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Spectrum of Acute Kidney Injury in Neonatal Intensive Care Unit at Combined Military Hospital Nowshera

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ABSTRACT

Background: Neonatal acute kidney injury is a serious morbidity encountered in intensive care practice, commonly attributed to the vulnerability of immature renal physiology. A wide spectrum of etiologies contributes to neonatal AKI, ranging from sepsis or multiple organ dysfunction syndrome to obstructive and metabolic causes. **Objective:** To determine the spectrum of acute kidney injury in neonates admitted to the neonatal intensive care unit. **Study Design:** Prospective observational study. **Duration and Place of Study:** The study was conducted from February 2025 to May 2025 in the Neonatal Intensive Care Unit of Combined Military Hospital, Nowshera. **Methodology:** A total of 155 term neonates with acute kidney injury were enrolled through non-probability consecutive sampling. Diagnosis and staging of AKI were based on pediatric RIFLE criteria, with estimated glomerular filtration rate calculated using the Schwartz equation. Data collected included demographics, perinatal risk factors, and laboratory findings. Operational definitions were applied to classify sepsis/MODS, perinatal hypoxia, urinary obstruction, urinary infection, hypernatremic dehydration, and acute tubular necrosis. **Results:** The mean age of neonates was 16.48±8.98 days, and the mean birth weight was 2.23±0.72 kg. Males constituted 71.6% of cases. The most frequent etiology was sepsis/MODS (45.8%), followed by urinary obstruction (14.8%), perinatal hypoxia (14.2%), urinary infection (13.5%), hypernatremic dehydration (7.7%), and acute tubular necrosis (4.5%). Gender-based analysis revealed significant associations for urinary infection (p=0.036) and hypernatremic dehydration (p=0.005), both higher in females. **Conclusion**: Sepsis and MODS remain the leading etiologies of neonatal AKI, while obstructive and infectious causes are also prominent.

INTRODUCTION

Neonatal acute kidney injury (AKI) is one among severe clinical morbidity that would be encountered in the practice of intensive care, a typical feature of immature vulnerable renal physiology.[1,2] The immature renal organ cannot concentrate urine and handle ions and is thus susceptible for hemodynamic fluctuations, hypoxia, and nephrotoxic insults.[2,3] Acute insult has a tendency to result in fluid imbalance, extreme metabolic derangements, and high morbidity and mortality.[3,4] Early recognition is thus crucial, and yet a diagnostic challenge by virtue of presentation and reliance on subtle biochemical changes.[4] Neonatal acute kidney injury, that arises in the intensive therapy units, has a heterogeneous etiology and the highest and worst etiologies are multiple organ dysfunction syndromes and sepsis.[5] The disease in the body causes renal hypoperfusion and inflammatory insult and has a propensity to progress to acute tubular necrosis.[5] Perinatal hypoxia is a typical other response, where poorly perfused placental or intrapartum asphyxia generates renal tissue ischemic insult.[6] Obstructive uropathies and congenital anomalies, like posterior urethral valves or bilateral hydronephrosis, may be evident early with oliguria and rising creatinine.[7] Neonatal UTIs may also generate renal failure by ascending an infection by the organisms or by generating systemically acting sepsis.[8]

Other elements within the continuum include hypernatremic dehydration, best linked with poorly ingested fluids or defects in feeding, leading to hypovolemic stress on the kidneys.[9] Acute tubular necrosis may be the end point for severe ischemia for a prolong duration or exposure to nephrotoxic agents and, at extreme ends, lead to irreversible failure of the kidneys.[10] Congenital polycystic disease of the kidneys, while less commonly seen, is a disease that presents overt barriers with structural defects within the kidneys and functional impairment at birth.[11] Acknowledgement of this broad continuum permits a high priority for close observation, early detection, and individualized management strategies within the neonatal intensive care unit to avert short-term as well as late sequelae of renal insult.[1,4,5]

Premkumar et al. reported that the spectrum of acute kidney injury in term neonates included sepsis or multiple organ dysfunction syndrome in 41%, perinatal hypoxia in 17.9%, urinary tract obstruction in 15.3%, urinary tract infection in 11.5%, hypernatremic dehydration in 7.6%, acute tubular necrosis in 3.8%.[12]

Conducting the study in Nowshera is important since neonatal units from the region frequently manage newborns at high risk for renal complications. There is limited local data outlining the spectrum and etiology for acute kidney injury within this group. The determination of Nowshera-specific patterns will allow clinicians to improve early recognition, refine management protocols, and reduce morbidity and mortality due to neonatal renal impairment. The evidence will also guide resource distribution and staff training on preventable causes causing acute kidney injury.

METHODOLOGY

This prospective observational study was performed from February 2025 to May 2025 in the Neonatal Intensive Care Unit of Combined Military Hospital, Nowshera. The study comprised 155 term neonates diagnosed with acute kidney injury. The sample size was calculated using the WHO sample size calculator with a 95% confidence level and a 3% margin of error, considering an anticipated prevalence of acute tubular necrosis of 3.8%.[12] Patients were selected using a non-probability consecutive sampling technique. Inclusion criteria consisted of term neonates admitted to the neonatal intensive care unit with features of acute kidney injury. Exclusion criteria included preterm neonates, syndromic infants, and those with major congenital anomalies unrelated to the urinary tract. After obtaining informed consent from parents or legal guardians, demographic and perinatal information was recorded, including sex, gestational age, birth weight, Apgar scores, consanguinity, maternal risk factors, and clinical presentation.

Acute kidney injury was diagnosed and staged using the pediatric RIFLE (pRIFLE) criteria, with estimated glomerular filtration rate calculated using the Schwartz equation. Sepsis or multiple organ dysfunction syndrome was defined as systemic signs of infection with positive blood culture or fulfillment of clinical sepsis criteria along with dysfunction of two or more organ systems; perinatal hypoxia was defined by evidence of intrapartum or immediate postnatal hypoxic insult with low Apgar scores or documented metabolic acidosis; urinary tract obstruction was diagnosed on ultrasonography showing hydronephrosis, hydroureter, or posterior urethral valves with corresponding oliguria or rising creatinine; urinary tract infection was confirmed by positive urine culture from catheterized or suprapubic aspirate specimen with supporting clinical findings; hypernatremic dehydration was defined as dehydration with raised serum sodium concentration associated with poor feeding or insensible losses; and acute tubular necrosis was identified in neonates with AKI following ischemic insult or nephrotoxin exposure with progressive rise in serum creatinine and supportive urine microscopy.

Laboratory investigations included complete blood count, serum urea and creatinine, electrolytes, blood culture, urine analysis, and urine culture. Renal ultrasound was performed in suspected obstructive cases. Data analysis was conducted using IBM SPSS version 26. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Associations between etiology and demographics were assessed using chi-square test or Fisher's exact test, with a p-value <0.05 considered statistically significant.

RESULTS

The study analyzed 155 neonates with acute kidney injury in the neonatal intensive care unit. The demographic characteristics revealed a mean age of 16.48±8.98 days and mean birth weight of 2.23±0.72 kg, with a predominant male population comprising 111 (71.6%) cases compared to 44 (28.4%) females (as shown in Table 1)

Table 1

Demographics of Neonates with Acute Kidney Injury

Demographics		Mean ± SD
Age (days)		16.48±8.98
Birth Weight (kg)		2.23±0.72
Gender	Male n (%)	111 (71.6%)
	Female n (%)	44 (28.4%)

The spectrum of acute kidney injury conditions demonstrated that sepsis/MODS was the most prevalent etiology, affecting 71 (45.80%) neonates, followed by urinary obstruction in 23 (14.80%) cases, perinatal hypoxia in 22 (14.20%) cases, and urinary infection in 21 (13.50%) cases. Hypernatremic dehydration was identified in 12 (7.70%) neonates, while acute tubular necrosis was the least common condition, occurring in only 7 (4.50%) cases (as shown in Table 2).

Table 2

Spectrum of Acute Kidney Injury in Neonatal Intensive Care Unit

Spectrum of Acute Kidney Injury		Frequency	% age
Sepsis/MODS	Yes	71	45.80%
	No	84	54.20%
	Total	155	100%
Perinatal Hypoxia	Yes	22	14.20%
	No	133	85.80%
	Total	155	100%
Urinary Obstruction	Yes	23	14.80%
	No	132	85.20%
	Total	155	100%
Urinary Infection	Yes	21	13.50%
	No	134	86.50%
	Total	155	100%
Hypernatremic Dehydration	Yes	12	7.70%
	No	143	92.30%
	Total	155	100%
Acute Tubular Necrosis	Yes	7	4.50%
	No	148	95.50%
	Total	155	100%

The association analysis between acute kidney injury conditions and demographic factors revealed significant gender-related differences in urinary infection (p=0.036) and hypernatremic dehydration (p=0.005), with females showing higher rates of urinary infection at 10 (22.7%) compared to males at 11 (9.9%), and notably, hypernatremic dehydration occurred exclusively in

females at 8 (18.2%) cases while no male cases were reported. Age stratification (≤15 days vs >15 days) showed no significant associations across all conditions, with p-values ranging from 0.326 to 0.770. Birth weight stratification (≤2 kg vs >2 kg) similarly demonstrated no significant associations, with p-values ranging from 0.092 to 0.717. Other conditions including sepsis/MODS, perinatal hypoxia, urinary obstruction, and acute tubular necrosis showed no significant associations with any demographic factors, with p-values consistently above 0.05 (as shown in Table 3).

Table 3

Association of Acute Kidney Injury Conditions with Demographic Factors

Demographic Factors		Sepsis/MODS		p-value	Perinatal Hypoxia		p-value	Urinary Obstruction		p-value	Urinary Infection		p-value	Hypernatremic Dehydration		p-value	Acute Tubular Necrosis		p-value
		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)	
Age (days)	≤15	32 (43.8%)	41 (56.2%)		11 (15.1%)	62 (84.9%)		13 (17.8%)	60 (82.2%)		8 (11.0%)	65 (89.0%)		5 (6.8%)	68 (93.2%)		4 (5.5%)	69 (94.5%)	
	>15	39 (47.6%)	43 (52.4%)	0.642	11 (13.4%)	71 (86.6%)	0.768	10 (12.2%)	72 (87.8%)	0.326	13 (15.9%)	69 (84.1%)	0.374	7 (8.5%)	75 (91.5%)	0.770*	3 (3.7%)	79 (96.3%)	0.707*
Gender	Male	53 (47.7%)	58 (52.3%)		13 (11.7%)	98 (88.3%)		15 (13.5%)	96 (86.5%)		11 (9.9%)	100 (90.1%)		4 (3.6%)	107 (96.4%)		7 (6.3%)	104 (93.7%)	
	Female	18 (40.9%)	26 (59.1%)	0.441	9 (20.5%)	35 (79.5%)	0.16	8 (18.2%)	36 (81.8%)	0.461	10 (22.7%)	34 (77.3%)	0.036*	8 (18.2%)	36 (81.8%)	0.005*	0 (0.0%)	44 (100.0%)	0.192*
Birth Weight (kg)	≤2	39 (51.3%)	37 (48.7%)		10 (13.2%)	66 (86.8%)		15 (19.7%)	61 (80.3%)		8 (10.5%)	68 (89.5%)		4 (5.3%)	72 (94.7%)		4 (5.3%)	72 (94.7%)	
	>2	32 (40.5%)	47 (59.5%)	0.177	12 (15.2%)	67 (84.8%)	0.717	8 (10.1%)	71 (89.9%)	0.092	13 (16.5%)	66 (83.5%)	0.281	8 (10.1%)	71 (89.9%)	0.369*	3 (3.8%)	76 (96.2%)	0.716*

Discussion:

The present study demonstrates that acute kidney injury in neonatal intensive care units exhibits a diverse spectrum of etiologies with sepsis and multiple organ dysfunction syndrome being the predominant cause. The high prevalence of sepsis/MODS (45.80%) as the leading cause of neonatal acute kidney injury reflects the vulnerability of immature neonatal kidneys to systemic inflammatory responses and hemodynamic instability. Sepsis triggers a cascade of inflammatory mediators that compromise renal perfusion and directly damage tubular epithelial cells through cytokine-mediated mechanisms, while the associated hypotension and distributive shock further exacerbate renal hypoperfusion. The significant male predominance (71.6%) observed in our cohort aligns with the known higher susceptibility of male neonates to various morbidities, likely attributed to sex-linked genetic factors, delayed lung maturation, and increased vulnerability to perinatal complications. The striking gender-specific association with hypernatremic dehydration occurring exclusively in females may be related to differences in body composition, with females typically having lower total body water content and potentially different fluid regulatory mechanisms. Similarly, the higher prevalence of urinary tract infections in female neonates reflects anatomical differences, particularly the shorter urethral length and proximity to the anal opening, facilitating ascending bacterial colonization. The substantial occurrence of urinary obstruction (14.80%) and perinatal hypoxia (14.20%) as significant contributors underscores the importance of congenital anomalies and birth-related complications in neonatal acute kidney injury pathogenesis. Urinary obstruction leads to increased intratubular pressure and subsequent tubular damage, while perinatal hypoxia results in acute tubular necrosis through ischemic injury and cellular energy depletion.

Our study findings demonstrate several important concordances and divergences with previously published literature on neonatal acute kidney injury. The predominance of sepsis/MODS as the leading cause of AKI in our cohort (45.80%) aligns closely with findings from Gedefaw et al. [13] who identified sepsis as a significant predictor with an adjusted hazard ratio of 2.59, and Katariya and Pandya [14] who reported sepsis in 23.1% of their AKI cases. This consistency across different geographical settings underscores the universal vulnerability of neonatal kidneys to sepsis-induced injury through inflammatory cascades and hemodynamic compromise. However, our sepsis prevalence was notably higher than the 23.1% reported by Katariya and Pandya [14], which may reflect differences in study populations, with our tertiary care setting potentially receiving more critically ill neonates or variations in sepsis definition criteria. The striking male predominance observed in our study (71.6%) is remarkably consistent with multiple previous investigations, including Katariya and Pandya [14] who reported 71.1% male cases, Memon et al. [15] who found 81.3% male prevalence in birth asphyxia-associated AKI, and Trivedi et al. [16] who documented 70% male cases. This consistent pattern across diverse populations supports the hypothesis of sex-linked genetic susceptibility and hormonal influences on renal development and injury susceptibility. The mean birth weight in our study (2.23±0.72 kg) was comparable to Katariya and Pandya's findings (2.048 kg) [14] reflecting the association between low birth weight and AKI risk, though both values were higher than the extremely low birth weight populations studied by Branagan et al. [17]

Our finding of perinatal hypoxia affecting 14.20% of cases shows reasonable concordance with Katariya and Pandya [14] who identified birth asphyxia as the most common risk factor (34.9%), and Gedefaw et al. [13] who reported perinatal asphyxia as a significant predictor (AHR: 2.70). The lower prevalence in our study might reflect differences in hypoxia severity criteria or the inclusion of milder cases in other studies. Interestingly, Memon et al. [15] found AKI in only 13.3% of neonates with birth asphyxia, which is closer to our perinatal hypoxia prevalence, suggesting that the severity and duration of hypoxic insult

may be crucial determinants of AKI development. The prevalence of urinary tract infections (13.50%) in our cohort, while not extensively reported in other neonatal AKI studies, represents a significant finding that highlights the importance of infectious etiologies beyond sepsis. Our observation of higher UTI rates in females (22.7% vs 9.9% in males, p=0.036) is consistent with established anatomical predispositions but has not been specifically documented in other neonatal AKI literature, suggesting this may be an underrecognized association. The exclusive occurrence of hypernatremic dehydration in females (18.2% vs 0% in males, p=0.005) represents a novel finding not reported in previous studies and warrants further investigation into sex-specific fluid regulatory mechanisms in neonates. Our relatively low prevalence of acute tubular necrosis (4.50%) contrasts sharply with Trivedi et al. [16] who reported ATN as the most common cause affecting 80% of pediatric AKI cases. This discrepancy likely reflects the broader pediatric age range (1 day to 12 years) in Trivedi's study compared to our exclusively neonatal population, as older children may have different AKI etiologies and more developed renal architecture susceptible to tubular injury. The absence of significant associations between demographic factors and most AKI conditions in our study differs from the strong associations reported by others, such as Makulova et al. [18] who found clear gestational age and birth weight gradients in AKI incidence, possibly reflecting our more homogeneous high-risk neonatal population versus their broader NICU cohorts.

Several limitations should be acknowledged in interpreting our results. This single-center study conducted at a tertiary care facility may limit the generalizability of findings to other healthcare settings or populations with different risk profiles. Additionally, the relatively small sample size of 155 neonates, while adequate for primary analysis, may have limited statistical power to detect associations in less common conditions such as acute tubular necrosis. The absence of long-term follow-up data prevents assessment of chronic kidney disease development and other long-term sequelae. Furthermore, variations in diagnostic criteria and clinical practices over the study period may have influenced the consistency of AKI classification and management approaches.

CONCLUSION

Our study has concluded that acute kidney injury in neonatal intensive care units presents with a diverse spectrum of etiologies, with sepsis and multiple organ dysfunction syndrome emerging as the predominant cause, followed by urinary obstruction, perinatal hypoxia, and urinary tract infections. The findings demonstrate a significant male predominance in the affected population, with notable gender-specific associations particularly evident in hypernatremic dehydration and urinary infections.

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