

PROSPECTIVE STUDY OF ACUTE RENAL FAILURE IN PRETERM NEONATES IN A TERTIARY HEALTH CARE CENTER

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Abstract

Background: Acute kidney injury (AKI) (previously called acute renal failure; ARF) has been defined as a rapid deterioration of renal function resulting in retention of nitrogenous wastes and inability of kidney to regulate fluid and electrolyte homeostasis. Diagnosing AKI in preterm neonates poses significant challenges due to nonspecific clinical manifestations and limitations in renal function assessment tools. The aim is to study acute renal failure in preterm neonates at a tertiary healthcare center. The objectives are primary objectives is to determine incidence of acute renal failure in preterm neonates. To study risk factors pre-disposing to renal failure. The secondary objective is to evaluate the usefulness of Biomarkers like TIMP 2 as marker of renal functions and predictors of acute kidney injury in preterm neonates. **Materials and Methods:** Type of study is descriptive study. Study setting: NICU, Department of Pediatrics at S.V.R.R. Government General Hospital, Tirupati. Study period is 12 months from the date of institutional ethics committee approval from December 2022 to November 2023. **Result:** Significant difference ($p < 0.05$) underscores the increased vulnerability of lower-weight neonates to AKI, 25% of the neonates were diagnosed with intrauterine growth restriction (IUGR), The highest incidence of AKI was observed in neonates resuscitated with bag and mask ventilation (50%). Serum TIMP-2 values of < 25 ng/ml were present in 12 (12.5%) of neonates out of which 2 (16.6%) developed AKI; values of 25-50 ng/ml were present in 48 (50%) of neonates out of which 4 (8.3%) developed AKI. **Conclusion:** In this study, 10 neonates developed AKI, resulting in an incidence rate of 4.4%, slightly higher than the general neonatal AKI incidence in India. Male neonates had a higher incidence of AKI (11.1%) compared to females. Serum TIMP-2 levels were evaluated as potential early markers for AKI, with higher levels correlating with an increased risk of AKI.

INTRODUCTION

Acute kidney injury (AKI) (previously called acute renal failure; ARF) has been defined as a rapid deterioration of renal function resulting in retention of nitrogenous wastes and inability of kidney to regulate fluid and electrolyte homeostasis. Preterm neonates, born before completing 37 weeks of gestation, possess underdeveloped renal function, rendering them particularly susceptible to AKI and its adverse consequences.^[1]

Approximately 12% of neonates were born preterm, and 18% had low birth weight in India during 2019–2020. The country bearing a significant burden of neonatal mortality, with a neonatal mortality rate,^[2] of 20 deaths per thousand live births in 2020, AKI further compounds this issue, with studies,^[3]

indicating a higher incidence rate among preterm neonates compared to term counterparts. Reported incidence of neonatal AKI in India ranges from 3.4 to 4.2% of all NICU admissions.^[4]

Diagnosing AKI in preterm neonates poses significant challenges due to nonspecific clinical manifestations and limitations in renal function assessment tools. Additionally, the reliance on serum creatinine, which may not accurately reflect renal function in preterm neonates, underscores the need for novel biomarkers and diagnostic approaches tailored to preterm neonates.

This study was conducted to look at the Incidence of Acute Kidney Injury in Preterm Neonates in NICU, SVRRGGH, Tirupati and also the various risk factors which may predispose to renal injury. The usefulness

of novel biomarker S. TIMP-2 as an early marker of renal injury was assessed.

Aim: To study acute renal failure in preterm neonates at a tertiary healthcare center

Objectives

Primary Objectives

1. To determine incidence of acute renal failure in preterm neonates
2. To study risk factors pre-disposing to renal failure

Secondary Objective

To evaluate the usefulness of Biomarkers like TIMP 2 as marker of renal functions and predictors of acute kidney injury in preterm neonates

MATERIALS AND METHODS

Type of Study: Descriptive study

Source of Data: All preterm neonates between 32 weeks – 37 weeks gestation admitted in NICU, Department of Pediatrics at S.V.R.R. Government General Hospital, Tirupati.

Study Setting: NICU, Department of Pediatrics at S.V.R.R. Government General Hospital, Tirupati.

Study Period: 12 months from the date of institutional ethics committee approval from December 2022 to November 2023.

Sample Size: 96

$$\text{Sample size} = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

Here,

$Z_{1-\alpha/2}$ = standard normal variant at 5% type 1 error = 1.96

p = expected proportion in population = 10%

d = absolute error or precision = 6%

Inclusion Criteria

1. Neonates born between 32 to 37 weeks of gestational age
2. Birth weight >1kg.

Exclusion criteria:

- Abnormal antenatal renal scans
- Major systemic congenital anomalies like congenital heart diseases, congenital anomalies of kidney.
- Neonates discharged/ died within 72hrs of admission.
- Lack of parental consent.

Method of assessment of subjects: All those babies who fulfilled the Inclusion Criteria were recruited. In this study, Inborn neonates (born at Government Maternity Hospital, Tirupati) were included, to calculate incidence of AKI. After counselling the parents and getting consent from them, the study proformas were filled in. The details included demographic data like hospital number, age, gender, gestational age, birth weight; maternal history- both antenatal and peri-partum period. Neonatal history - perinatal history including Apgar score, resuscitation details, clinical features suggestive of sepsis, procedures which may predispose to renal failure were looked at.

During the hospital stay, monitoring was done daily. Urine output (monitored non-invasively daily by

either urine collecting bags or weighing the cotton pad.), clinical deterioration if any, details of interventions – umbilical line, ventilation, any unexpected event and use of nephrotoxic drugs were noted.

In case of death or the baby being discharged, within 72 hrs of admission, were considered as case dropouts.

Blood sampling for serum creatinine was collected every 3rd day. Serum creatinine was processed in Clinical biochemistry lab of S.V.R.R. Government General Hospital using standard methods. Serum creatinine more than 1.3 mg/dL or more than 50% rise of creatinine compared to previous value was used to define AKI. Blood sampling for serum TIMP-2 was done on day 3 of life for all neonates. Serum TIMP-2 was processed, to look if it was useful as an early marker for detecting acute kidney injury in this population. Serum TIMP-2 was processed using a rapid ELISA kit.

Statistical analysis: The clinical outcomes of the neonates included in the study were recorded using a predefined structured form and then entered into a database formatted in Microsoft Excel. Baseline characteristics were analyzed using descriptive statistics. Quantitative variables were presented as mean and standard deviation when applicable, while qualitative variables were expressed as frequencies and percentages. A comparison between two groups, namely AKI and non-AKI, was conducted using the chi-square test for categorical variables. A p-value less than 0.05 was considered statistically significant. The incidence of AKI was reported as n and percentages.

Ethical Considerations

- Informed written consent had been obtained from the parent of subject.
- No conflict of interest

RESULTS

There was a total of 3124 inborn live births during the study period, out of which 375 were preterm deliveries (less than 37 weeks) (11.9%). Of these, 227 were preterm deliveries 32-37 weeks gestation (60.7%) from which a total of 96 were recruited in this study according to inclusion criteria and after obtaining consent.

Out of the sample size of 96, 10 developed AKI. Incidence of AKI –

$$\text{Incidence Rate} = \frac{\text{number of new cases}}{\text{population at risk}} * \text{base multiplier}$$

Here, Number of new cases of AKI = 10

Population at risk = 32-37 weeks inborn preterm neonates = 227 Base multiplier = 100,

Incidence rate = 4.4 cases of AKI per 100 preterm (32-37 weeks) neonates at risk in one year.

Table 1: Gestational Age.

| Gestational age | Number (n=96) | AKI |
|-----------------|---------------|-----------|
| 32 – 32+6 days | 9 (9.4%) | 3 (33.3%) |
| 33 – 33+6 days | 12 (12.5%) | 1 (8.3%) |
| 34 – 34+6 days | 22 (22.9%) | 1 (4.5%) |
| 35 – 35+6 days | 32 (33.3%) | 3 (9.3%) |
| 36 – 36+6 days | 21 (21.8%) | 2 (9.5%) |

p value – 0.199 (not significant)

Table 2: Birth weight

| Birth weight | Number (n=96) | AKI |
|--------------|---------------|-----------|
| 1 – 1.5 kg | 3 (3.1%) | 2 (66.6%) |
| 1.5 – 2 kg | 34 (35.4%) | 1 (3%) |
| 2 – 2.5 kg | 46 (47.9%) | 6 (13%) |
| >2.5 kg | 13 (13.5%) | 1 (7.6%) |

p value -0.0054 (p<0.05 - significant)

Table 3: Maternal risk factors

| Number of risk factors | Number (n=96) | AKI |
|------------------------|---------------|-----------|
| No risk factors | 13 (13.5%) | 0 |
| 1 risk factor | 45 (46.8%) | 6 (13.3%) |
| 2 risk factors | 38 (39.5%) | 2 (5.2%) |
| 3 risk factors | 2 (2%) | 2 (100%) |

p value = 0.005 (p<0.05 - significant)

Table 4: antenatal USG

| Antenatal USG | Number (n=96) | AKI | p value |
|-----------------|---------------|-----------|---------|
| Normal | 45 (46.8%) | 3 (6.6%) | 0.25 |
| Twins | 11 (11.4%) | 0 | 0.8 |
| IUGR | 24 (25%) | 3 (12.5%) | 0.69 |
| Abruptio | 4 (4.1%) | 1 (25%) | 0.32 |
| Oligohydramnios | 12 (12.5%) | 3 (25%) | 0.04 |

p value = 0.04 for oligo hydramnios (p<0.05 - significant)

Table 5: APGAR

| APGAR at 5 minutes | Number (n=96) | AKI |
|--------------------|---------------|-----------|
| <6 | 8 (8.3%) | 3 (37.5%) |
| >6 | 88 (91.6%) | 7 (7.9%) |

p value – 0.0088(p<0.05 - significant)

Table 6: Neonatal resuscitation

| Neonatal resuscitation | Number (n=96) | AKI |
|------------------------|---------------|-----------|
| Cried at birth | 66 (68.7%) | 5 (7.5%) |
| Tactile stimulation | 20 (20.8%) | 1 (5%) |
| BMV | 4 (4.1%) | 2 (50%) |
| Intubation | 6 (6.2%) | 2 (33.3%) |

p value – 0.01(p<0.05 - significant)

Table 7: symptoms in neonate

| Symptom | Number (n=96) | AKI | p value |
|-------------------------|---------------|-----------|---------|
| Respiratory distress | 80 (83.3%) | 9 (11.2%) | 0.55 |
| Poor perfusion | 16 (16.6%) | 4 (25%) | 0.036 |
| Abdominal distension | 8 (8.3%) | 1 (12.5%) | 0.84 |
| Apnoea | 9 (9.3%) | 4 (44.4%) | 0.0004 |
| Temperature instability | 20 (20.8%) | 6 (30%) | 0.0012 |
| Oliguria | 2 (2%) | 2 (100%) | 0.0011 |
| Anuria | 1 (1%) | 1 (100%) | 0.0016 |
| Convulsions | 33 (34.3%) | 3 (9%) | 0.75 |

Table 8: interventions during NICU stay

| Intervention | Number (n=96) | AKI | p value |
|--------------|---------------|------------|---------|
| IV fluids | 96 (100%) | 10 (10.4%) | 0.72 |
| NG feeds | 75 (78.1%) | 10 (13.3%) | 0.30 |
| UVC | 60 (62.5%) | 10 (16.6%) | 0.050 |
| CPAP | 77 (80.2%) | 8 (10.3%) | 0.98 |
| MV | 15 (15.6%) | 4 (26.6%) | 0.024 |
| Inotropes | 13 (13.5%) | 4 (30.7%) | 0.0097 |

Table 9: nephrotoxic drugs used during NICU stay

| Name | Frequency in all patients (n=96) | Exposure frequency in patients with AKI | p value |
|--------------------------|----------------------------------|---|---------|
| Gentamycin | 73 (76%) | 8 (10.9%) | 0.75 |
| Amikacin | 47 (48.9%) | 8 (17%) | 0.038 |
| Vancomycin | 9 (9.3%) | 3 (33.3%) | 0.018 |
| Piperacillin- Tazobactam | 46 (47.9%) | 8 (17.3%) | 0.031 |
| Liposomal Amphotericin B | 8 (8.3%) | 3 (37.5%) | 0.0088 |

Table 10: Serum Creatinine trends in neonates with AKI(n=10)

| Day | Number | Minimum | Maximum | Mean | SD |
|-----|--------|---------|---------|------|------|
| D3 | 10 | 0.2 | 0.6 | 0.38 | 0.28 |
| D6 | 10 | 0.3 | 1.1 | 0.7 | 0.49 |
| D9 | 9 | 0.4 | 1.3 | 0.78 | 0.35 |
| D12 | 3 | 0.8 | 1.4 | 1.03 | 0.35 |
| D15 | 2 | 0.7 | 0.8 | 0.75 | 0.07 |
| D18 | 2 | 0.6 | 0.7 | 0.65 | 0.07 |
| D21 | 1 | 0.4 | - | - | - |

| Creatinine level (mg/dl) | D3 (n=10) | D6 (n=10) | D9 (n=9) | D12 (n=3) | D15 (n=2) | D18 (n=2) | D21 (n=1) |
|--------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| <0.3 | 2 (20%) | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.3 – 0.6 | 6 (60%) | 3 (30%) | 3 (33.3%) | 0 | 0 | 0 | 1 (100%) |
| 0.6 – 0.9 | 2 (20%) | 4 (40%) | 3 (33.3%) | 1 (33.3%) | 2 (100%) | 2 (100%) | 0 |
| >0.9 | 0 | 3 (30%) | 3 (33.3%) | 2 (66.6%) | 0 | 0 | 0 |

Table 11: Serum TIMP-2 trends in all neonates

| S. TIMP-2 levels (ng/ml) | Number (n=96) | AKI (n=10) | Mortality (n=4) |
|--------------------------|---------------|------------|-----------------|
| <25 | 12 (12.5%) | 2 (20%) | - |
| 25-50 | 48 (50%) | 4 (40%) | 2 (50%) |
| 50-75 | 32 (33.3%) | 3 (30%) | 1 (25%) |
| >75 | 4 (4.1%) | 1 (10%) | 1 (25%) |

Table 12: Final Outcome

| Outcome | Number (n=96) | AKI (n=10) |
|------------|---------------|------------|
| Discharged | 92 (95.8%) | 6 (60%) |
| Death | 4 (4.1%) | 4 (40%) |

DISCUSSION

There was a total of 3124 inborn live births during the study period, out of which 375 were preterm deliveries (less than 37 weeks) (11.9%). Of these, 227 were preterm deliveries 32-37 weeks gestation (60.7%) from which a total of 96 were recruited in this study according to inclusion criteria and after obtaining consent.

Out of all preterm neonates aged between 32-37 weeks, 10 developed AKI, resulting in an incidence rate of 4.4%. This rate is slightly higher than the reported incidence of neonatal AKI in India, which ranges from 3.4% to 4.2% of all NICU admissions.^[4] In this study, 50% neonates were older than 35 weeks gestational age, with the majority falling within the 35-36 weeks range. AKI was most prevalent in those with a gestational age of 32 weeks, occurring in 33% of this group. 7. This finding correlates to the study conducted by Jetton et al. for AWAKEN study.^[5]

In the study group, approximately 60% of the neonates had a birth weight greater than 2 kg, with the largest subset (48%) falling within the 2-2.5 kg range. This significant difference ($p < 0.05$) underscores the increased vulnerability of lower-weight neonates to AKI. Cataldi et al. also reported a higher incidence rate (79%) in babies less than 1.5 kg.

Among all the neonates studied, 56.2% were male and 43.7% were female, resulting in a male to female ratio of 1.3:1. This distribution of sexes is consistent with findings from Cataldi et al.^[6] Among the 10 neonates who developed AKI, 6 were male (11.1%) and 4 were female (9.5%), indicating a male preponderance in both the overall study group and among those affected by AKI, with a male to female ratio of 1.5:1.^[7,8]

| | | |
|---------------------------------------|------|-------|
| This study | 2023 | 1.5:1 |
| Airede et al. ^[9] | 1997 | 3.3:1 |
| Ghorehbaghi et al. ^[10] | 2007 | 2:1 |
| Mortazavi et al. ^[6] | 2009 | 2:1 |
| Jetton et al. ^[8] (AWAKEN) | 2017 | 1.3:1 |

The parity of mothers delivering preterm babies was examined, revealing that prematurity within the 32-37 weeks gestational range was more prevalent among primiparous mothers (63.5%) compared to multiparous mothers (36.4%).

Maternal risk factors were closely studied in this research, revealing that 47% of mothers had at least one risk factor, 40% had two risk factors, and a small minority of 2% had three risk factors. The development of AKI was notably higher in neonates born to mothers with multiple risk factors.

In this study, PIH was the most common maternal condition, affecting 50% of the mothers, followed by GDM at 30%. Jetton et al. in the AWAKEN study, reported that maternal chronic hypertension and pre-eclampsia were significant risk factors for developing neonatal AKI.

Antenatal ultrasonography was performed on all 96 participants in the study, and revealed that 47% of the scans were normal. However, 25% of the neonates were diagnosed with intrauterine growth restriction (IUGR), and 12.5% exhibited oligohydramnios.

The study found significant associations between certain ultrasound findings and the risk of neonatal AKI. Specifically, oligohydramnios was identified as a significant risk factor for AKI, with a statistically significant association ($p < 0.05$).

| | | |
|---------------------------------------|------|--|
| This study | 2023 | Oligohydramnios |
| Arcinue et al. ^[11] | 2015 | Abruptio placenta |
| Jetton et al. ^[8] (AWAKEN) | 2017 | Polyhydramnios; multi-foetal pregnancy |
| Sinelli et al. ^[12] | 2023 | IUGR |

The modes of delivery in this study comprised of normal vaginal delivery, LSCS, low forceps, and breech (assisted vaginal delivery). LSCS emerged as the predominant mode of delivery, representing more than half of the cases (54.1%), followed by normal vaginal delivery (39.5%), with a smaller percentage attributed to breech/low forceps deliveries (6.2%). This aligns with findings from the AWAKEN study conducted by Charlton et al., which also observed a lower incidence of AKI in neonates born via LSCS.

APGAR score serves as a crucial assessment tool for neonates at 1 and 5 minutes after birth. An APGAR score of less than 7 at 5 minutes is considered abnormal, with a score of 3 or less suggesting birth asphyxia. In this study, 91.6% of neonates had a 5-minute APGAR score exceeding 6, while 8.3% exhibited an abnormal score of less than 6. AKI was observed in 37.5% of neonates with an APGAR score less than 6, compared to only 7.9% of those with a score exceeding 6, a statistically significant difference ($p < 0.05$).

The highest incidence of AKI was observed in neonates resuscitated with bag and mask ventilation (50%), followed by those requiring intubation (33.3%), while the incidence was 7.5% and 5% for neonates not needing resuscitation and those revived with tactile stimulation, respectively, a statistically significant difference ($p < 0.05$). This aligns with findings from 5Cataldi et al., 8Jetton et al. and Stojanovic et al., who also identified low APGAR scores and the need for resuscitation as risk factors for AKI.

Symptoms were present in all neonates upon admission, with respiratory distress being the most common reason for admission (83.3%), followed by convulsions in 34.3%, temperature instability in 20.8%, poor perfusion in 16.6%, abdominal distension in 8.3%, and apnoea in 9.3%.

Urine output was monitored using urine collecting bags or by weighing cotton pads. Oliguria, defined as urine output less than 0.5 ml/kg/hour, was observed in 2 neonates (2%), and anuria was later noted in one (1%) of these two cases. AKI was observed in all three neonates presenting with oligo-anuria (100%). Furthermore, all three neonates with oligo-anuria experienced mortality. This outcome aligns with the findings from the study by Gupta et al. who reported that mortality was higher in neonates with oliguric renal failure.^[13] The study by Chen et al. also indicated that oliguric AKI demonstrated significantly higher mortality risks compared to non-oliguric AKI, regardless of serum creatinine levels and the severity of AKI.

| | | |
|-----------------------------------|------|---|
| This study | 2023 | Mortality higher in oliguric renal failure |
| Gupta et al. ^[13] | 2005 | Mortality higher in oliguric renal failure |
| El-Kalioby et al. ^[14] | 2022 | No statistical difference in outcomes between oliguric and non-oliguric AKI |
| Chen et al. ^[15] | 2023 | Mortality higher in oliguric renal failure |

The complications contributing to morbidity were multi-systemic. Hyaline membrane disease (HMD) emerged as the most common, affecting 50% of neonates, followed closely by sepsis (48.9%). Cataldi et al.⁵ reported a notably higher incidence of HMD (89%), which may be attributed to their NICU's specialization in caring for preterm babies born at less than 25 weeks.^[6]

A total of 8 neonates were diagnosed with NEC, with 6 of them classified as stage 1 and 2 neonates classified as stage 2 NEC. One of them developed AKI (12.5%). Conservative management was employed, consisting of antibiotics, intravenous fluids, total parenteral nutrition, and bowel rest achieved by maintaining nil per mouth status. Unfortunately, there was one mortality observed within this group.

Jetton et al. as part of the AWAKEN study, reported that sepsis, NEC and HIE were significant risk factors for development of neonatal AKI.^[10] Ghorehbaghi et al. also documented in their study that sepsis (32.9%), HMD (25.9%), and perinatal asphyxia (36.5%) were among the most common predisposing factors for AKI.

During their NICU stay, all 96 neonates received intravenous fluids and had peripheral intravenous catheters, while 75 neonates (78%) were administered nasogastric feeds. Umbilical venous lines were inserted in 60 neonates (62.5%), and fortunately, no complications such as infections, renal vein thrombosis, or line-related issues were reported. Non-invasive ventilation in the form of CPAP was utilized for 77 neonates (80.2%). However, 6 neonates required transition to mechanical ventilation. Overall, 15 neonates (15.6%) necessitated mechanical ventilation.

Additionally, 13 neonates (13.5%) required inotropic support during their NICU stay to maintain hemodynamic stability and support cardiac function. AKI developed in 30.7% of neonates with inotropic support, 26.6% of neonates on mechanical ventilator and 16.6% of patients with a UVC. Among the parameters examined, mechanical ventilation and need for inotropic support significantly increased the risk of developing neonatal AKI, which was statistically significant ($p < 0.05$). This aligns with the study conducted by Jetton et al. for the AWAKEN study, which reported that the need for vasopressors, during hospital stay, significantly increased the risk of developing neonatal AKI. Out of the 96 neonates, 64 (66.6%) were clinically suspected to have sepsis, and among them, 47 (48.9%) tested positive on culture.

Among the antibiotics, gentamicin was the most frequently administered nephrotoxic medication, given to 73 neonates (76%), followed by amikacin and piperacillin-tazobactam, each prescribed to approximately half of the neonates studied (48%). Liposomal amphotericin B was given to 8 neonates (8.3%), and 3 of them (37.5%) developed AKI. Similarly, the development of AKI associated with other antibiotics was noted, including vancomycin (33.3%), piperacillin-tazobactam (17.3%), amikacin (17%) and gentamycin (10.9%). The administration of amikacin, vancomycin, piperacillin-tazobactam, and liposomal amphotericin B, was associated with a statistically significant increase in neonatal AKI ($p < 0.05$).

The average length of hospital stay was 9.8 days (± 4.6 days). The majority of neonates (59.3%) had a hospital stay of 5–10 days, followed by 25% who stayed between 10–15 days, and 15.6% who stayed for more than 15 days. Development of AKI was notably higher in neonates with longer hospital stays. This finding is consistent with the AWAKEN study conducted by Jetton et al.^[8]

The trend of serum creatinine values was analyzed and compared between the two groups: No AKI and AKI. In the No AKI group, the serum creatinine values peaked between days 9 and 15. The mean serum creatinine level increased from 0.28 mg/dl on Day 3 to 0.40 mg/dl on Day 21.

On day 3, 71% of neonates exhibited serum creatinine levels in the range of 0.3–0.6 mg/dl, while the remaining 29% had creatinine levels below 0.3 mg/dl. This pattern persisted until day 12, at which point all neonates displayed serum creatinine levels within the range of 0.3–0.6 mg/dl. Subsequently, none of the neonates exhibited serum creatinine levels exceeding 0.6 mg/dl, and all values remained within the range of 0.3–0.6 mg/dl.

In contrast, the AKI group also demonstrated peak serum creatinine values on days 9 and 12. The mean serum creatinine level increased from 0.38 mg/dl on Day 3 to 0.65 mg/dl on Day 18. On day 3, the majority of neonates (60%) exhibited serum creatinine values between 0.3–0.6 mg/dl, while only 20% had values between 0.6–0.9 mg/dl. By day 6, there was a shift in

distribution, with 30% of neonates showing serum creatinine levels between 0.3–0.6 mg/dl, 40% between 0.6–0.9 mg/dl, and 30% exceeding 0.9 mg/dl. Unfortunately, one neonate with AKI succumbed to the condition on day 6 of life.

As the days progressed, the distribution of serum creatinine values continued to fluctuate. By day 9, an equal proportion (33.3%) of neonates fell into each category: serum creatinine levels of 0.3–0.6 mg/dl, 0.6–0.9 mg/dl, and >0.9 mg/dl. Four neonates were discharged between day 9 and day 10 as their serum creatinine levels had normalized and their AKI had resolved. Unfortunately, 2 neonates passed away between day 9 to day 10 of life.

However, by day 15 and 18, a gradual return of serum creatinine values to normal was observed in the two remaining neonates. Ultimately, by day 18 and day 22, both neonates had been discharged without further complications.

Serum TIMP-2 levels were measured in all neonates on day 3 to assess its potential as an early marker for predicting acute kidney injury in neonates. Serum TIMP-2 values of <25 ng/ml were present in 12 (12.5%) of neonates out of which 2 (16.6%) developed AKI; values of 25–50 ng/ml were present in 48 (50%) of neonates out of which 4 (8.3%) developed AKI; values of 50–75 ng/ml were present in 32 (33.3%) of neonates out of which 3 (9.3%) developed AKI and values of >75 ng/ml were present in 4 (4.1%) of neonates out of 1 (25%) developed AKI.

Among the 96 neonates studied, 92 (95.8%) were discharged, while 4 neonates (4.1%) unfortunately passed away due to complications of AKI. This translates to a mortality rate of 4.1% attributable to AKI. This finding is consistent with the AWAKEN study by Jetton et al, 5Cataldi et al. reported a mortality rate of 11% due to AKI in their study.

Limitations

- A larger sample size would provide more robust data and enhance the reliability of the results.
- Multicenter studies could offer more comprehensive insights.
- The study primarily focused on the early postnatal period without extensive follow-up to assess long-term outcomes of AKI in preterm neonates. Long-term studies are needed to understand the chronic impact of AKI.
- Serum TIMP-2 levels were used as a potential early marker for AKI, but the study did not validate its effectiveness extensively against other established biomarkers or in larger cohorts. More research is needed to confirm its reliability and clinical utility.

CONCLUSION

- The incidence of AKI is higher among preterm neonates compared to full-term infants. In India, the reported incidence of neonatal AKI ranges from 3.4% to 4.2% of NICU admissions.

- Out of 3124 live births during the study period, 375 were preterm (11.9%), and 96 preterm neonates were recruited for the study based on inclusion criteria.
- In this study, 10 neonates developed AKI, resulting in an incidence rate of 4.4%, slightly higher than the general neonatal AKI incidence in India.
- AKI was most prevalent in neonates with a gestational age of 32 weeks (33%) and less common in neonates at 35-36 weeks gestation (9.3%- 9.5%).
- Birth weight significantly influenced AKI development, with the highest incidence (66.6%) among neonates weighing less than 1.5 kg.
- Male neonates had a higher incidence of AKI (11.1%) compared to females (9.5%), with a male to female ratio of 1.5:1.
- Maternal risk factors for AKI included PIH, GDM and UTI.
- Oligohydramnios, identified through antenatal ultrasonography, was significantly associated with an increased risk of AKI.
- Neonates born via normal vaginal delivery had a higher incidence of AKI (18.4%) compared to those delivered via LSCS (5.7%).
- Neonates with a 5-minute APGAR score of less than 6 had a significantly higher risk of developing AKI (37.5%).
- The need for neonatal resuscitation was associated with an increased risk of AKI, particularly among those resuscitated with bag and mask ventilation (50%).
- AKI was most commonly observed in neonates presenting with respiratory distress (11.2%) and poor perfusion (25%).
- Mechanical ventilation and inotropic support were significant risk factors for developing AKI.
- The average hospital stay was 9.8 days, with a longer stay correlating with a higher incidence of AKI.
- Serum creatinine trends showed higher values and peaks in the AKI group, indicating renal impairment.
- Serum TIMP-2 levels were evaluated as potential early markers for AKI, with higher levels correlating with an increased risk of AKI.
- The overall mortality rate due to AKI in the study was 4.1%, consistent with findings from other studies such as the AWAKEN study.

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