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Original Research Article

ACUTE KIDNEY INJURY IN HOSPITALIZED NEWBORNS: ASSOCIATED RISK FACTORS AND OUTCOME

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ABSTRACT

Background: Acute kidney injury (AKI) is a significant complication among neonates admitted to Neonatal Intensive Care Units (NICUs), so early recognition and management of risk factors are crucial for improving clinical outcomes. This study aimed to identify the risk factors and outcomes of AKI among neonates admitted to a tertiary care center in North East India.

Materials and Methods: A hospital-based prospective analytical study was conducted in the NICU of Silchar Medical College and Hospital (SMCH) from June 2021 to May 2022. A total of 140 neonates were included in the study and were assessed for AKI using the KDIGO for neonates and nRIFLE criteria. Demographic, clinical, and laboratory data were collected, and statistical analysis was performed using IBM SPSS (version 26). Chi-square and regression analyses were applied to identify independent risk factors.

Results: Among 140 neonates enrolled, 36 (25.7%) developed AKI. Significant maternal risk factors included pregnancy-induced hypertension (p=0.032), preterm premature rupture of membranes (p=0.043), and antenatal steroid use (p=0.032). Neonatal factors independently associated with AKI were inborn delivery (p=0.018), birth asphyxia (p<0.001), shock (p=0.024), sepsis (p=0.001), umbilical catheterization (p=0.025), and dehydration (p=0.001). The mortality rate among AKI cases was 41.7%. Use of mechanical ventilation (p=0.037), congestive heart failure (p=0.043), and AKI (p=0.005) were significant predictors of neonatal mortality.

Conclusion: AKI is a prevalent condition in NICU neonates, with high morbidity and mortality. Early identification and management of associated risk factors are crucial for improving neonatal outcomes as mortality increased with severity, reaching 100% in Stage 3. Further research is needed to explore preventive interventions and long-term renal implications in neonates with AKI.

Keywords: Acute Kidney Injury, Neonates, Risk Factors, Renal Dysfunction, KDIGO, nRIFLE.

INTRODUCTION

Acute kidney injury (AKI) is a common complication encountered in neonates admitted to neonatal intensive care units (NICUs) worldwide.[1,2] The exact prevalence of AKI in the newborn population remains unknown, although varying incidences ranging from 6-24% have been reported in NICUs.[3,4] AKI is defined as a rapid reduction in kidney function, as evidenced by an absolute increase in serum creatinine of ≥0.3 mg/dL (>26.4 micromol/L), a percentage increase in serum creatinine of ≥50% (1.5-fold from baseline), or a decrease in urine output (<1mL/kg per hour for 24 hours).[5,6] Several underlying risk factors, including asphyxia, respiratory distress syndrome, preterm birth, sepsis, umbilical artery catheterization, early medication administration (especially aminoglycosides), volume depletion, and urogenital abnormalities, can influence AKI development.[7-11]

Survivors of AKI may develop permanent renal damage in up to 40% of cases.[12] In the north-eastern region of India, AKI epidemiology in a general NICU has been scarcely studied. Therefore, this study aims to explore the risk factors associated with AKI in admitted neonates and assess their outcomes in a tertiary care centre of Northeast India.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based prospective analytical study conducted at the Department of Paediatrics of a tertiary care hospital named Silchar Medical College and Hospital (SMCH) of Cachar district of Assam from June 2021 to May 2022.

Study participants, inclusion, and exclusion criteria

All neonates admitted between the study period in the in NICU of SMCH with risk factors and symptoms of AKI either at admission or during the course of treatment were evaluated for enrolment/eligibility in the study with due consent of the parents or caretakers.

Patients were included based on the following criteria : Neonates with.

1. Peri-natal asphyxia. 2. Respiratory distress syndrome. 3. Sepsis. 4. Prematurity. 5. Use of mechanical ventilation.	6. Presence of dehydration. 7. Umbilical catheterization. 8. Maternal use of ACE inhibitors. 9. Congestive heart failure.

Patients were excluded based on the following criteria

1. Neonates who died within 24 hrs of admission. 2. With maternal history of azotaemia. 3. With congenital anomalies of urinary system.	4. With post operative AKI. 5. On drugs altering GFR.

Sample size and sampling

The study used purposive sampling where all neonates admitted between the study period in the in NICU of SMCH with risk factors and symptoms of AKI either at admission or during the course of treatment were evaluated for enrolment in the study. Altogether 140 newborns were enrolled in the study after applying inclusion and exclusion criteria.

Procedure and Data collection

Detailed history taking and clinical examination were followed by laboratory investigations. The diagnosis of AKI was established by measuring the serum creatinine level or urine output as per KDIGO AKI Criteria. In babies, who fulfilled the criteria for AKI, repeat estimations of serum creatinine were done every 48 h (or earlier if indicated) till it was normalized or the baby was discharged from the hospital. Normal serum creatinine values used for this study were 0.3–1.0 mg/dl. 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 24 h, <1ml/kg/h for 24 h, and <0.7 ml/kg/h for 24 h or anuria for 12 hour was defined as Stages 1, 2 and 3 oliguric renal failure, respectively.[14,15] Semi-structured proforma was used for collecting data on socio-demographic characteristics, clinical examination and laboratory investigation results.

Data Analysis

Data was entered into Microsoft Excel and analysis was done using IBM SPSS (version 26, trial version). Data were tested for normal distribution. Quantitative data was expressed as mean (± Standard Deviation) and categorical variables were summarised as frequencies with percentages. Chi square test/Fisher exact test was applied as test of significance. A p-value of <0.05 was considered as significant in this study.

Ethical Consideration

The institutional ethical committee of Silchar Medical College approved the study and informed written consent was taken in the participant's own language before data collection.

RESULTS

Basic characteristics of neonates are described in Table 1. There were 54% of mothers who were between 21 and 30 years, followed by 26% of mothers who were below 20 years of age, and the remaining 20% mothers belong to the more than 30 years age group. The mean maternal age was 24.6 ± 4.7 years with range between 17 and 34 years. Preterm Premature rupture of membrane (PPROM) was the commonest morbidity seen in mothers (21.40%) followed by pregnancy induced hypertension (PIH, 18.60%), antepartum hemorrhage (APH, 13.60%), ante-natal/peri-natal use of steroids (12.10%) and anti-hypertensives (10.00%). Other risk factors for AKI in neonates are gestational diabetes mellitus GDM (6.50%) and chorioamnionitis (5.00%). Among the neonatal factors birth asphyxia was the most common risk factor seen in 55 neonates (39.30%), followed by shock in 46 neonates (29.70%), respiratory distress in 39 neonates (27.90%), sepsis in 36 neonates (25.70%), umbilical vein catheterization in 23 neonates (16.20%), mechanical ventilation in 20 neonates (14.30%), dehydration in 18 neonates (12.90%) and congestive heart failure in 7 neonates (5.00%). However, combination of risk factors was present in most of the neonates. [Table 2]

Table 1: Basic characteristics of sample (N=140)

Gestational Age (In Weeks)	**Frequency**	**Percentage**
28-33 weeks	21	15.00 %
34-36 weeks	45	32.00 %
≥ 37 weeks	74	53.00 %
Birth Weight (In gram)	**Frequency**	**Percentage**
< 1000 grams	1	0.70 %
1000- 1499 grams	28	20.00 %
1500- 2499 grams	48	34.30 %
>2500 grams	63	45.00 %
Gender	**Frequency**	**Percentage**
Male	83	59.00 %
Female	57	41.00 %
Mode of Delivery	**Frequency**	**Percentage**
Normal vaginal Delivery	83	59.00 %
Lower Segment Caesarean Section (LSCS)	57	41.00 %
Site of Delivery	**Frequency**	**Percentage**
Inborn	64	46.00 %
Out born	76	54.00 %

Table 2: Proportion of the neonatal risk factors for AKI

Risk Factors	**Frequency**	**Percentage**
Birth asphyxia	55	39.3%
Shock	46	32.9%
Respiratory Distress	39	27.9%
Sepsis	36	25.7%
Umbilical vein Catheterization	23	16.4%
Mechanical ventilation	20	14.3%
Dehydration	18	12.9%
Congestive Heart Failure	7	5.0%

Note: Risk factors are not mutually exclusive

In the study 36 (25.7%) newborns were diagnosed to have AKI and the majority 22 (61%) had stage I AKI (Figure 1A & 1B). Serum creatinine was done on day of admission followed by every 48 hours till the serum creatinine level came below 1.5 mg/dl. The mean serum creatinine level on day 1 was 1.21 ± 0.45 mg/dL, on day 3 was 1.10 ± 0.48 mg/dL and on day 5 was 0.99 ± 0.31 mg/dL. Urine output monitoring was done in all included neonates either by diaper method or by catheterization wherever needed, and then they were categorized into different subgroups according to nRIFLE criteria. Majority (80%) had urine output >1.5 ml/kg/hr over 24 hours, followed by 12.1% of neonates who had 1-1.5 ml/kg/hr, 6.4% who had <1 ml/kg/hr and 1.5% <0.7 ml/kg/hr over 24 hours. The ratio of males to females for the occurrence of AKI in our study was 1.57:1.

Figure 1A: Prevalence of AKI (N=40)

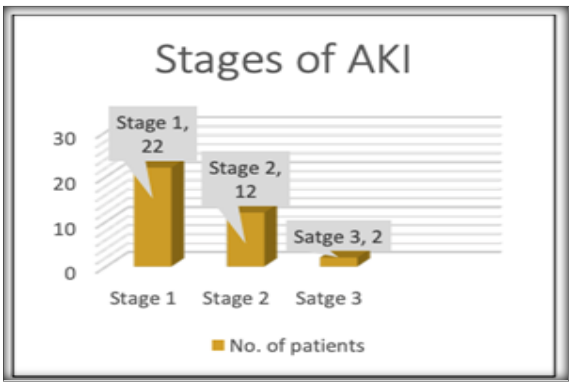

Figure 1B: Stages of AKI (N=36)

It is observed that among the risk factors gestational age, birth weight, site of delivery, PIH, PROM, steroids use, birth asphyxia, sepsis, umbilical catheter, use of mechanical ventilation, oliguria, and shock were significantly associated with developing AKI among neonates admitted in this facility (Table 3).

Further, regression analysis was done to assess the independent association of the risk factors with AKI. It is observed that risk factors like Inborn delivery, Birth asphyxia, Shock, Sepsis, Umbilical catheterization and Dehydration were independently associated with AKI in the newborns. [Table 4]

Table 3: Risk factors for acute kidney injury

Risk Factors of AKI		AKI				Total		p-Value	OR	95% CI of OR
		Yes		No						
		N	%	N	%	N	%			
Gestational age	< 37 weeks	23	63.9	43	41.3	66	47.1	0.014 *	2.51	1.15-5.5
	≥ 37 weeks	13	36.1	61	58.7	74	52.9			
Birth Weight	Low Birth Weight	25	69.4	52	50.00	77	65	0.043 *	2.27	1.01-5.09
	Normal	11	30.6	52	50.00	63	45			
Site of Delivery	Inborn	22	61.1	42	40.4	64	45.7	0.031*	2.32	1.07-5.04
	Out born	14	38.9	62	59.6	76	54.3			
PIH	Yes	11	30.6	15	14.4	26	18.6	0.032 *	2.61	1.07-6.39
	No	25	69.4	89	85.6	114	81.4			
PROM	Yes	12	33.3	18	17.3	30	21.4	0.043 *	2.39	1.01-5.64
	No	24	66.7	86	82.7	110	78.6			
Steroids	Yes	8	22.2	9	8.7	17	12.1	0.032 *	3.02	1.06-8.55
	No	28	77.8	95	91.3	123	87.9			
Umbilical catheter	Yes	10	27.8	13	12.5	23	16.4	0.033 *	2.69	1.06-6.84
	No	26	72.2	91	87.5	117	83.6			
Mechanical Ventilation	Yes	12	33.3	8	7.7	20	14.3	<0.001*	6	2.2-16.31
	No	24	66.7	96	92.3	120	85.7			
Oliguria	Yes	11	30.6	0	0	11	7.9	<0.001*	∞	
	No	25	69.4	104	100	129	92.1			
Shock	Yes	17	47.2	29	27.9	46	33.1	0.028 *	2.31	1.06-5.06
	No	19	52.7	75	72.1	94	66			

*Statistically Significant

Table 4: Regression Analysis of Risk factors for Acute Kidney Injury

Parameter Estimates								
AKI (outcome)	B	Std. Error	Wald	Df	Sig. (p value)	Exp(B)	95% Confidence Interval for Exp(B)	
							Lower Bound	Upper Bound
Intercept	-0.644	6.984	0.009	1	0.927			
Birth weight	0.000	0.001	0.140	1	0.708	1.000	0.998	1.003
Gestational age (in weeks)	-0.239	0.218	1.205	1	0.272	0.787	0.514	1.206
Sex	0.271	0.591	0.211	1	0.646	1.312	0.412	4.181
Inborn	1.846	0.777	5.641	1	0.018	6.334	1.381	29.055
Mode of delivery	0.679	0.641	1.123	1	0.289	1.972	0.562	6.921
PIH	0.530	0.733	0.523	1	0.470	1.699	0.404	7.149
PPROM	1.506	1.596	0.890	1	0.346	4.507	0.197	102.953
GDM	-1.703	1.460	1.361	1	0.243	0.182	0.010	3.183
Chorioamnionitis	-2.067	1.813	1.300	1	0.254	0.127	0.004	4.418
APH	-1.651	1.068	2.388	1	0.122	0.192	0.024	1.557
Steroids	0.250	1.304	0.037	1	0.848	1.285	0.100	16.552
Birth asphyxia	5.733	1.571	13.318	1	0.000	308.904	14.210	6714.920
Dehydration	5.710	1.700	11.287	1	0.001	301.921	10.794	8445.332
Umbilical catheterization	5.058	2.170	5.045	1	0.025	157.23	1.905	2976.701
Shock	2.112	0.936	5.093	1	0.024	8.265	1.320	51.750
Sepsis	3.165	0.971	10.619	1	0.001	23.685	3.530	158.922
Mechanical ventilation	1.807	1.015	3.172	1	0.075	6.093	0.834	44.512
Congestive heart failure	0.669	1.163	0.330	1	0.566	1.951	0.200	19.079

The newborns were followed up to assess whether they were successfully discharged or expired and it was found that majority of the babies 123 (83.6%) could be successfully discharged while 17 (12.14%) babies could not survive. Also among the babies developing AKI, 21 (58.3%) were discharged successfully while the rest 15 (41.7%) failed to survive. (Table 5). Further, mortality rates rose with the severity of AKI. Stage 1 (S1) had a 27.3% mortality, which increased considerably in Stage 2 (S2) to 58.3%. Stage 3 (S3) showed the worst outcome, with a 100% mortality. [Table 6]

Table 5: Outcome of newborns with AKI

AKI	Expired		Discharged		Grand Total	
	N	%	n	%	N	%
Present	15	41.7%	21	58.3%	36	24.2%
Absent	2	1.9%	102	98.1%	104	69.8%
Grand Total	17	12.1%	123	82.6%	140	100.0%

Table 6: Outcome of newborns as per different stages of AKI.

AKI Stages	Expired		Discharged		Grand Total
	N	%	N	%	
S1	6	27.3%	16	72.7%	**22**
S2	7	58.3%	5	41.7%	**12**
S3	2	100.0%	0	0.0%	**2**
No AKI	2	1.9%	102	98.1%	**104**
Grand Total	**17**	**12.1%**	**123**	**87.9%**	**140**

Note: Percentage shown in the table is row-wise.

To further understand the factors contributing to death of the babies regression analysis was done which reflected that babies under Mechanical Ventilators, babies developing Congestive Heart Failure and AKI were significant factors leading to deaths. [Table 7]

Table 7: Regression analysis of Risk factors for Death among the admitted cases

Parameter Estimates									
Death (outcome)		B	Std. Error	Wald	df	Sig. (p-value)	Exp(B)	95% Confidence Interval for Exp(B)	
								Lower Bound	Upper Bound
	Intercept	2.213	9.454	0.055	1	0.815			
	Birth weight	-0.001	0.002	0.118	1	0.731	0.999	0.996	1.003
	Gestational age (in weeks)	-0.244	0.313	0.605	1	0.437	0.784	0.424	1.449
	Male	-0.294	0.866	0.115	1	0.734	0.745	0.136	4.072
	Inborn	0.132	0.978	0.018	1	0.892	1.141	0.168	7.754
	Chorioamnionitis	0.892	1.580	0.318	1	0.573	2.439	0.110	53.995
	Steroids	-0.057	1.588	0.001	1	0.971	0.945	0.042	21.250
	Birth asphyxia	4.051	2.306	3.086	1	0.079	57.474	0.626	5277.587
	Shock	1.501	1.235	1.476	1	0.224	4.486	0.398	50.515
	Sepsis	-0.473	1.445	0.107	1	0.743	0.623	0.037	10.586
	Mechanical ventilation	2.528	1.215	4.330	1	0.037	12.531	1.158	135.586
	Congestive heart failure	3.312	1.639	4.082	1	0.043	27.449	1.104	682.318
	AKI	3.108	1.104	7.922	1	0.005	22.380	2.570	194.917

DISCUSSION

This study was conducted in a tertiary care centre in Northeast India to assess the association of the risk factors of acute kidney injury (AKI) among neonates admitted to the neonatal intensive care unit (NICU). The study employed modified Kidney Disease Improving Global Outcomes (KDIGO) criteria for neonates, which have been used in previous paediatric studies, to allow for comparison with existing literature.[6] The proportion of AKI in this study was found to be 25.7% (36 neonates), which is constant with previous reports in the literature.[16-18] Gohiya P et al reported 21% incidence of AKI in their study,[16] while Jetton J.G et all reported an incidence of 29.9% of AKI in neonates in their multicentric study.[18]

Of the 36 neonates with AKI, 22 had stage I (61.1%), 12 had stage II (33.33%), and 2 had stage III disease (5.5%). The mean age of onset of AKI was 1.86 ± 2.52 days, which is lower than what has been previously reported.[16] Gohiya P et al reported the mean age of new-borns with AKI as 3.49 ± 0.23 days, while 37.4% neonates have stage I AKI, 36.4% and 26.2% had AKI of stage II and III respectively.[16] Maternal factors such as pregnancy-induced hypertension, preterm premature rupture of membranes, and antenatal steroids were significant predictors of neonatal AKI in this study, which is consistent with previous studies.[19,20] Shalaby MA et al reported that gestational age and perinatal asphyxia were associated with increased incidence of AKI and its related mortality.[19] Bolat F et al reported high prevalence of AKI among those new born who suffered from respiratory distress syndrome, sepsis, asphyxia, dehydration, congenital anomalies of urinary tract, low birth weight , PIH, PPROM and administration of antenatal corticosteroid use.[20] Which are similar to our study, but we have not included congenital anomalies of urinary tract in our study. Neonatal factors such as birth asphyxia, sepsis, shock, umbilical catheterization, and dehydration were also found to be independently associated with the occurrence of neonatal AKI, similar to previous study by Shalaby MA et al.[19] Oliguria and elevated serum creatinine levels were significantly associated with the occurrence of AKI, which is in line with the findings of Youssef et al.[21] In their study Youssef et all reported that 29.6 % new born presented with oliguria, while 70.4% presented with normal urine output. The mortality rate among neonates with AKI in this study was 41.7%, which is similar to previous studies. Youssef et al reported 52.9% mortality, while Nandhagopal N et al reported mortality rate of 45.71% in their studies.[21,22] Of the neonates who died, six had stage I AKI, seven had stage II AKI, and two had stage III AKI with increasing order of mortality- 27.3% in Stage 1, 58.3% in Stage 2, and 100% in Stage 3. Similar findings were reported by

Gohiya P et al with significantly high mortality (89.9 %) in AKI Stage III.

Our study highlights the importance of early recognition and management of risk factors for AKI in neonates, including prematurity, low birth weight, maternal PIH, PPROM, and antenatal steroid use, as well as neonatal factors such as birth asphyxia, sepsis, shock, umbilical catheterization, oliguria, and mechanical ventilation use. Further studies are needed to explore potential interventions that could reduce the incidence of AKI in neonates and improve their clinical outcomes.

Limitation of Study

Possible limitations to our study is that the sample size was smaller, Novel biomarkers of kidney injury also needed to be tested for early diagnosis of AKI, long term follow-up needed to look for development of chronic kidney disease (CKD) in neonates with AKI.

CONCLUSION

This study found a high number of cases of AKI in neonates admitted to the NICU in Northeast India. Maternal and neonatal factors like site of delivery, birth asphyxia, sepsis, umbilical catheter, mechanical ventilation, dehydration were identified as significant factors leading to AKI. Also, oliguria and elevated serum creatinine levels at the time of admission were found to be associated with the occurrence of AKI. Early diagnosis and timely intervention in AKI are critical, as mortality rates increased with severity, reaching 100% in Stage 3, while neonates without AKI had the highest survival rates.

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