International Journal of Contemporary Pediatrics
Gopalan D et al. Int J Contemp Pediatr. 2024 Feb;11(2):162-166
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20240091

Original Research Article

Clinical profile and outcome of acute kidney injury in preterm neonates in a level three neonatal intensive care unit

Divya Gopalan*, Palak T. Hapani

Department of Paediatrics, P. D. U. Government Medical College, Rajkot, Gujarat, India

Received: 29 November 2023
Accepted: 02 January 2024

***Correspondence:**
Dr. Divya Gopalan,
E-mail: g.divya_11@yahoo.co.in

ABSTRACT

Background: Acute kidney injury is an important cause of neonatal mortality and morbidity. Preterm neonates, in particular are a vulnerable population as they are associated with various risk factors, predisposing them to multi-organ injury. Data on AKI in preterm neonates in India are limited. There are several gaps including the risk factors, demographic profile and associations with other comorbidities which remain unanswered. The objectives of this study were to study the clinical profile, outcomes and various associated risk factors of AKI in preterm neonates.
Methods: It is a prospective observational study conducted in neonatal intensive care unit of a government medical college hospital in Rajkot, Gujarat, India. 300 preterm neonates with AKI were selected and demographic details, risk factors associated with AKI and outcomes were studied.
Results: It was found that among 300 newborns under study, 82% were males, 92% had sepsis, 65% had respiratory distress syndrome, 32% had birth asphyxia, 29% had shock, 30% had exposure to nephrotoxic drugs, 54% had requirement for mechanical ventilation, 94% patients were discharged and 6% patients expired.
Conclusions: The most common risk factor associated with AKI was sepsis. The other important risk factors are birth asphyxia, respiratory distress syndrome, and shock. Monitoring of serum creatinine can help in early detection of acute kidney injury.

Keywords: Acute kidney injury, Preterm neonates, Serum creatinine

INTRODUCTION

Acute kidney injury (AKI) is defined as a sudden decline in kidney function resulting in derangements in fluid balance, electrolytes and waste products. It is fairly common in the newborn population and a major contributor of neonatal morbidity and mortality.[1] The precise prevalence is unknown but the available data shows variable incidence of AKI in the Neonatal Intensive Care Units (NICUs) around the globe-it is from 6-24%. Of these, pre-renal type of AKI was found to be most common. There is no definite data available on incidence of renal failure in preterm babies in India.[2] Preterm babies were selected for this study as they are vulnerable to several complications; predisposing them to multi-organ injury. Due to various complications that preterm neonates are exposed to in the early weeks of life, multiple interventions with prolonged hospitalization is required. Premature infants may be born with less than half of the nephrons compared with term neonates, predisposing them to chronic kidney disease (CKD) early on in life and as they age. AKI can also lead to CKD, and premature neonates with AKI may be at very high risk for long-term kidney problems. AKI in neonates is often multifactorial and may result from prenatal, or postnatal insults as well as any combination thereof.[3] The most common among these are perinatal asphyxia and sepsis. In addition to these, incomplete nephrogenesis places

preterm neonates at more risk for renal failure than term babies. As non- oliguric renal failure is more common in neonates, by the time oliguria sets in, significant renal injury has already taken place and diagnosis may be delayed. Novel biomarkers like urine NGAL (Neutrophil Gelatinase associated Lipocalcin) has been proved to be useful in diagnosing acute kidney injury in other situations and age groups.[4]

The measurement and interpretation of renal function in premature neonates is complicated by in utero events, maternal drug exposure, gestational age, birth weight, severity of postnatal illness, renal development and changing muscle mass. The serum creatinine in preterm infants can increase initially before it declines to a steady state and does not necessarily represent acute kidney injury. Preterm birth is often associated with diseases affecting placental function and/or maternal renal function. The term neonate has more mature renal tubular function, which can appropriately respond to homeostatic needs. The tubular function is immature in preterm infants, with a decreased ability to reabsorb electrolytes and proteins and a decreased ability to concentrate urine. The data available on AKI in preterm neonates in India is limited. More importantly there are several gaps including the risk factors, demographic profile and association with other comorbidities which remain unanswered.[2] This is a prospective observational study where the clinical profile, various associated risk factors and outcomes of AKI in preterm neonates are discussed.

METHODS

Study design, location and participants

This study was a prospective observational study. The study was conducted in the Neonatal Intensive Care Unit (NICU) of Department of Paediatrics, PDU Government Medical College, Rajkot, Gujarat, India. It was conducted from September 2018 to March 2020. The study involved 300 preterm neonates with acute kidney injury admitted in NICU as per the inclusion criteria.

Inclusion and exclusion criteria

Inclusion criteria were; All newborn babies with: Serum creatinine>1.5 mg/dl and Gestational age <37 weeks.
Exclusion criterion was; Consent not given for study.

Sample size

Sample size was calculated based on prevalence of renal failure. Prevalence of renal failure worldwide ranges from 6 to 24% as mentioned in a study on acute kidney injury in neonates by Pradhan et al.[5]

$$N = 4\,p\,(100 - p)/L2$$

Where, n is the sample size, p is the expected prevalence, and L is allowable error of 5%. Sample size was calculated to be 292 (~300). Data entry was done in Microsoft Excel and analysis was done using SPSS 20. For qualitative data, frequency and percentage were calculated.

Procedure

Written informed consent was obtained from either of the parents or the guardian of the patient in vernacular language. Gestational age was assessed according to new Ballard scoring system. Details which included demographic data like hospital number, age, gender, birth weight; maternal history, perinatal history, resuscitation details, investigations and details of interventions; umbilical venous catheter, mechanical ventilation, and administration of nephrotoxic drugs were noted. Serum creatinine more than 1.5 mg/dl was used to define AKI. Serum creatinine was processed in Clinical biochemistry lab of PDU Government Medical College, Rajkot using Jaffe's method. Urine output was monitored at regular intervals either by weighing the diapers or by measuring amount of urine collected by catheterization.

RESULTS

A total of 300 neonates fulfilling the inclusion criteria were included in the study and their clinical profile, risk factors for AKI and outcomes were studied.

Distribution according to gestational age

It was found that there were 15% babies (45) born with less than 28 weeks gestational age, 33% babies (99) having gestational age between 28 to 32 weeks and 52% babies (156) born with gestational age >32 weeks.

Table 1: Gender distribution (n=300).

Gender	N	%
Male	246	82
Female	54	18
Total	300	100

Gender based distribution

It was found that male babies were more affected than females. 82% male babies (246) and 18 female babies (54%). The male: female ratio was 4.5:1 (Table 1).

Table 2: Distribution based on sepsis (n=300).

Sepsis	N	%
Present	276	92
Absent	24	8
Total	300	100

Distribution based on birth weight

It was found that most of the babies had birth weight between 1000 to 1500g. There were 12% babies (36) with

birth weight <1000g; 53% babies (159) with birth weight between 1000 to 1500g; 35% babies (105) with birth weight between 1500 to 2500g.

Distribution of birth weight for gestational age

There were 69% babies (206) who were born appropriate for gestational age; and 31% babies (94) who were born small for gestational age. There were no preterm babies who were born large for gestational age in this study.

Distribution of babies requiring mechanical ventilation

It was found that 54% (163) of babies required mechanical ventilation whereas 46% (137) of babies did not require mechanical ventilation.

Distribution of babies with meconium aspiration syndrome

There were 12% babies (36) with meconium aspiration syndrome and 88% babies (264) without meconium aspiration syndrome.

Distribution of sepsis

AKI was more common in neonates with sepsis. There were 92% (276) babies with sepsis, and 8% (24) babies without sepsis (Table 2).

Distribution of birth asphyxia

There were 32% babies (97) who had birth asphyxia and 68% babies (202) who did not have birth asphyxia.

Distribution of postnatal exposure to nephrotoxic drugs

There were 30% babies (90) who had exposure to nephrotoxic drugs like vancomycin, amikacin and acyclovir and 70% babies (210) who did not have exposure to nephrotoxic drugs.

Respiratory distress syndrome (RDS)

There were 65% babies (195) who had respiratory distress syndrome and 35% babies (105) who did not have respiratory distress syndrome.

Shock

There were 29% babies (87) who had shock and 71% babies (213) who did not have shock.

Final outcome

Out of total of 300 patients, 94% (282) patients were discharged and 6% (18) patients expired (Table 3).

Table 3: Final outcome (n=300).

Outcome	N	%
Discharge	282	94
Death	18	6
Total	300	100

Table 4: Factors associated with AKI.

Factors associated	%
Sepsis	92
Respiratory distress syndrome	65
Birth asphyxia	32
Shock	29
Exposure to nephrotoxic drugs	30
Mechanical ventilation	54
Male gender	82
Meconium aspiration syndrome	12

DISCUSSION

Acute kidney injury in the study

Preterm babies are a vulnerable population and are exposed to various risk factors; predisposing them to multi-organ injury. Due to the myriad of complications which preterm neonates are exposed to in the early weeks and multiple interventions with prolonged hospitalization, these babies are predisposed to acute kidney injury and its long-term consequences.

Table 5: Comparison of sepsis in AKI.

Study	Year	Incidence of sepsis (%)
Durga et al[21]	2017	64
N Nagaraj et al[9]	2016	80
Hossein et al[11]	2014	77.5
Bansal et at[2]	2010	91
El Badawy et al[12]	2015	75.6
Current study	2020	92

Factors predisposing to acute kidney injury are usually multifactorial, the most common among these being perinatal asphyxia and sepsis. Both these factors are common in preterm babies.[2] This study was conducted in a level 3 neonatal intensive care unit between September 2018 and March 2020. During the study period, babies born at less than 37 completed weeks of gestational age were recruited for the study and those with serum creatinine levels more than 1.5mg/dl were considered to have acute kidney injury. The various risk factors associated with AKI were compared with other studies and discussed below. Acute kidney injury was defined as an absolute value of more than 1.5 mg/dl. Different studies have used different cut-off values of creatinine. Cataldi et al reported AKI in preterm babies in a case control study, where creatinine of more than 1.3 mg/dl was used to define AKI.[6] Mortazavi et al looked at both term and preterm babies, wherein creatinine of more than

1.5 mg/dl was used to define AKI.[7] A study from Serbia in 2014 by Stojanovic et al defined AKI as rise in creatinine more than 0.3 mg/dl compared to the previous value.[8] In this study, there were 82% male babies (246) and 18 female babies (54%).

Table 6: Comparison of studies on incidence of birth asphyxia in AKI.

Study	Year	Incidence of birth asphyxia
Stojanovic et al[8]	2014	60
Medani et al[13]	2013	54
Durkan et al[22]	2011	56
Aslam et al[14]	2014	44
Current study	2020	32

The male: female ratio was 4.5:1. Nagaraj et al conducted an observational study in 2016 in 450 neonates over an eight-month period and found that AKI was more common in preterm males with male to female ratio of 1.8:1.[9] Timovska et al in a study conducted in 770 newborns over a 3-year period found that AKI was more common in males with a male to female ratio of 2.1:1.[8] Our study is comparable to both of the above studies. In our study, it was found that 92% of the patients had sepsis and sepsis was the leading cause of AKI. In a prospective study conducted in 2017 by Durga et al including 50 babies, it was found that 64% of babies with AKI had sepsis. In a prospective observational study conducted by Nagaraj et al in 2016, including 54 neonates with AKI, it was found that 80% of the neonates had sepsis.[7] Sepsis, along with birth asphyxia was the leading cause of AKI in this study also. In a cross-sectional study conducted by Hossein et al in 2014, it was found that 77.5% of the patients with AKI had sepsis.[9] In a descriptive study done in 2010 by Bansal et al it was found that 91% of the neonates with AKI had sepsis.[2] Sepsis was the most common factor associated with AKI. In a case control study including 100 neonates done by El Badawy et al in 2015, it was seen that 75.6% of babies with AKI had sepsis, which was the most common factor associated with AKI.[10] Our study is comparable to the studies done by Hossein et al. APGAR score (appearance, pulse, grimace, activity and respiration) is an assessment score of neonates at 1 and 5 minutes of life. The 5-minute Apgar less than 7 is abnormal and 3 or less is suggestive of birth asphyxia. In this study, it was found that 32% had birth asphyxia. In a study done by Stojanovic et al in 2014, including 150 preterm neonates, it was found that 60% of the babies had birth asphyxia.[8] In a prospective study including 85 neonates done by Medani et al in 2013, 54% had AKI.[11] In a cross-sectional study done by Aslam et al it was found that 44% of babies with acute kidney injury had birth asphyxia.[11]

In the current study, it was found that 29% of babies with AKI had shock. In a prospective and observational study done by Katariya et al with a sample size of 140, it was found that 28.5% of the patients with AKI also had shock which is comparable to our study.[12] In a prospective study done by Bansal et al it was found that amongst the 74 patients who had AKI, 56.7% had shock.[2] In a case control study including 100 neonates done by El Badawy et al it was found that 39% of the patients had shock.[9] In a retrospective case control study done by Jagrawal et with 107 cases, it was found that 70.5% of the babies with AKI had shock.[13] In the current study, it was found that 65% of the babies with AKI had respiratory distress syndrome. In a prospective study done by Bansal et al in 2010, it was found that amongst the 74 patients who had AKI, 2.7% had respiratory distress syndrome.[2] In a cross sectional study done by Nikavar et al in 2018, 26% of the babies with AKI had RDS.[14] In a retrospective study done by Bolat et al including 162 babies with AKI, it was found that 38% of the neonates had respiratory distress syndrome.[15] In a prospective study done by Timovska et al it was found that amongst 50 babies with AKI, 24% had respiratory distress syndrome.[10] In a case control study done by El Badawy et al including 41 neonates, it was found that 70.5% of the babies had exposure to nephrotoxic drugs.[12] In a case control study done with 59 neonates with AKI by Viswananthan et al it was found that 52% of the babies had exposure to nephrotoxic drugs like cephalosporin.[19] In a case control study done by Cataldi et al with 81 neonates, it was found that 50% had exposure to nephrotoxic drugs like cephalosporins and aminoglycosides.[6] In this study the percentage of extreme preterm babies was 15%. In a case control study done by Cataldi et al with 81 neonates, it was found that 48% of babies were extreme preterm babies whereas in a retrospective study done by Felipin et al it was found that percentage of extreme preterm babies was 60%.[6,20] In the current study, it was found that 40% of the babies were having birth weight less than 1000grams, 40% of babies were having birth weight between 1000-1500 grams, and 20% were having birth weight between 1500-2500 grams. In a retrospective study done by Felipin et al it was found that 60% of the babies were having birth weight of less than 1000 grams, 30% of babies were having birth weight between 1000-1500 grams; 10% of babies were having birth weight between 1500-2500 grams.[20] In this study, it was found that 31% of babies were small for gestational age (SGA). In a study done by Viswananthan et al in 2011, 41% of babies were SGA and in study done by Bolat et al it was found that 33.3% of babies were SGA.[18,19] The results in our study were comparable to both these studies. In a study done by Cataldi et al it was found that 13% of patients were SGA.[6] In the current study, 54% of babies required mechanical ventilation. In a study done by Cataldi et al, it was found that 82% of babies required mechanical ventilation.[6] In a study done by Bolat et al it was found that 53% of babies required mechanical ventilation which is comparable to our study.[18]

CONCLUSION

Acute kidney injury is an important cause of morbidity and mortality in preterm neonates. The most common

risk factor associated with AKI was sepsis. The other important risk factors were birth asphyxia, respiratory distress syndrome, shock and exposure to nephrotoxic drugs. Other associated factors are requirement for mechanical ventilation and male gender. Monitoring of serum creatinine can help in early detection of acute kidney injury. Regular clinical examination and investigations for associated risk factors like sepsis and shock would also help in early identification and timely management of AKI.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Coleman C, Tambay Perez A, Selewski DT, Steflik HJ. Neonatal Acute Kidney Injury. Front Pediatr. 2022;10:842544.
2. Bansal SC, Nimbalkar AS, Kungwani AR, Patel DV, Sethi AR, Nimbalkar SM. Clinical Profile and Outcome of Newborns with Acute Kidney Injury in a Level 3 Neonatal Unit in Western India. J Clin Diagn Res. 2017;11(3):SC01-4.
3. Gallo D, de Bijl-Marcus KA, Alderliesten T, Lilien M, Groenendaal F. Early Acute Kidney Injury in Preterm and Term Neonates: Incidence, Outcome, and Associated Clinical Features. Neonatology. 2021; 118(2):174-9.
4. Pejović B, Erić-Marinković J, Pejović M, Kotur-Stevuljević J, Peco-Antić A. Detection of acute kidney injury in premature asphyxiated neonates by serum neutrophil gelatinase-associated lipocalin (sNGAL) sensitivity and specificity of a potential new biomarker. Biochem Med. 2015;25(3):450-9.
5. Pradhan DD, Meher BK, Panda SK, Samal D. Prevalence and factors affecting prognosis in neonates with acute kidney injury in a neonatal intensive care unit. J Clin Neonatol. 2018;7:237-42.
6. Cataldi L, Leone R, Moretti U, De Mitri B, Fanos V, Ruggeri L, et al, Potential risk factors for the development of acute renal failure in preterm newborn nfants: a case-control study. Arch Dis Child Fetal Neonatal Ed. 2005;90:F514-9.
7. Fakhrossadat M, Sedigeh HS, Nayyer N. Acute Kidney Failure in Neonatal Period. IJKD 2009;3:136-40.
8. Stojanović V, Barišić N, Milanović B, Doronjski A. Acute kidney injury in preterm infants admitted to a neonatal intensive care unit. Pediatr Nephrol. 2014; 29(11):2213-20.
9. Nagaraj N, Berwal PK, Srinivas A, Berwal A. A study of acute kidney injury in hospitalized preterm neonates in NICU. J Neonat Perinat Med. 2016;9(4): 417-21.
10. Silvana NT, Svetlana C, Tosheska-Trajkovska K. Acute kidney injury in neonates. MASA. 2015;82:34-9.
11. Momtaz HE, Sabzehei MK, Rasuli B, Torabian S. The main etiologies of acute kidney injury in the newborns hospitalized in the neonatal intensive care unit. J Clin Neonatol. 2014;3(2):99-102.
12. El-Badawy AA, Makar S, Abdel-Razek AR. Incidence and risk factors of acute kidney injury among the critically ill neonates. Saudi J Kidney Dis Transpl. 2015;26:549-55.
13. Medani SA, Kheir AE, Mohamed MB. Acute kidney injury in asphyxiated neonates admitted to a tertiary neonatal unit in Sudan. Sudan J Paediatr. 2014;14(2): 29-34.
14. Aslam M, Arya S, Chellani H, Kaur C. Incidence and predictors of acute kidney injury in birth asphyxia in a tertiary care hospital. J Clin Neonatol. 2017;6(4):240.
15. Katariya KL, Pandya NK. Clinical profile of neonates with acute renal injury in neonatal intensive care unit at GMERS Medical College and General Hospital, Gotri, Vadodara, Gujarat, India. Int J Contemp Pediatr. 2019;6:1136-42.
16. Jagrawal G, Arora V, Gunawat M, Malik P. Acute renal failure in neonatal septicemia. Int Jour Biomed Res. 2016;7(5):260-4.
17. Nickavar A, Khosravi N, Mazouri A. Predictive Factors for Acute Renal Failure in Neonates with Septicemia, Arch Pediatr Infect Dis. 2017;5(4): e61627.
18. Bolat F, Comert S, Bolat G, Kucuk O, Can E, Bulbul A, et al. Acute kidney injury in a single neonatal intensive care unit in Turkey. World J Pediatr. 2013; 9(4):323-9.
19. Viswanathan S, Manyam B, Azhibekov T, Mhanna MJ. Risk factors associated with acute kidney injury in extremely low birth weight (ELBW) infants. Pediatr Nephrol. 2012;27(2):303-11.
20. Felipin LCS, Oliveira RR, Merino MFGL, Rodrigues BC, Higarashi IH. Associated factors for acute kidney injury in preterm infants. Rev Bras Enferm. 2019; 72(3):118-24.
21. Durga D, Rudrappa S. Clinical profile and outcome of acute kidney injury in neonatal sepsis in a tertiary care centre. IJCP. 2017:4:2
22. Durkan AM, Alexander RT. Acute kidney injury post neonatal asphyxia. J Pediatr. 2011;158(2 Suppl):e29-33.

Cite this article as: Gopalan D, Hapani PT. Clinical profile and outcome of acute kidney injury in preterm neonates in a level three neonatal intensive care unit. Int J Contemp Pediatr 2024;11:162-6.