinical history and relevant investigations performed. Renal failure classified by pRIFLE. Dialysis was performed when needed and outcomes are analysed. Statistical analysis used: Descriptive statistics for continuous variables. Pearson chi-square test for categorical data using Epi infoTM7 statistical software. Results: The incidence of AKI is 11.53 % (21/182). Neonates were 28.57% (6) and infants were 71.42% (15). Male female ratio was 3.2 (16/5). Infections were the commonest aetiology in 76.19% (16) with highest being sepsis 23.80% (5). Most common clinical features were oliguria 61.9% (13) followed by fever 57.1% (12). Most common laboratory features elevated total WBC count in 76.19% (16) and hypoalbuminemia 52.38% (11). Peritoneal dialysis was done in 38.09% (8) of babies. Complete recovery seen in 80.95% (17) and mortality in 19.4% (4) of babies. Sepsis contributed to mortality in 75 % (3) babies. Conclusions: Acute kidney injury in neonates and infants is not uncommon and needs frequent renal function monitoring for prevention.

Keywords: acute kidney injury, neonates, infants, pRIFLE

1. Introduction

Acute kidney injury is defined by an acute and reversible increment in serum creatinine levels associated or not with a reduction in urine output. It is a complex disorder varying in severity from mild injury to complete shut down of renal function (1).

The epidemiology of acute kidney injury has changed in the past few years with advances in medical field. Still acute kidney injury contributes to significant mortality and morbidity in children and adults (2). Evaluating acute kidney injury in infants and neonates is a challenge as renal function, serum creatinine and eGFR vary by the growth of the baby (3).

The incidence of acute kidney injury in foreign studies done in infants and children varies between 3-10% (4). There are only few studies done on the epidemiology of acute kidney injury in children most of them being conducted in special groups like post neonatal asphyxia (5), low birth weight (6) and post cardiac surgery (7). Data on the epidemiology in neonates and infants are scarce (8,9), especially in countries like India where there is a lack of standardisation for documentation.

So we conducted a prospective observational study to evaluate epidemiology, clinical profile and outcome predictors in infants and neonates over a 1 year period. pRIFLE criteria is used for classification of acute kidney injury as described by Acute Dialysis Quality Initiative (ADQI) group of investigators (10).

2. Subjects and Methods

This is a prospective observational study conducted in the Department Of Nephrology, King George Hospital Visakhapatnam, in association with Department Of Paediatrics. The study was conducted from December 2013 To November 2014. Neonates and infants admitted with acute kidney injury or who developed acute kidney injury

during hospital stay were referred to nephrology. All babies who presented or developed clinical features or abnormal laboratory parameters suggestive of acute kidney injury were included. The clinical features include edema, bladder mass, kidney mass, reduced urine output, passage of dark or blood stained urine and hypertension. The laboratory features include rise in serum creatinine, blood urea, metabolic acidosis, abnormal sodium, potassium, calcium homeostasis. We excluded babies more than 1 year of age, post operative and cases with chronic kidney disease. Acute kidney injury classified by pRIFLE¹⁰ as defined by the Acute Dialysis Quality Initiative (ADQI) on AKI classification system. Based on babies' length and Schwartz Formula eGFR was calculated and percentage decrease in eGFR was used to assort RIFLE stage.

The standard management of acute kidney injury includes obtaining a relevant clinical history followed by a thorough physical examination. Blood and serum chemistries and urine analysis with a spot P/c wherever necessary were sent. Imaging tests included chest x ray PA view, electrocardiography, echocardiography, and ultrasound and ordering special tests like CT scan and other investigations where necessary. Informed consent was taken from parents. Blood and urine culture sensitivity tests were sent when infection was suspected. Malaria was diagnosed by either smear or QBC positive. viral screening for HIV, HbsAg, Anti HCV were done in all children. Indications for renal replacement therapy included patients with one or more of the following oligoanuria, dysnea, uremic features, uncorrectable metabolic acidosis and hyperkalemia. Peritoneal dialysis was done to babies who require dialysis. All patients were monitored throughout their hospital stay until death or recovery.

Sepsis was diagnosed on basis of either a positive sepsis screen and/or a positive blood culture in symptomatic neonates. Sepsis screen were considered positive if > 2 of the 4 criteria were present, which includes: 1) C-Reactive Protein (CRP) > 0.6mg/dl 2) Micro Erythrocyte Sedimentation Rate (ESR) > age in days + 2mm or > 15mm

fall in 1st hour 3) leucopenia Total leukocyte count <5000/cmm with low absolute neutrophil count (<2000cells/ cmm) and 4) Immature: total neutrophil ratio >0.2.CRP was measured by turbidimetric immunoassay.

3. Statistical Analysis

All statistics were performed using Epiinfo™ 7 statistics. Continuous variables were analysed by descriptive statistics like mean, standard deviation. Categorical variables analysed by Pearson Chi Square Test.p value less than 0.05 was taken as statistically significant.

4. Results

During the study period of 1year, total no. Of admissions of infants and neonates were 182, of which about 21 babies developed acute kidney injury, an incidence of 11.53%.Among the 21 total, infants were 15(71.42%) in number and neonates were 6(28.57%). Male babies were 16(76.19%) and female babies were 5(23.80%) in number. All babies were in pRIFLE “F” Failure stage.

Aetiology:

Various infections causing acute kidney injury were noted in 16(76.19%) babies. In infants, the causes of acute kidney injury included pneumonia-3(20%), post gastroenteritis-3(20%),dengue-2(13.33%),sepsis -2(13.33%) , malarial(6.67%)congestive heart failure 1(6.67%) and renal tubular acidosis 2(13.33%). In neonates, aetiologies causing acute kidney injury were neonatal sepsis 3(50%),pneumonia1(16.67%) and posterior urethral valves-urinary retention in 2 babies(33.33%).Overall sepsis was the most common cause leading to acute kidney injury in 5(23.80%) babies followed by pneumonia in 4 babies(19.04%). The various aetiologies leading to acute kidney injury in each age group are shown in Table 1.

Table 1: Aetiology of Acute kidney injury In Neonates And Infants.

Etiology	<1y (n=15)		<1mon (n=6)	
Infections	12	80%	4	66.7%
Sepsis in children	2	13.33%	-	-
Neonatal sepsis	-	-	3	50%
Malaria	1	6.67%	-	-
Dengue	2	13.33%	-	-
post gastroenteritis	3	30%	-	-

Pneumonia	3	30%	1	16.67%
Pyelonephritis	1	6.67%	-	-

Table 2: Aetiology Of Acute kidney injury In Neonates And Infants

ETIOLOGY	<1y (n=15)		<1mon (n=6)	
CHF	1	6.7%		
PUV- obstruction			2	33.3%
RTA	2	13.34%		
Sickle crisis				
Overall other causes	3	20%	2	33.3%

Clinical Profile

Most common clinical features noted were oliguria-13(61.9%) followed by fever-12(57.1%), CNS manifestation-12(57.1%), shortness of breath-9(42.8%) and edema-5(23.8%).Only 5(23.8%) babies were low birth weight (<2.5kg). Two (9.5%) neonates had history of birth asphyxia. Four (19.4%) out of the 21 babies were a product of 1st degree consanguineous marriage. Hypertension seen in 1(4.7%)baby and hypotension noted in 8(38.09%) babies. The clinical profile in neonates and infants is shown in Figure 1.

Laboratory profile included anaemia in 1(4.7%), raisedTWBCcount in 16(76.19%), thrombocytopenia in 3(14.28%), low serum albumin in 11(52.38%), hypernatremia in 4(19.4%), hypocalcaemia in 8(38.09%), hypokalaemia in 5(23.8%) and hyperkalaemia in 2(9.5%). Blood cultures were positive in 6(23.57%) babies.

5. Dialysis:

Peritoneal dialysis was done in 8(38.09%) patients,out of which 3 (37.5%) of babies died and 5(62.5%) babies recovered.Two (25%) are neonates and 6 (75%) are infants.Aetiologies causing acute kidney injury in the dialysis population are sepsis 4 (50%), pneumonia-1(1.25%), dengue1(1.25%), post gastroenteritis 2(25%).

Mortality:

Seventeen babies(80.95%) completely recovered and 4(19.4%) babies died. Sepsis contributed to death in 3(75%) babies and pneumonia in 1(25%) baby.Comparative analysis of babies survived and who did not survive is shown in Table 3. Only positive blood culture was statistically significant to contribute to mortality.

Table 3: Comparative Analysis Of Mortality Vs Survival

	Mortality (n=4)		Survivors (n=17)		Odds ratio	Confidence intervals	Statistical significance P<0.05
Age							
<1mon	2	50%	4	23.52%	3.25	0.3-31.07	NS
>1mon	2	50%	13	76.47%			
Males	3	75%	13	76.47%	0.92	0.07-11.53	NS
Females	1	25%	4	23.52%			
Sepsis	3	75%	2	11.76%	15	0.9-228.9	NS
Other infections	1	25%	10	58.81%			
Oliguria	3	75%	12	70.58%	1.25	0.10-15.10	NS
Non oliguria	1	25%	5	29.41%			
Shortness of breath					3.37	0.28-39.32	NS
Yes	3	75%	8	47.05%			
No	1	25%	9	52.94%			

Edema								
Yes	1	25%	5	29.41%	0.8	0.06-9.66	NS	
No	3	75%	12	70.58%				
Low birth weight								
Yes	2	50%	3	17.64%	4.6	0.45-47.63	NS	
No	2	50%	14	82.35%				
Hypotension Vs normotension	1	25%	6	35.29%	0.55	0.04-6.62	NS	
	3	75%	10	58.81%				
Haemoglobin					14	1.05-185.5	NS	
<10	3	75%	3	17.64%				
>10	1	25%	14	82.35%				
Total count								
>11000	4	100%	12	70.58%	-			
<11000	0	0%	5	29.41%				
Platelets								
<100000	2	50%	2	11.76%	0.88	0.10-7.85	NS	
>100000	2	50%	15	88.23%				
Serum albumin								
<3g/dl	2	50%	9	52.94%	7.5	0.64-87.19	NS	
>3g/dl	2	50%	8	47.05%				
Hyponatremia	1	25%	8	47.05%	1.55	0.11-20.61	NS	
Hyperkalemia	3	75%	1	5.88%	0.18	0.009-3.89	NS	
Blood culture positivity	3	75%	2	11.76%	22.5	1.50-335.35	S	

6. Discussion

Acute kidney injury in neonates and infants in literature has been described in special populations like post asphyxia⁵, low birth weight(6), post cardiac surgery (7), sick neonates (11), preterm(12) etc. Data on Epidemiology and outcomes in non sick neonates and infants with acute kidney injury is scarce (8,9). We report a prospective observational study determining epidemiological pattern of acute kidney injury in babies less than 1year of age over a 1year period .In our study, the incidence of acute kidney injury is 11.53%. The incidence of neonatal acute kidney injury varies between 1-24% reported in literature(13,14). The incidence of neonatal acute kidney injury in a Thailand study is 6.3%(15). Scott et a(16) noted a higher incidence of acute kidney injury in their study in neonates and infants. Incidence of 3.8% was noted in study done Ashok et al in India(17).

In our study, 71.4% were infants and 28.6% were neonates. Male babies were 76.19% and female babies were 23.8%. Similar to our study, studies done by Pradhan et al(11), Richard et al(18), Nariman et al (19), males were predominant. All babies were in pRIFLE stage F probably as this study was done in a referral centre.

Infections were the most common aetiology causing acute kidney injury contributing to 76.2% of babies. Sepsis was the predominant cause followed by pneumonia. Similar rates of neonatal sepsis causing acute kidney injury were noted in various studies(6,11,19).

This is in contrast to the study done by Narmiman et al(19), post gastroenteritisacute kidney injury was the predominant cause followed by haemolytic uremic syndrome. Most common clinical features noted were oliguria 62%, fever 57%, central nervous system features 57%, shortness of breath in 49% and edema in 23.8%. Similar clinical features

were noted in studies done by Narmimanetal(19) and Pradhanetal(11).

Only 23.8% of babies were low birth weight (<2500gm). This is in contrast to Pradhan et al(11) study were 60.2% were low birth weight. Hypotension was more common than hypertension in our study. Elevated total WBC count in 76.2% patients is consistent with the common etiology sepsis causing acute kidney injury. Hyponatremia and hypokalemia were more common in our study probably due to immaturity of tubules and impaired concentrating ability present normally at that age(20).

Peritoneal dialysis was done in 35.1% of patients of which 37.5% died and 62.5% recovered. Sepsis and post gastroenteritisacute kidney injury were the most common aetiologies in the dialysis group. The percentage of patients who required dialysis in study done by Nariman etal(19) is 44%. Similar to our study, sepsis and post gastroenteritisacute kidney injury were the common aetiologies in dialysis group.

Mortality rate was 19.4%. Sepsis contributed to mortality in 75% and pneumonia 25%.The mortality rates reported in literature in neonates range 2-11%. Mortality in Nariman etal (19)study was 8%.Mortality rate in study by Scott et al (16) was31.2%. Of the factors contributing to mortality only positive blood culture status was found to be statistically significant consistent with the sepsis being commonest etiology leading to death of the babies in this study.

This study was a first prospective observational study to include neonates and infants. This study also alerts the treating paediatrician the importance of infections causing acute kidney injury and higher mortality with acute kidney injury despite improvements in perinatal care. Major limitation is a small sample size and lack of long term outcomes of these babies.

To conclude, acute kidney injury in neonates and infants is not uncommon and requires careful and frequent renal function monitoring as it is a preventable condition.

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