

Predisposing factors and outcome of acute kidney injury in neonates

S Ramesh

From Department of Pediatrics, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India

Correspondence to: S Ramesh, 108-A, 4th Street, Meenakshi Garden, Opposite to VG Hospital, GN Mills PO, Coimbatore - 641 029, Tamil Nadu, India. Phone: +91-9962823975. E-mail: drsramesh95@gmail.com

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ABSTRACT

Introduction: Acute kidney injury (AKI) influences the risk of mortality in sick neonates. Predicting AKI on the basis of risk factors may help in early intervention and improved outcome. **Objective:** The aim of this study is to identify the predisposing factors, clinical features, and outcome of AKI in neonates. **Methodology:** A retrospective study was carried out from September 2011 to August 2015. AKI was diagnosed if any one of the following is present: (1) Baby's serum creatinine more than 1.5 mg/dl for at least 24–48 h with normal maternal renal function, (2) baby's serum creatinine increases by more than 0.3 mg/dl over 48 h. All babies with AKI during the study were included in the study. **Result:** Twenty-five babies with AKI were studied. Male predominance was seen. Babies presented at a median age of 3 days interquartile range ([IQR] 2–5) with the median gestational age of 36 weeks (IQR 28–40) and median birth weight of 2490 g (IQR 1885–2875). Perinatal asphyxia (44%), blood culture positive sepsis (24%) and excess weight loss due to inadequate feeds (20%) were common causes for AKI. About half of the cases have received mechanical ventilation and/or inotropes. Nephrotoxic drug exposure was seen in 44% of cases. Only one-third of the babies had oliguria. Fluid boluses, diuretics, and sodium bicarbonate to correct acidosis were commonly used for medical management. Only 12% of cases required peritoneal dialysis. One baby expired. **Conclusion:** Perinatal asphyxia, sepsis, excess weight loss, and cardiopulmonary compromise predisposes to AKI in neonates. Many babies improve with medical management.

Key words: Acute kidney injury, Cardiopulmonary compromise, Excess weight loss, Perinatal asphyxia, Sepsis

Acute kidney injury (AKI) is commonly seen in newborns admitted to neonatal intensive care unit. It was found to have an independent influence on the risk of mortality in sick neonates [1]. The terminology “AKI” has now replaced “acute renal failure.” AKI is a disorder of renal function with clinical manifestations ranging from mild dysfunction to complete a uric kidney failure [2]. Thus, the concept of AKI includes not only established renal failure but also functional impairment relative to the physiological demand [3].

Predicting AKI on the basis of risk factors may help in prompt identification and early treatment of this condition in critically ill neonates. Jetton and Askenazi have recognized newborns with the following conditions as being at increased risk for AKI: Perinatal hypoxia, prematurity and very low birthweight (VLBW), congenital heart disease, especially requiring cardiopulmonary bypass, requiring extracorporeal membrane oxygenation, sick near-term/term infants, sepsis, and congenital anomalies of kidney and urinary tract [4]. Thus, understanding the etiological profile and outcome of AKI in our neonatal population is of utmost importance to reduce the disease burden in our country. Hence, this study was conducted to describe the predisposing factors, clinical features, and outcome of AKI in newborn babies.

MATERIALS AND METHODS

The study was done in a level 3 neonatal unit of a teaching hospital in Tamil Nadu state of India. This study was done using retrospective data from September 2011 to August 2015 over a period of 4 years. A baby was said to have AKI if any one of the following two conditions is present: (1) Baby's serum creatinine more than 1.5 mg/dl for at least 24–48 h if mother's renal function is normal, (2) baby's serum creatinine increases by more than 0.3 mg/dl over 48 h [3]. All babies admitted during the study with the diagnosis of AKI were included in the study. The study was approved by the Institutional Ethics Committee.

The babies with AKI were identified by screening the diagnosis list of cases admitted during the study. Their case records were retrieved from the medical records department and scrutinized for their eligibility. Babies who satisfied the inclusion criteria were included in the study. The following baseline data were collected as follows: gender, gestational age as completed weeks, birth weight in grams, and age at diagnosis of AKI. The presence of predisposing condition for AKI such as perinatal asphyxia, sepsis, excess weight loss, renal anomalies, exposure to nephrotoxic drugs, patent ductus arteriosus, cardiac failure, umbilical arterial line, and necrotizing enterocolitis were noted.

Clinical parameters such as hydration status, urine output, blood pressure, hemodynamic compromise, respiratory problem, and any surgical procedure done were also recorded. Laboratory data collected include maximum serum creatinine, maximum blood urea, electrolyte abnormalities, acid-base status, and blood cell count and blood culture. The following serum electrolyte values were considered as normal: Sodium 135–145 mEq/L, potassium 3.5–5.5 mEq/L, ionized calcium 1–1.4 mEq/L, and bicarbonate 20–28 mEq/L. The treatment received for AKI, duration of hospital stay, and outcome were also entered in the pro forma.

Perinatal asphyxia was defined as requirement of positive pressure ventilation at birth. Babies with microbial growth in blood culture were considered to have sepsis. Any baby with weight loss more than 10% of their birth weight was said to have excess weight loss. Aminoglycosides, vancomycin, and amphotericin were considered as nephrotoxic drugs. Oliguria was defined as urine output <1 ml/kg/h. The data were collected in the designed pro forma and entered in Microsoft Excel sheet 2007. Epi info 2017 statistical software was used for analysis. The descriptive data were presented as a median \pm interquartile range (IQR), and numerical data were presented as percentage.

RESULT

During the study, there were 2876 admissions to the neonatal unit and twenty-five babies had AKI. All 25 babies were included in the study. Male predominance was seen in the study population. Median gestational age was 36 weeks (IQR 28–40), and median birth weight was 2490 g (IQR 1885–2875). One-third of the babies were born preterm. Median age at presentation with AKI was 3 days (IQR 2–5) (Table 1).

Perinatal asphyxia was the underlying cause in about half of the cases in the study population. Blood culture positive sepsis was observed in about one-fourth of the babies. One-fifth of the cases had dehydration, excess weight loss, and hypernatremia due to inadequate feeds. The renal anomaly was seen in two babies as follows: One had hypoplastic kidneys and other had medullary nephron calcinosis. Cardiac failure due to supraventricular tachycardia was seen in one baby. Exposure to nephrotoxic drugs was observed in about half of the cases. Three babies had patent ductus arteriosus and two had an umbilical arterial catheter (Table 2).

One-fourth of the cases had dehydration and 12% had edema. Almost one-third of the babies had oliguria. About 50% of the cases were on mechanical ventilator. Hemodynamic compromise requiring inotropic support was observed in about 50% of the cases. Parenteral nutrition was given for one-fourth of the cases and blood component therapy was given to about half of the babies (Table 3).

Hypocalcemia, low serum bicarbonate, metabolic acidosis, and hypernatremia each were seen in about half of the cases. About one-third of the babies had hyperkalemia. Anemia and thrombocytopenia each were seen in about 30% of the cases (Table 4). Fluid bolus (40%), diuretic therapy (36%), and

Table 1: Baseline characteristics of the study population

Characteristics	Observations
Male: female ratio	1.78:1
Median gestational age (weeks) (n=15)	36 (28–40)
Number of preterm babies (%)	9 (36)
Median birth weight (g)	2490(1885–2875)
Median age at diagnosis (days)	3 (2–5)

Table 2: Predisposing factors for AKI in the study population

Characteristics	Observations (%)
Perinatal asphyxia	11 (44)
Sepsis	6 (24)
Dehydration due to inadequate feeds	5 (20)
Renal anomaly	2 (8)
Nephrotoxic drugs exposure	11 (44)
Patent ductus arteriosus	3 (12)
Congestive cardiac failure	1 (4)
Umbilical arterial catheter	2 (8)

AKI: Acute kidney injury

Table 3: Clinical characteristics of the study population

Characteristics	Observations (%)
Hydration status	
Dehydration	6 (24)
Edema	3 (12)
Oliguria	9 (36)
Respiratory support	
Oxygen	4 (16)
CPAP	3 (12)
Mechanical ventilation	13 (52)
Circulatory support	
On single inotrope	7 (28)
On two or more Inotropes	5 (20)
Parenteral nutrition	7 (28)
Blood component therapy	14 (56)

CPAP: Continuous positive airway pressure

Table 4: Abnormal laboratory parameters in study population

Characteristics	Observations
Median maximum serum creatinine (mg/dl)	1.73(1.56–2.29)
Median maximum blood urea (mg/dl)	61 (41.5–112)
Hypernatremia (%)	10 (40)
Hyponatremia (%)	7 (28)
Hyperkalemia (%)	9 (36)
Hypokalemia (%)	3 (12)
Hypercalcemia (%)	3 (12)
Hypocalcemia (%)	14 (56)
Low serum bicarbonate (%)	14 (56)
Metabolic acidosis (%)	8/15 (53)
Anemia (%)	8 (32)
Thrombocytopenia (%)	7 (28)

sodium bicarbonate infusion (36%) for acidosis correction were commonly used as medical management. Only three babies

(12%) required peritoneal dialysis. About three-fourth of cases improved and got discharged. Seven cases left against medical advice and one expired (Table 5).

DISCUSSION

In this study, perinatal asphyxia, culture positive sepsis, and excess weight loss were the common causes for AKI in neonates. A study from Thailand has found that sepsis was the most common cause of AKI followed by hypovolemia, renal and urinary tract anomalies, congestive heart failure, and birth asphyxia [5]. In a prospective study from Egypt, Youssef *et al.* have found sepsis, respiratory distress syndrome, mechanical ventilation, perinatal asphyxia, and dehydration as the common predisposing factors for AKI in neonates [6]. Sepsis was identified as a predisposing factor in about three-fourth of the cases with AKI by Momtaz *et al.* [7]. Askenazi *et al.* have found that babies with AKI had low Apgar score at 5 min, low cord blood pH and required mechanical ventilation in delivery room [8]. Selewski *et al.* in a review on neonatal AKI has suggested that babies with birth weight <1500 g, perinatal asphyxia, low apgar scores, on extracorporeal membrane oxygenation and undergoing cardiac surgery need closer surveillance of renal function to identify AKI early [9].

About half of the babies in this study were sick requiring mechanical ventilation and/or inotropic support and 44% of the babies have been exposed to nephrotoxic drugs. Critically ill neonates are at risk of having AKI, as they are commonly exposed to nephrotoxic medications and have frequent infections that lead to multi-organ failure [2]. Youssef *et al.* have found that 51.9% of their AKI babies were on mechanical ventilator [6]. Respiratory support with high mean airway pressure and low mean arterial pressure were associated with renal failure in extremely low birthweight babies in a study by Viswanathan *et al.* [10]. Bansal *et al.* had observed an association between mortality and need for mechanical ventilation and shock in babies with AKI [11].

Male predominance observed in this study was also noted by Askenazi *et al.* and Bansal *et al.* [8,11]. Male gender was found to have statistically significant correlation with the occurrence of AKI [11]. However, Momtaz *et al.* had found female predominance in their study [7]. Oliguria was observed in only one-third of the study population. Similarly, Youssef *et al.* have found oliguria

in only 29.6% of their babies [6]. Infants are commonly stated to have nonoliguric renal failure [2]. However, Momtaz *et al.* have found oliguria in 77.6% of their cases [7]. Bezerra *et al.* have observed an association between reduced urine output and mortality in neonates admitted to intensive care units [12]. Most of the cases in this study improved with conservative management which includes fluid boluses, diuretics, and sodium bicarbonate. Jetton and Askenazi state that currently there are little data on treatment options for AKI in neonates [13]. A trial of diuretics can be tried in oliguric neonates with AKI. The primary therapy for severe AKI is renal replacement therapy, and the indications are refractory acidosis, uremia, electrolyte disturbances, and fluid overload [9]. Only 12% of babies in this study required peritoneal dialysis. However, Momtaz *et al.* state that 36.7% of their babies required peritoneal dialysis [7].

AKI has an independent impact on survival after correction for comorbidities, complications, and severity of illness [2]. Chertow *et al.* have found that an increase of serum creatinine of >0.3 mg/dl was independently associated with mortality [14]. In a study by Vachvanichsanong *et al.*, sepsis-induced AKI had the highest mortality rate with an overall mortality rate of 38.8% and nearly 14 times the risk of death compared to hypovolemia-induced AKI [5]. Among babies with perinatal asphyxia and AKI, the mortality rate was 71.4% [15]. VLBW babies with AKI had 2.4 times higher chance of death compared to those babies without AKI [16]. However, there was only one death in this study population. Premature infants who developed AKI in the neonatal period are at risk of hypertension, chronic kidney disease, and metabolic syndrome [2,17]. Thus, long-term follow-up these cases are required.

This study has identified the important predisposing factors for AKI in neonates of our geographical region. However, the study is limited by its retrospective nature and small sample size. A large-scale prospective study is needed to have a clear understanding of the epidemiology and outcome of AKI in neonates.

CONCLUSION

Perinatal asphyxia, sepsis, excess weight loss, and cardiopulmonary compromise requiring mechanical ventilation and/or inotropes were the common predisposing factors for AKI in neonates. Many babies improved with conservative medical management. Vigilant monitoring of renal function is required in babies with these predisposing factors.

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Table 5: Treatment and outcome of the study population

Characteristics	Observation (%)
Treatment	
Fluid bolus	10 (40)
Diuretics	9 (36)
Sodium bicarbonate infusion	9 (36)
Peritoneal dialysis	3 (12)
Median duration of hospital stay (days)	7 (3–13)
Outcome	
Improved	18 (72)
Left against medical advice	7 (28)
Expired	1 (4)

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