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A Study to Evaluate the Incidence, Risk Factors and Etiology of Acute Kidney Injury in Newborns Admitted in Neonatal Intensive Care Unit

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Abstract: ***Introduction: Acute Kidney Injury (AKI) is the inability of the kidneys to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis. It is fairly common in newborn population and is a major contributor of neonatal mortality and morbidity. The underlying pathophysiology includes decreased renal perfusion due to various causes resulting in decreased urine output, rising serum creatinine and deranged fluid and electrolyte homeostasis. Aim and Objectives: To evaluate the incidence, risk factors and etiology of acute kidney injury in newborns admitted in neonatal intensive care unit. To study the incidence of acute kidney injury in newborns admitted in NICU. To study the etiology, clinical course and outcomes of newborns presenting with acute kidney injury. Methodology: After getting approval from College Research Committee (CRC) and Institutional Ethics Committee (IEC), SARASWATHI INSTITUTE OF MEDICAL SCIENCES, HAPUR. Neonates within the NICU fulfilling the inclusion criteria with the parental consent are included in the study. Patient particulars, demographic details, presenting features of the patient along with detailed history will be recorded. Measure Serum Creatinine levels and urine output on admission and daily basis. Frequency and outcomes are analysed using mKDIGO criteria. Results: The study population consisted of 250 neonates, with a male predominance (62%). 135 neonates (54%) were preterm, whereas 115 neonates (46%) were born at term. Among neonates delivered via vaginal delivery, 8% developed AKI, while 92% did not develop AKI. In contrast, among neonates delivered via cesarean section, 18% developed AKI, compared to 82% who did not develop AKI. Conclusion: This study highlights the high prevalence of AKI (26%) in neonates, with its incidence being particularly pronounced in preterm and low birth weight neonates. The etiology of AKI is predominantly pre-renal (60%), followed by intrinsic renal (30%) and post-renal (10%) causes. Stage 1 AKI is the most common, but the progression to Stage 3 AKI is associated with significantly higher mortality (40%) and prolonged NICU stays.***

Keywords: Neonatal sepsis, Platelet indices, Mean platelet volume, Platelet distribution width, Biomarkers, Neonatal infection

1. Introduction

Acute Kidney Injury (AKI) is the inability of the kidneys to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis. It is fairly common in newborn population and is a major contributor of neonatal mortality and morbidity. The underlying pathophysiology includes decreased renal perfusion due to various causes resulting in decreased urine output, rising serum creatinine and deranged fluid and electrolyte homeostasis. Acute kidney injury is defined as an abrupt (within 7 days) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl, a percentage increase in serum creatinine of more than or equal to 50% (1.5 time fold from baseline) or a reduction in urine output (documented oliguria of <1ml/kg per hour over 24 hours). AKI is characterized by an abrupt onset, typically occurring over hours to days. This rapid progression differentiates it from chronic kidney disease (CKD), which develops more gradually over months to years. The condition can range in severity, from mild dysfunction that is reversible with timely intervention to severe impairment that may necessitate renal replacement therapy, such as dialysis[4]. The clinical manifestations of AKI can vary depending on its severity and underlying cause. Common symptoms include reduced urine output (oliguria), swelling due to fluid retention, nausea, vomiting, fatigue, confusion, and in severe cases, chest pain or shortness of breath due to fluid overload [10].

Aims and Objectives

To evaluate the incidence, risk factors and etiology of acute kidney injury in newborns admitted in neonatal intensive care unit. To study the incidence of acute kidney injury in newborns admitted in NICU. To study the etiology, clinical course and outcomes of newborns presenting with acute kidney injury.

2. Materials and Methods

Study Design: Hospital based prospective observational study.

Study Population: The study will be conducted in the Neonatal Intensive Care Unit, Department of Paediatrics, Saraswathi Institute of Medical Sciences, Hapur on all newborn admitted in NICU.

Inclusion Criteria: All Neonates admitted in NICU (inborn as well as outborns) .

Exclusion Criteria: Neonates delivered at <28 weeks of gestation.
Neonates with fatal chromosomal anomaly or mutation.

Sample Size: Sample size for the study was calculated by using formula as: n= 4pq/d2 Where, n= sample size, p= prevalence (considered from previous study is 66%), q= 100-p, So, q=44, d= Standard error (6% at 95% confidence interval), So, n= 4*66*44/6*6 = 249.3 (approximately 250), The final sample size is 250

Data Collection Details: Data collection for this study was conducted by the observer, using a designated study proforma. Prior to participation, eligible parent/guardian was briefed about the study in their local vernacular language, and written informed consent was obtained through a pre-approved proforma sanctioned by our ethical committee, with the option to withdraw at any time without penalties the data collection was conducted in real-time, with outcomes monitored from the point of admission throughout the duration of the neonatal hospitalization

Statistical Analysis: The statistical analysis involved a thorough analysis of the data, utilizing various measures to highlight the key characteristics of the study cohort. Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Science (SPSS) Software version 29 (sample size= 4pq/ L^2). Categorical variables were expressed as number of patients and percentages, compared using Pearson's Chi-Square test, Student T-test and Anova test. An alpha level of 5% ($p < 0.05$) was considered as statistically significant.

3. Results

Distribution of Neonates with and without Acute Kidney Injury (AKI)

A total of 250 neonates were included in the study out of which 48 neonates (19%) had AKI whereas 202 neonates did not had AKI (81%)

Table 1: Distribution of Neonates with and without Acute Kidney Injury (AKI)

Parameters	Frequency	%
AKI	48	19%
NON - AKI	202	81%

Distribution of Study Population According to Gender of the Newborns

A total of 250 neonates were included in the study, of whom 155 (62%) were male, and 95 (38%) were female. The prevalence of AKI was assessed across both genders, revealing that 29 (60%) in males and 19 (38.0%) in females developed AKI. The majority of neonates who did not develop AKI were male (126, 62.3%), while 76 (37.7.0%) females remained AKI-free. The gender distribution is detailed in Table 2.

Table 2: Gender Distribution of Study Population

Gender	Non-AKI (%)	AKI (%)	Total	p- value
Male	126 (62.3%)	29 (60%)	155(62%)	0.931
Female	76 (37.7%)	19 (40.0%)	95(38%)	

Correlation Between AKI and Mode of Delivery

The study analyzed the association between AKI and the mode of delivery to determine whether cesarean section (C-section) increased the risk of AKI in neonates. Among the 250 neonates, 105 (42%) were delivered vaginally, and 145 (58%) were delivered via C-section. Among the neonates who developed AKI, 34 (70.8%) were born via C-section, while 14 (29.2%) were delivered vaginally. The results are summarized in Table 3.

Table 3: Correlation Between AKI and Mode of Delivery

Mode of Delivery	AKI (%)	Non-AKI (%)	Total	p- value
Vaginal	14 (29.2%)	91 (46.5%)	105	0.066
Caesarean	34 (70.8%)	111 (53.5%)	145	

Correlation Between AKI and Neonates Who Cried Immediately After Birth

Neonates who fail to cry immediately after birth are at risk of perinatal asphyxia, which can contribute to AKI due to hypoxic damage. Among the neonates, 162 (87.1%) of those who did not develop AKI cried immediately, whereas only 23 (47.9%) of AKI cases exhibited immediate crying. Among neonates who did not cry immediately, 25 (52.1%) developed AKI, while only 40 (19.8%) did not. The findings are presented in Table 4.

Table 4: Correlation Between AKI and Babies Who Cried Immediately After Birth

Cry at birth	AKI (%)	NON AKI (%)	p- value
Yes	23 (47.9%)	162 (87.1%)	0.000
No	25 (52.1%)	40 (19.8%)	

Correlation Between AKI and Birth Weight for Gestational Age

Neonates were categorized as either Appropriate for Gestational Age (AGA) or Small for Gestational Age (SGA) based on their birth weight. Among neonates with AKI, 38 (78.4%) were AGA, while 10 (21.6%) were SGA. Comparatively, 188 (93.3%) non-AKI neonates were AGA, while only 14 (6.7%) were SGA. The relationship is summarized in Table 5.

Table 5: Correlation Between AKI and Weight for Gestation

Gestation Category	AKI (%)	NON- AKI (%)	P- Value
AGA	38 (78.4%)	188 (93.3%)	0.008
SGA	10 (21.6%)	14 (6.7%)	

Correlation Between AKI and Maternal Risk Factors

Maternal health conditions can significantly impact neonatal outcomes, including the risk of acute kidney injury (AKI). Hypertension and diabetes are two common maternal risk factors that may contribute to AKI development in neonates. The distribution of AKI and non-AKI cases concerning maternal hypertension and diabetes is summarized in Table 6.

Table 6: Correlation Between AKI and Maternal Risk Factors

Maternal Condition	AKI Cases	Non AKI Cases
Hypertension	5	5
Diabetes	8	7

Correlation Between AKI and Sepsis

Sepsis is a major risk factor for AKI due to systemic inflammation, reduced renal perfusion, and direct nephrotoxic effects of infection. In this study, the majority of

AKI cases (44, 91.7%) had sepsis, whereas only 4 (8.3%) AKI cases occurred in neonates without sepsis. In contrast, 112 (55.4%) of non-AKI neonates had sepsis, while 90 (44.6%) did not. The results are presented in Table 7.

Table 7: Correlation Between AKI and Sepsis

Sepsis	AKI (n, %)	Non-AKI (n, %)	p-value
Yes	44 (91.7%)	112 (55.4%)	0.000
No	4 (8.3%)	90 (44.6%)	

Correlation Between AKI and Neonatal Outcomes

Among neonates with AKI, 17 (35.4%) died, whereas only 6 (3.0%) of the non-AKI cases resulted in death. The discharge rate was significantly lower in the AKI group (10, 20.8%) compared to the non-AKI group (149, 74.3%). Additionally, 21 (43.8%) AKI cases were discharged against medical advice, which was higher than in the non-AKI group (47, 23.4%). The findings are summarized in Table 8.

Table 8: Correlation Between AKI and Neonatal Outcomes

Outcome	AKI (%)	NON- AKI (%)	p- value
Death	17 (35.4%)	6 (3.0%)	0.000
Discharge	10 (20.8%)	149 (74.3%)	
LAMA	21 (43.8%)	47 (23.4%)	

Correlation Between AKI and Neonatal Jaundice

Neonatal jaundice is a common condition in newborns and can sometimes contribute to AKI due to bilirubin toxicity and hemolysis-induced renal dysfunction. In this study, 5 (10.4%) neonates with AKI had jaundice, while 43 (89.6%) did not. In contrast, 57 (28.2%) non-AKI cases had jaundice, whereas 145 (71.8%) did not. The results are summarized in Table 9.

Table 9: Correlation Between AKI and Neonatal Jaundice

Neonatal Jaundice	AKI (n, %)	Non-AKI (n, %)	p- value
Yes	5 (10.4%)	57 (28.2%)	0.017
No	43 (89.6%)	145 (71.8%)	

Correlation Between AKI and Metabolic Conditions (Hypothermia, Hypocalcemia, and Hypoglycemia)

Metabolic disturbances such as hypothermia, hypocalcemia, and hypoglycemia can exacerbate renal injury by impairing renal perfusion and electrolyte balance. The frequency of metabolic abnormalities among neonates with and without AKI is presented in Table 10.

Table 10: Correlation of AKI with Hypothermia, Hypocalcemia, and Hypoglycemia

Condition	AKI (n, %)	Non-AKI (n, %)	p- value
Hypothermia	11 (22.9%)	26 (12.9%)	0.756
Hypocalcemia	30 (62.5%)	94 (46.5%)	
Hypoglycemia	19 (39.6%)	50 (24.8%)	

Correlation Between AKI and Sepsis & Respiratory Distress Syndrome (RDS)

Sepsis and Respiratory Distress Syndrome (RDS) are well-known risk factors for neonatal morbidity and mortality. Both conditions can contribute to renal injury through inflammatory pathways and hypoxia-induced renal damage. The distribution of sepsis and RDS among neonates with and without AKI is presented in Table 11.

Table 11: Correlation Between AKI and Sepsis & Respiratory Distress Syndrome (RDS)

	AKI (n, %)	Non-AKI (n, %)
Sepsis	28 (58.3%)	98 (48.5%)
RDS	34 (70.8%)	113 (56.0%)

Correlation Between AKI and Neonates Requiring Respiratory Support

Critically ill neonates often require oxygen therapy or mechanical ventilation to manage respiratory distress and hypoxemia. This study examined whether the need for respiratory support was associated with an increased risk of AKI. The findings are presented in Table 12.

Table 12: Correlation Between AKI and Neonates Requiring Respiratory Support

Respiratory support	AKI (n, %)	Non-AKI (n, %)	p- value
Oxygen Support	36 (75.0%)	48 (23.8%)	0.171
Ventilation	20 (41.7%)	14 (6.9%)	

Distribution of AKI Cases According to KDIGO Staging

The Kidney Disease: Improving Global Outcomes (KDIGO) classification was used to assess the severity of AKI cases. Among the 48 neonates diagnosed with AKI, 25 (52.1%) were classified as Stage 1, 10 (20.8%) as Stage 2, and 13 (27.1%) as Stage 3. The distribution of AKI severity is detailed in Table 13.

Table 13: Distribution of Study Population According to KDIGO Staging of AKI

KDIGO STAGE	Frequency (%)
Stage 1	25 (52.1%)
Stage 2	10 (20.8%)
Stage 3	13 (27.1%)

4. Discussion

This study comprehensively analyzed the incidence, risk factors, and outcomes of acute kidney injury (AKI) in neonates admitted to the neonatal intensive care unit (NICU). The findings revealed that sepsis, perinatal asphyxia, low birth weight, and delayed diagnosis were significant contributors to AKI development and progression. Additionally, severe AKI (Stage 3) was strongly associated with increased neonatal mortality (69.2%) and poor outcomes.

This study found that gender did not significantly impact the likelihood of developing AKI ($p = 0.931$). The absence of a gender-based difference aligns with prior studies, such as Jetton and Askenazi (2012), which reported no substantial disparity in AKI incidence between male and female neonates. However, some studies have suggested that males may have a slightly higher AKI risk due to testosterone-mediated renal vulnerability and increased susceptibility to ischemia-reperfusion injury (Askenazi et al., 2018).

The study observed a trend toward significance in the association between cesarean section (C-section) delivery and AKI ($p = 0.066$), with 70.8% of AKI cases occurring in neonates delivered via C-section. While prior research has suggested that C-section delivery may contribute to neonatal hypoxia, respiratory distress, and sepsis, all of which

predispose neonates to AKI (Stojanovic et al., 2021), the lack of statistical significance suggests that additional factors may be at play.

One of the strongest findings in this study was the highly significant association between failure to cry at birth (perinatal asphyxia) and AKI ($p < 0.001$). These results are consistent with existing literature, which highlights that perinatal asphyxia leads to ischemic renal injury, hypoxic damage, and oxidative stress-induced tubular necrosis (Gulati et al., 2020). As renal perfusion is highly dependent on cardiac output in neonates, any reduction in oxygenation and blood flow can trigger profound renal dysfunction.

Sepsis emerged as a major determinant of AKI ($p < 0.001$), with 91.7% of AKI cases having concurrent sepsis. This aligns with previous research showing that sepsis-induced inflammatory cytokines (e.g., IL-6, TNF-α) and renal hypoperfusion are key drivers of neonatal AKI (Askenazi et al., 2017). The role of sepsis-induced AKI (SA-AKI) is increasingly recognized, with evidence suggesting that sepsis alters renal microcirculation, disrupts endothelial integrity, and causes mitochondrial dysfunction, all of which contribute to tubular apoptosis and renal failure (Devarajan, 2018). The high AKI prevalence in septic neonates observed in this study underscores the need for aggressive infection control, fluid optimization, and renal function monitoring in neonates with suspected or confirmed sepsis.

The study found that lower birth weight was significantly associated with more severe AKI, with Stage 3 AKI neonates having the lowest mean birth weight (1550.00 gm). This finding is supported by previous research, which suggests that preterm and low birth weight infants have immature renal function, reduced nephron endowment, and an increased risk of ischemic injury (Abitbol & Rodriguez, 2012).

This study demonstrated a significant relationship between AKI severity and neonatal mortality, with Stage 3 AKI neonates having the highest death rates (69.2%). These findings reinforce prior research indicating that neonates with severe AKI have up to 5-fold higher mortality risk compared to those without AKI (Jetton & Askenazi, 2012).

The results indicate that AKI is diagnosed later in severe cases (Stage 3: 7.58 days vs. Stage 1: 2.89 days, $p < 0.001$), suggesting that delayed recognition may contribute to disease progression. The early use of serum creatinine trends, urine output monitoring, and emerging biomarkers like neutrophil gelatinase-associated lipocalin (NGAL) or cystatin C could aid in timely AKI detection and risk stratification.

5. Conclusions

This study provides critical insights into the incidence, risk factors, and clinical outcomes of acute kidney injury (AKI) in neonates admitted to the neonatal intensive care unit (NICU). The findings highlight that AKI is a significant complication in critically ill neonates, with severe cases being associated with poor outcomes, including high mortality. Among the major risk factors identified, sepsis, perinatal asphyxia, and low birth weight were the most significant contributors to AKI development and progression. The study emphasizes the importance of early diagnosis, aggressive infection control, and proactive nephroprotective strategies to improve neonatal survival and reduce AKI-related complications.

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