STUDY OF INCIDENCE, RISK FACTORS, AND OUTCOME OF ACUTE KIDNEY INJURY IN NEONATAL INTENSIVE CARE UNIT AT TERTIARY CARE CENTER

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ABSTRACT

Acute Kidney Injury (AKI) remains a notable cause of morbidity and mortality in neonates and the costs of care for patients with AKI are also very expensive, particularly in developing countries like Nepal. The global burden of AKI is quite high specially in low-middle-income countries and has very limited data on the incidence of AKI worldwide and the data vary generally in different studies This is a hospital based retrospective cross-sectional study of neonates admitted at Nepal Medical College and Teaching Hospital (NMCTH) from January 2022 till January 2023. Among 318 admitted newborns, incidence of AKI was found to be 18 (5.7%) with male to female ratio of 3:1 in AKI group. The mean length of hospital stay was 13 days, which was longer in AKI group in comparison to non AKI group which was 6.3 days. The rate of neonatal AKI varied within the gestational age cohorts: lower the gestational age more chance of AKI as 28 -32 weeks (n=3/17, 17.6 %) had more incidence of AKI in compare to older gestational age as 32–36 weeks (n=3/50, 6%), and ≥37 weeks (n=12/250, 4.8 %). Meconium stained liquor and pregnancy induced hypertension were the maternal risk factors found to be associated with the development of AKI. Respiratory distress syndrome (RDS) was the commonest cause of neonatal AKI (44.40%), followed by neonatal sepsis (38.90%) and fluid overload (38.90%). In term of outcomes all the cases were discharged from non AKI group while among AKI group mortality was 4/15 (22.2%). Stage 3 AKI had poor prognosis with 100% mortality. Use of nephrotoxic drugs was the main cause of morbidity and mortality of AKI in both discharged and expired group. This showed that this vulnerable population need to be taken care early with effective management and awareness should be developed for the better understanding of the epidemiology of AKI in neonates as there is high risk of developing chronic kidney disease (CKD).

KEYWORDS

Acute kidney injury, neonatal sepsis, asphyxia, oliguria

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INTRODUCTION

Acute kidney injury (AKI) is frequent and common cause of a heavy burden of illness (morbidity and mortality). Not only this, but also the costs of care for patients with AKI are very high.[1] AKI is defined as the decline or abrupt loss of kidney function and is marked by an accumulation of waste products, imbalance of fluid and electrolyte, and change of acid-base homeostasis.[2-4] Soon after birth, there are significant changes in renal blood flow (RBF), Glomerular filtration rate (GFR) and tubular function. As RBF increases, GFR in neonates increases from 10–20 ml/min/1.73 m^2 to 30–40 ml/min/1.73 m^2 by 2 weeks of life and by 2 years of age reaches an adult GFR value.[5] Neonates are more vulnerable to AKI than older children because of their functionally immature kidneys.[6] As most neonates have frequent infections and are exposed to nephrotoxic medications during their management, this may lead to multi-organ failure.[7]

AKI is a common problem in neonates especially admitted in neonatal intensive care unit (NICU) but the proof is limited.[8] The global burden of AKI is approximately 13.3 million cases per year, with 85.0% from low-middle-income countries. There is limited data on the incidence of AKI worldwide and the data vary generally in different studies which depend on the setting and the populations investigated.[9,10] The incidence of AKI in neonates scale from 2.6% to 25.0% of all admissions in NICU.[11] A huge multi-centric study found gestation wise distribution of AKI cases to follow a U-shaped distribution with the highest rates of AKI in the preterm (22–29 weeks) and near term (>36 weeks) newborns.[7] Critically ill neonates and premature neonates are at threat for chronic kidney disease (CKD), although the imposed pathophysiology, incidence, risk factors, and outcomes are not yet known. AKI is one of the most alarmingly high-risk factors for future CKD in both pediatrics and adults.[12]

There are marked differences in the epidemiology of AKI in neonates between developing and the developed countries. Increased prevalence of neonatal sepsis, lack of awareness about neonatal AKI and poor access to pediatric nephrologists may be the reason behind it in the developing countries. The cornerstone of treatment and management of AKI in neonates is prevention, careful monitoring and early detection.[13] Nepal as one of the developing countries have very limited data about the incidence of AKI in NICU. To detect the incidence, the etiological profile and outcome of AKI is important for prevention, early detection and rational therapeutic modalities. This study aims to identify the incidence of AKI in NICU by carefully monitoring kidney injury, the high risk factors associated with AKI and to find the cause of mortality in AKI patients as well as the short-term outcomes in such infants.

METHODS AND METHODS

This is a hospital based retrospective study of neonates admitted at Nepal Medical College Teaching Hospital (NMCTH) from January 2021- December 2022. Ethical approval for the study was taken from the Institutional Review Committee (Ref. No. 43-079/080) of NMCTH. All neonates admitted in NICU, during the period were included in the study. Neonates who died within the first 24 hours of admission, neonates with chromosomal abnormalities, malformations incompatible with life as complex congenital heart disease and major kidney malformations, neonates who left against medical advice (LAMA) and neonates with a maternal history of AKI were excluded.

AKI was labeled using the KDIGO classification modified for newborns which considers increased serum creatinine values over baseline values as well as urine output over time in hours or both. The elevation of serum creatinine value by 1.5, 2, and 3 times from the baseline values was considered as Stage 1, 2, and 3 of renal failure, respectively. Similarly, urine output ≤1.5 ml/kg/h for 8 h, <1 ml/kg/h for 24 h, and <0.7 ml/kg/h for 24 h or anuria for 12 h was defined as Stages 1, 2, and 3 oliguric renal failure, respectively.[14]

Maternal and neonatal detail sociodemographic [name, age, sex, weight at admission, gestational age, mode of delivery, maternal risk factors]; associated contributing conditions, including perinatal asphyxia, sepsis, respiratory distress syndrome, dehydration due to feeding problems, oliguria, heart failure, nephrotoxic drug administration, urologic anomalies, and mechanical ventilation with its duration; and clinical data were entered into predesigned proforma. The outcome of cases diagnosed with acute kidney injury was further categorized in terms of improved, mortality and duration of hospital stay was noted.

Descriptive analysis was done by the use of frequency, percentage, mean, median, standard deviation and range as per the nature of data and inferential analysis was done by using chi-square test. Data were collected and analyzed using SPSS-18).

RESULTS

Among 318 newborns admitted in NICU, 18 (5.7%) babies developed AKI as defined by nRIFLE criteria. Among the total population 209 (65.7%) were male with male to female ratio of 1: 1.9 who got admitted in NICU, while in AKI group 15/18 (83.3%) were males with male to female ratio of 3:1. The mean birth weight and gestational age in AKI and non AKI groups were similar. The mode of delivery in AKI group was caesarean section which was 14/18 (77.8%) which was similar to non AKI group (Table 1).

The rate of neonatal AKI varied within the gestational age cohorts: in neonates of 28 -32 weeks, 3/17 (17.6 %) had AKI in compare to older gestational age, where AKI was present in 3/50 (6.0%), in neonates of 32-36 weeks, and 12/250 (4.8 %) in neonates of ≥37 weeks (Table 1). Among 18 cases of AKI, 11 (61.1%) was diagnosed by both serum creatinine and urine output: 6 (33.3%) by serum creatinine and 1 (5.56%) by urine output (Table 2).

Of the 18 with AKI, 6 had stage 1 (33.33%), 8 had stage 2 (57.14%), while 4 had stage 3 AKI (22.22%) (Fig. 1).

Table 1: Demographics of the overall patients in AKI and non AKI and stratified into gestational age.

Variables	Total no of Cases		28-32 weeks (n= 17)		33-36 weeks (n= 50)		>-37 weeks (n= 251)	
	AKI (n=18)	Non –AKI (n=300)	AKI (n= 3)	Non –AKI (n= 14)	AKI (n= 3)	Non -AKI (n= 47)	AKI (n= 12)	Non –AKI (n= 239)
Gestational age, (wk)	36 ± 2.9	37.4 ±2.08	31±1	31.7 ± 0.46	35.6± 0.57	35± 1.18	38.2± 1.13	38.2 ± 1.15
Birth weight, gm	2700±700	2927±619	800± 430	2100 ±600	2430±570	2300±500	3100±540	3090±520
Sex (male)	15(83.3%)	194 (64.7%)	3 (100.0%)	9 (64.3%)	2 (66.7%)	29 (61.7%)	10 (83.3%)	155 (65.1%)
Parity								
Single	12 (66.7)	129 (59.7)	2 (66.7%	10 (71.4%)	1 (33.3%)	24 (51.0%)	9 (75.0%)	145 (60.7%)
Multiple	6 (33.3)	121 (40.3)	1(33.3%)	4 (28.6%)	2 (66.7%)	23 (48.9%)	3 (25.0%)	94 (39.3%)
Amniotic fluid								
Oligohydraminous	0	10 (3.3)	0	0	0	4	0	6
Normal	18 (100)	290 (96.7)	3	14	3	43	12	233
Polyhydraminous	0	0	0	0	0	0	0	0
Mode of delivery								
NVD	4 (22.2)	71 (23.7)	0	4	2	4	2	63
C-section	14 (77.8)	229 (76.3)	3	14	3	43	12	233

Table 2: Laboratory finding and clinical feature of neonates with acute kidney injury

	Total no of Cases		28-32 weeks (n= 17)		33-36 weeks (n= 50)		>-37 weeks (n= 251)	
Parameter	AKI (n=18)	Non –AKI (n=300)	AKI (n= 3)	Non –AKI (n= 14)	AKI (n= 3)	Non -AKI (n= 47)	AKI (n= 12)	Non –AKI (n= 239)
AKI by serum cr	6 (33.3%)	0	2 (66.7%)	0	2 (66.7%)	0	2 (16.7%)	0
AKI by both serum cr and urine output	11 (61.1%)	0	1 (33.3%)	0	1 (33.3%)	0	9 (75%)	0
AKI by urine output	1(5.56%)	0	0	0	0	0	1 (8.3%)	0

Table 3 : Association of maternal conditions in AKI and non AKI

Variables	Non-AKI (n= 300) (%)	AKI (n= 18) (%)	P Value
Meconium stained	37 (12.3)	4 (22.2)	0.224
Hypertension during pregnancy	14 (4.7)	2 (11.1)	0.224
Others maternal risk (Premature rupture of membrane, Abrutio placenta)	17 (5.7)	1 (5.6)	0.984

Table 4: Neonatal risk factors associated with acute kidney injury			
Variables	**Non-AKI (%)**	**AKI (%)**	**P Value**
Birth weight			
Low birth weight	61 (20.3)	4 (22.2)	
Normal	227 (75.7)	13 (72.2)	0.925
Large for gestational age	12 (4)	1 (5.6)	
Gestational age			
Term	239 (79.7)	12 (66.7)	0.189
Preterm	61 (20.3)	6 (33.3)	
Sepsis blood culture positive	19 (6.3)	7 (38.9)	0.001
Meconium aspiration syndrome	37 (12.3)	4 (22.2)	0.224
Respiratory distress syndrome	16 (5.4)	8 (44.4)	0.001
Persistent pulmonary hypretension of newborn	0	3 (18.8)	
Necrotizing enterocolitis	0	2 (11.1)	
Fluid overload	0	7 (38.9)	
Birth asphyxia	17 (5.7)	4 (22.2)	
Neonatal resuscitation	20 (6.7)	3 (16.7)	

Table 5: Prognostic factors associated with acute kidney injury (n = 18)		
	Outcomes	
Risk factors	**Discharged n=14 (77.8%**	**Expired n=4 (22.2%)**
Shock		
Present	4 (28.57%)	2 (50%)
Absent	10 (71.4%)	2 (50%)
Sepsis blood culture		
Positive	5 (35.7%)	1(25%)
Negative	9(64.3%)	3(75%)
Mechanical ventilation		
Yes	6 (42.9%)	2(50%)
No	8(57.1%)	2(50%)
Birth asphyxia		
Yes	2 (14.3%)	1(25%)
No	12 (85.7%)	3 (75%)
Nephrotoxic drugs		
Used	9 (57.14%)	4 (100%)
Not used	5 (42.85%)	0

Meconium stained liquor and pregnancy induced hypertension were the maternal risk factors found to be associated with the development of AKI in the newborn in this study (Table 3). Among the neonatal risk factors, respiratory distress syndrome (44.4%) was the commonest cause of neonatal AKI followed by neonatal sepsis (38.9%) and fluid overload (38.9%) respectively. Other neonatal risk factors associated with neonatal AKI were birth asphyxia and neonatal resuscitation which was present in 22.2 % and 16.7% of neonates respectively. Meconium aspiration syndrome (MAS), necrotizing enterocolitis (NEC) and persistent pulmonary hypretension of newborn (PPHN) were also found to be other important risk factors for AKI in this study (Table 4).

Use of nephrotoxic drugs was the main predictor of mortality with AKI in both discharged and expired group. Shock, use of mechanical

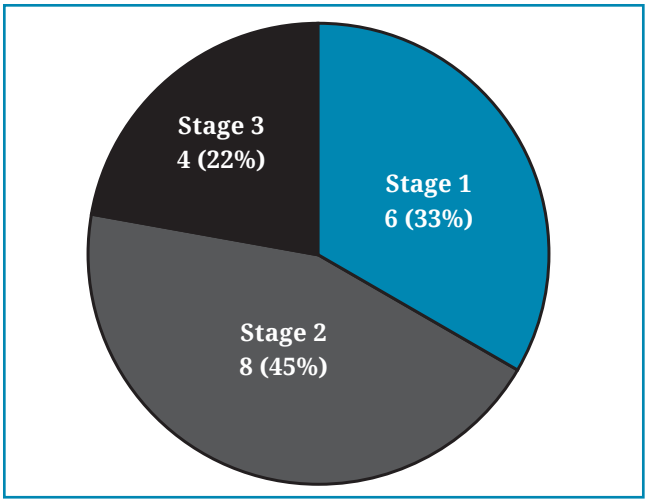

Fig. 1: Neonatal AKI as per staging

Table 6: Outcomes of AKI

Variables	AKI (n=18)	Non –AKI (n=300)
Length of hospital stay	13.3± 11	6.3 ±4.9
Mortality	4 (22.2%)	0

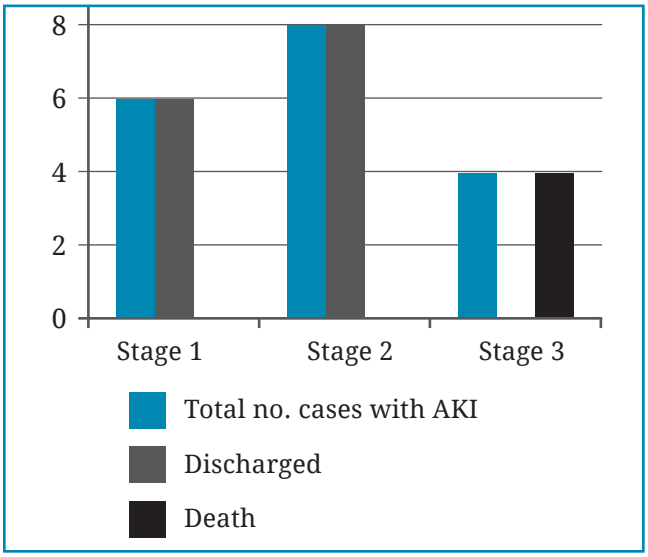

Fig. 2: Outcomes of AKI according to staging

ventilation and neonatal sepsis (culture proven), were also found to be poor prognostic factors associated in AKI group (Table 5).

The duration hospital stay in AKI group was longer (13.3± 11) in compare to non AKI group. While evaluating outcomes of neonatal AKI, 4/18 (22.2%) were expired (Table 6). There were 4 case of Stage 3 AKI and had poor prognosis with 100% mortality. All of these parents refused for dialysis (Fig. 2).

DISCUSSION

AKI is a common problem with various etiologies and one of the independent markers of survival in neonatal population.[13] The incidence of neonatal AKI varies in different studies, while the incidence of AKI in this study was 5.7%, which was similar to studies done by Timovska *et al*[2] and Palle *et al*,[15] which was around 6.5 %. In the study done by Nandhagopal *et al*[16] the incidence was 21.8%, while Kapoor *et al*[1] found to have 9.6%, similarly, in the study done in Nepal by Poudel *et al*[17] the incidence of AKI was 37.5%, similar to the assessment of worldwide acute kidney epidemiology in neonates (AWAKEN) cohort study, 30% of NICU admitted neonates had AKI[7] which was quite higher than in this study. The reason behind that the low incidences of AKI in this study, may be due to early recognization and prompt management of the risk factors of AKI. Most of the neonates admitted in NICU were inborn with good antenatal care. The varying incidence of AKI in different hospitals may be due to some geographical variations, economical situation and cultural believes. In the present study, male neonates had higher incidence of AKI with male female ratio of 3:1, which was quite comparable to other studies.[11,16,17] This may be probably due to some predisposing factors as neonatal sepsis and respiratory distress syndrome, which was more prevalent in male compared to female.[2]

In this study the rate of neonatal AKI was high in lower gestational age in compare to older gestational age, which was similar to study done by Youssef *et al*,[18] while the study done by Mortazavi *et al*,[19] reported that lower gestational age had less frequency of AKI in compare to higher gestational age. In this study the mean duration of hospital stay was longer in AKI group in compare to non AKI group which was 13 days and 6.3 days respectively which was similar to other investigators.[7,16,20]

AKI was diagnosed by both serum creatinine and urine output. In this study oliguric AKI was more in compare to non-oliguria which accounted for 33.3%, which was similar to study done by Kapoor *et al*[11] and Mortazavi *et al*.[19] While in the study done by Youssef *et al*,[18] non-oliguric AKI was more frequent than oliguric AKI, with 70.4% of patients being non-oliguric.

In this study RDS (44.4%) was the commonest cause of neonatal AKI followed by neonatal sepsis and fluid overload, which accounted for 38.9% each. Most of the study showed that neonatal sepsis was the commonest cause of neonatal AKI, which was higher than this study

which range from 28.5%-63.0%.[11,18,19] Similar study done by Poudel *et al*[17] had found that use of nephrotoxic drugs and neonatal sepsis were most common causes of AKI in neonates. Study done by Timovska *et al*[2] observed asphyxia was the most common risk factor associated with AKI which accounted for 38.0%, while in this study asphyxia and neonatal resuscitation were also one of the predisposing risk factors for development of AKI in compared to neonates without AKI, presented for 22.2% and 16.7%. In the similar study by Mortazavi *et al*[19] and Kapoor *et al*[11] found asphyxia in 29.8% and 22.2%, respectively.

The overall mortality of neonate was higher in AKI group than in non AKI group, in this study mortality rate was 22.2% and all were from AKI group which was within the range (15.0% -40.0%) of other different studies.[11,17-19,21,22] In this study use of nephrotoxic drugs was the main cause of AKI in both discharged and expired group which was similar with other study.[17] While the other studies showed that sepsis, mechanical ventilation, surgical procedures were the important associated risk factors for the mortality with AKI neonates.[11,18] In this study all 4 patients of stage 3 AKI had poor prognosis. All 4 (100.0%) patients expired, as the parents couldn't afford renal replacement therapy due to financial constraints. In this study, sepsis and mechanical ventilation were not significant in term of prognostic factors in the neonates with AKI. As 25.0% neonates died due to sepsis ,while 37.5% AKI neonates with sepsis were discharged and around 50.0% AKI neonates on mechanical ventilation were discharged and had similar rate of mortality. This could be explained by that most of the newborns in this study group were inborn and required less invasive procedures.

Thus special attention needs to be paid while doing procedures, need promptly, timely referral, proper management and less use of nephrotixic drugs could decrease the rate of mortality, which was lacking in our setting especially due to financial constraints, low resources and lack of specialized manpower. The limitations of this study are; it is a retrospective study and sample size is small.

In conclusion, AKI is a treatable condition with early detection. In the field of clinical practice, AKI in this vulnerable population needs to be taken care early with effective management Awareness should be developed for the better understanding of the epidemiology of AKI as these neonates have high risk of developing CKD.

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