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ORIGINAL ARTICLE

Incidence and risk factors of acute kidney injury in term neonates.

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ABSTRACT… Objective: To determine the incidence and risk factors of acute kidney injury in term neonates. **Study Design:** Prospective Observational study. **Setting:** Neonatal Intensive Care Unit (NICU) of National Institute of Child Health, Karachi, Pakistan. **Period:** October 2024 to March 2025. **Methods:** A total of 190 neonates suspected to have AKI and admitted to the NICU were enrolled. The development of AKI during the study or discharge from the NICU was noted. Risk factors of AKI were also evaluated. Multivariate binary logistic regression analysis was performed for the determination of risk factors associated with the development of AKI in neonates taking p<0.05 as statistically significant. **Results:** Among 190 term neonates, 104 (54.7%) were male, and the mean age at admission was 2.92±1.89 days. There were 72 (37.9%) neonates who developed AKI, with stage 1 in 58.3%, stage 2 in 26.4%, and stage 3 in 15.3%. Mortality was higher in the AKI group (11.1% vs. 3.4%, p=0.035). Multivariate logistic regression identified maternal diabetes (adjusted odds ratio [aOR]: 3.22), pregnancy-induced hypertension (aOR: 2.85), IUGR (aOR: 3.75), and longer NICU stay (aOR per day: 1.16) as independent risk factors for AKI. Mortality was significantly high in AKI neonates (11.1% vs. 3.4%, p=0.035). **Conclusion:** This study demonstrated a high incidence of AKI among term neonates, with maternal diabetes, pregnancy-induced hypertension, maternal infection, IUGR at birth, and prolonged NICU stay identified as significant and independent risk factors.

Key words: Acute Kidney Injury, Maternal Diabetes, Mortality, NICU, Pregnancy Induced Hypertension.

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INTRODUCTION

In the neonatal intensive care unit (NICU) population, acute kidney injury (AKI) is highly prevalent, affecting all gestational groups, and is linked to substantial morbidity and mortality.[1-4] According to reports, neonatal AKI increases hospital stays, which raises healthcare costs drastically, exerting an extraordinary burden on nations with low-income economies.[5] The kidneys of newborns are not as developed as those of older children, making them more vulnerable to AKI.[6,7] According to several studies, the occurrence of neonatal AKI ranges between 18% and 70%.[8-12]

Different diagnostic criteria in newborns are employed, owing to which neonatal AKI presents a diversity in its occurrence, and these are difficult to follow in premature newborns as well.[13-16] Neonatal AKI can now be diagnosed with greater precision through the KDIGO modified diagnostic and classification criteria, which are based on quantitative changes in serum creatinine levels and/or a decrease in urine output.[17-21]

The rising sepsis prevalence and lack of awareness regarding neonatal AKI emphasize the need to evaluate incidence and associated risk factors.[18] In Pakistan, not much of the research has been done on AKI, more specifically on neonatal AKI, focusing on its prevalence, risk factors, and outcomes in various populations. This study was planned to determine the incidence and risk factors of AKI in term neonates. The findings of this study would not only add to the existing literature on the subject from Pakistani settings but also help clinicians improve diagnosis, prevent progression, intervene earlier, and better manage fluid balance in achieving improved long-term outcomes for neonates who experience AKI.

METHODS

This prospective observational study was conducted at the Neonatal Intensive Care Unit, National Institute of Child Health, Karachi, Pakistan, from October 2024 to March 2025 after achieving authorization from the Ethics Committee of the institution (letter

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number: IERB-21/2024). A sample size of 190 was calculated considering the anticipated frequency of AKI in neonates with gestational age >36 weeks as 41%[12], using a 95% confidence interval and a precision of 7%. The inclusion criteria were neonates with gestational age > 37 weeks and admitted to the NICU. All patients born within the hospital premises showing manifestation for AKI screening were enrolled into the study. Patients with urinary retention, dehydration, abnormal serum creatinine values at birth, and those requiring nutritional support through intravenous fluids were considered. The exclusion criteria were patients with <48 hours of stay in the NICU. Patients with lethal chromosomal anomalies, major kidney malformations, or those undergoing cardiac surgery within the first week of birth were also excluded. Sample selection was done employing a non-probability consecutive sampling technique. Parents/caregivers were briefed about the objective and safety of the study to take their consent to enroll their patients into the study. Demographic details of neonates like gender, age, and gestational age were noted. Maternal characteristics like maternal diabetes, pregnancy-induced hypertension, maternal infections at or near the time of delivery, and intrauterine growth restriction (IUGR) at birth were recorded. All neonates were treated as per the hospital protocol. AKI was defined and staged based on KDIGO criteria.[17]

The data was analyzed using "IBM-SPSS Statistics" version 26.0. The numerical variables were presented as mean and standard deviation (SD). The categorical variables were summarized through frequencies with percentages. The chi-square or the Fisher's exact test was applied to compare categorical variables. Numerical variables were compared using the independent t-test. Binary logistic regression was applied to determine factors associated with AKI, and adjusted odds ration (aOR) with 95% confidence interval (CI) was calculated. A p-value ≤0.05 was taken as statistically significant.

RESULTS

In a total of 190 term neonates, 104 (54.7%) were male, and 86 (45.3%) female. The mean age at admission was 2.92±1.89 days. Maternal diabetes was documented in 22 (11.6%) cases, pregnancy-induced hypertension in 18 (9.5%), and maternal infection in 28 (14.7%) cases. The incidence of AKI was noted in 72 (37.9%) neonates. According to the KDIGO criteria, 42 (58.3%) of the affected neonates had stage 1 AKI, 19 (26.4%) had stage 2, and 11 (15.3%) had stage 3. The duration of NICU stay was significantly longer in neonates with AKI (13.12±5.62 vs. 8.87±3.62 days, p<0.001). Maternal diabetes (22.2% vs. 5.1%, p<0.001), pregnancy-induced hypertension (16.7% vs. 4.2%, p=0.004), and maternal infection at or near delivery (25.0% vs. 8.5%, p=0.002) were significantly more frequent among neonates who developed AKI. IUGR at birth was more common in neonates who developed AKI (p=0.001). Table-1 is showing association of AKI in neonates with neonatal and maternal characteristics.

TABLE-I

Association of AKI with neonatal and maternal characteristics

Variables		Acute Kidney Injury		P-Value
		Yes (n=72)	No (n=118)	
Gender	Male	38 (52.8%)	66 (55.9%)	0.672
	Female	34 (47.2%)	52 (54.1%)	
Age at admission (days)		2.82±2.14	3.06±1.75	0.401
Gestational age (weeks)		38.01±1.25	38.28±1.03	0.217
Birth weight (kg)		2.65±0.35	2.73±0.31	0.102
NICU stay (days)		13.12±5.62	8.87±3.62	<0.001
Maternal diabetes		16 (22.2%)	6 (5.1%)	<0.001
Pregnancy induced hypertension		12 (16.7%)	5 (4.2%)	0.004
Maternal history of infection		18 (25.0%)	10 (8.5%)	0.002
Intrauterine growth restriction at birth		12 (16.7%)	4 (3.4%)	0.001

The stage of AKI at diagnosis was associated with both length of stay and risk factor burden, with stage 3 neonates having the longest median duration of NICU admission (median 15 days, IQR: 11–19). Of the 72 neonates with AKI, 6 (8.3%) required renal replacement therapy. Mortality was reported in 8 (11.1%) neonates with AKI in comparison to 4 (3.4%) neonates without AKI (p=0.035). Multivariate logistic regression identified maternal

diabetes (aOR:3.22, 95% CI:1.41–7.34, p=0.005), pregnancy-induced hypertension (aOR:2.85, 95% CI:1.09–7.47, p=0.032), IUGR at birth (aOR:3.75, 95% CI:1.16–12.16, p=0.027), and longer duration of NICU stay (aOR per day:1.16, 95% CI:1.07–1.26, p<0.001) as independent risk factors for AKI (Table-II).

TABLE-II

Multivariate logistic regression analyzing risk factors of AKI

Variables	Adjusted Odds Ratio	95% Confidence Interval (Lower-Upper)	P-Value
Maternal diabetes	3.22	1.41-7.34	0.005
Pregnancy induced hypertension	2.85	1.09-7.47	0.032
Maternal infection	2.31	1.01-5.27	0.048
Intrauterine growth restriction at birth	3.75	1.16-12.16	0.027
NICU stay (per day increase)	1.16	1.07-1.26	<0.001

DISCUSSION

The overall incidence of AKI was relatively high in the present study (37.9%). Agarwal et al.[22], through the Indian multicenter TINKER registry, reported an AKI incidence of approximately 26.6%. Farhadi et al.[23], in Iran observed a 26.6% prevalence of AKI, suggesting that geographic, ethnic, and healthcare system differences, along with varying inclusion criteria and AKI definitions, can influence observed rates. In contrast, Gedefaw et al.[24], in a study from Ethiopia, documented an incidence of 20.2% among NICU neonates, employing both clinical and laboratory definitions. The higher incidence in the current cohort may be attributed to a combination of rigorous screening, heightened surveillance for subtle changes in renal function, and possibly the burden of underlying maternal conditions common in the Pakistani population.

Stratification of AKI severity revealed that most affected neonates in this study experienced stage 1 AKI (58.3%). Farhadi et al.[23], reported relatively equal distribution among AKI stages but with a predominance of prerenal cases. The slightly higher proportion of stage 1 AKI may reflect early detection and intervention strategies implemented at the study center, as well as heightened clinical vigilance due to the use of standardized KDIGO criteria. In the TINKER registry.[22], and Rutledge et al.[25], a similar trend toward higher rates of mild AKI was observed, suggesting that improved diagnostic protocols globally are leading to earlier diagnosis, though the burden of severe AKI persists.

Maternal diabetes was present in 22.2% of AKI cases compared to 5.1% in non-AKI neonates. This association has been documented previously, where the metabolic and vascular effects of maternal hyperglycemia predispose neonates to compromised renal perfusion and glomerular injury.[26] Gedefaw et al.[24], similarly identified maternal and perinatal comorbidities as key predictors of AKI, while Agarwal et al.[22], and Farhadi et al.[23], also highlighted maternal diabetes and hypertension as recurrent risk factors in their respective cohorts. In the present study, pregnancy-induced hypertension was present in 16.7% of AKI neonates versus 4.2% in non-AKI neonates (aOR: 2.85, 95% CI: 1.09–7.47). This observation reinforces the importance of optimizing maternal health and antenatal care to mitigate preventable neonatal complications. Maternal infection at or near delivery was another significant risk factor, identified in 25.0% of AKI cases compared to 8.5% in non-AKI neonates (p=0.002). Infection-related inflammatory responses and sepsis are known contributors to renal hypoperfusion and direct nephrotoxic injury.[27] Gedefaw et al.[24], found that neonatal sepsis was an independent predictor of AKI, consistent with global trends in NICU populations. The high prevalence of perinatal infection underscores the need for infection prevention protocols, timely diagnosis, and appropriate antimicrobial therapy in perinatal and neonatal care settings.[25]

This study showed significant association between longer duration of NICU stay and the risk of AKI, with an aOR of 1.16 per additional day of admission (p<0.001). Rutledge et al.[25], observed that recurrent AKI (rAKI) in neonates was associated with prolonged hospitalization, with a median length of stay more than threefold higher than those without AKI. This relationship may reflect both the increased severity of illness among neonates developing AKI and the contribution of iatrogenic factors such as

nephrotoxic medications, invasive procedures, and nosocomial infections. The present study also explored the outcomes associated with AKI in the neonatal period. The requirement for renal replacement therapy was documented in 8.3% of neonates with AKI, a figure broadly consistent with previous cohorts reporting 5–15% rates of dialysis or hemofiltration in severe cases. In-hospital mortality among neonates with AKI was 11.1% (p=0.035). This increased mortality risk echoes the findings of El-Badawy et al.[28], who reported a threefold increase in mortality among AKI cases, and Alayed et al.[29], who found that AKI contributed to prolonged PICU stays, resource utilization, and increased case fatality. Gedefaw et al.[24], in their study found that neonates with perinatal asphyxia and sepsis demonstrated increased mortality rates, further substantiating the life-threatening nature of neonatal AKI.

Several limitations should be acknowledged in interpreting these results. The single-center design and exclusive inclusion of inborn term neonates limit the generalizability to outborn populations, preterm infants, or those with complex congenital conditions. The observational nature of the study introduces potential confounding and selection biases, and the follow-up was restricted to in-hospital outcomes without assessment of long-term renal function or growth.

CONCLUSION

This study demonstrates a high incidence of AKI among term neonates, with maternal diabetes, pregnancy-induced hypertension, maternal infection, IUGR at birth, and prolonged NICU stay identified as significant and independent risk factors. The findings reinforce the critical importance of antenatal risk factor modification, early diagnosis, and vigilant supportive care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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3	**Hira Nawaz:** Methodology, proof reading.
4	**Nimra Fatima:** Literature review.
5	**Aasma Kayani:** Critical revision.