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Original Article

Prediction and Risk Stratification of Acute Kidney Injury in Neonates Using STARZ Scoring Model

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Abstract

Background: Neonates admitted to NICU are vulnerable to acute kidney injury which can lead to worse outcomes. STARZ score is an AKI specific risk stratification score that can be used to predict the risk of AKI at any time within 7 days post admission in the NICU.

Materials and methods: A prospective observational study conducted from January to March 2024 in NICU at a tertiary care center. STARZ score was applied to neonates fulfilling the inclusion criteria during any time post 12 hours admission and the risk of AKI was predicted. Some variables were recorded at the time of admission and some after 12 hours. Each variable was assigned a score and a cut off >31.5 was proportional to the probability of AKI within 7 days of admission. High risk neonates were then vigilantly monitored during the course of hospitalization.

Results: Out of 127 neonates included, 33 neonates had AKI during the hospital stay. 88(69.3%) of the neonates were identified as at-risk neonates for developing AKI. The neonates with higher probability score were monitored and 33 had AKI of varied stages. In the AKI group, 21(63.6%) had mortality and 12(36.3%) were discharged for home. Maximum mortality was seen in stage 3 AKI.

Conclusion: STARZ score was simple and easy to predict the risk of AKI in neonates during anytime post 12 hours admission in NICU. 26% of the neonates had AKI of varied stages according to KDIGO classification with maximum mortality seen with stage 3 AKI.

Key words: AKI, STARZ score, NICU, KDIGO

Introduction

Acute kidney injury (AKI) is defined as a sudden impairment in renal function leading to accumulation of nitrogenous wastes and dysregulation of fluid electrolyte and acid-base homeostasis. [1]

The incidence of neonatal AKI varies from 18 to 70% and it is an important contributor to neonatal morbidity and mortality2. In the largest epidemiologic study till date, the Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN) study, it was seen that 30 % of the neonates admitted to NICU develop AKI and that the incidence of AKI was different across the gestational age groups. [2]

Incidence of AKI varies in high-risk groups, like 19 % preterm neonates, 39 % in newborns who receive hypothermia for severe perinatal asphyxia [3]. 52 % in newborns undergoing cardiopulmonary bypass surgery [4,5]. 71% in newborns with congenital diaphragmatic hernia who receive extracorporeal membrane oxygenation [6,7] and very low birth weight neonates. [8-10]

The definition of neonatal AKI has been evolved. In various clinical textbooks, AKI is defined as a sudden decrease in GFR and retention of nitrogenous waste products in the body [11].

Though it is clinically correct definition, but it lacks specificity due to which various definitions had emerged in past years. The Acute Dialysis Quality Initiative (ADQI) introduced the Risk, Injury, Failure, Loss, and End Stage Renal Disease (RIFLE) scheme in 2004, which offered a consistent framework for categorizing AKI. [12] According to this criterion the least severe category “risk” was defined as a 50% increase in serum creatinine or >25% decrease in eGFR presumed to have occurred within 7 days. KRT was added to stage 3 of the Acute Kidney Injury Network (AKIN) Classification System in 2005, which replaced the RIFLE's Loss and ESRD stages as well as the eGFR criterion. [2]

The most recent definition criteria were introduced by KDIGO in 2012. In neonates, a modified version of kidney disease: Improving Global Outcomes (KDIGO) AKI definition has been made as standardized definition after the consensus. In April 2013 in National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) workshop made a current consensus definition for neonatal AKI which will be used for the research and clinical care.[13]

In view of increasing incidence and marked vulnerability to AKI in neonates, there is a need for extensive research on utility of new biomarker or risk stratification score for early detection/prediction of AKI. Various risk stratification score for mortality in critically ill children have been successfully implemented in critical care units. Two most common scores being paediatric risk of mortality (PRISM) and paediatric index of mortality (PIM) [14-16] but their use in assessing outcomes in neonates is poor. There is no such score which can be used in resource limited settings. Renal angina index (RAI) is the only AKI specific risk stratification score that has been extensively studied in multiple paediatric cohorts but it is not useful in neonates.

It is highly important to identify the neonates admitted in NICU who are at risk of developing AKI, and periodic assessments for early identification AKI are to be done in them, so as to start early preventive and therapeutic measures. It has been seen that the main basis of treatment of AKI in neonates is prevention, vigilant monitoring and early detection.

STARZ (Sethi, Tibrewal, Agarwal, Raina, Wazir) score is a scoring model developed to predict the risk of AKI in neonates post admission to the NICU. This score can help in predicting risk in resource limited settings. [17]

Patients and Methods

Study design

This was a prospective observational study conducted in Neonatal ICU in the

Department of Paediatrics in a tertiary care centre after approval by Institutional Ethics Committee and written consent from participant's guardians with time duration from January 2023 to March 2024. This study was conducted to predict probability of acute kidney injury in Neonatal ICU using STARZ score model and to stratify risk of acute kidney injury using STARZ score model.

Inclusion criteria

- All inborn neonates admitted in NICU with established IV access to receive IV fluids for at least 48 hours.
- All out born neonates coming to NICU within 24 hours of life with record history of IV fluids, antibiotics and resuscitation.

Exclusion criteria

- Death within 48 hrs. of admission
- Neonates who received IV for <48 hrs. or only for administration of medications
- Neonates with obvious congenital anomalies.
- Neonates with congenital anomalies of kidney and urinary tract detected in antenatal scans.

Data collection

Total 540 neonates admitted in NICU during the study period, out of which 127 neonates were included in this study after meeting the inclusion criteria. Demographic details, Maternal details & Neonatal details were recorded at the time of admission in NICU (Table 2 &3). STARZ criteria were applied on the neonates fulfilling the inclusion criteria after 12 hours of admission in NICU. AKI was defined as increase in serum creatinine of >0.3mg/dl or >50% from the previous lowest value or a urinary output of <1 ml/kg/h on postnatal days 2-7 as per KDIGO criteria.18Data was collected during the first week of hospitalization & was continuously assessed until neonate was discharged, transferred out of NICU or died.

Variables were recorded at the time of admission and some at 12 hours of life (Table No. 1). The variables in STARZ

criteria were simple to extract and use.17STARZ model predicted the incidence of AKI at any time within 7 days post admission in the NICU. Each of the variable was assigned a score on a scale of 0-100 and a cut off >31.5 was proportional to probability of AKI within 7 days of admission. This criterion helped to identify at risk neonates for early prevention so as to improve the quality of life. The neonates with a higher stratification score needed intense monitoring and daily kidney function assessment. This helped in reducing the morbidity and mortality associated with AKI.

- A score of <37 will indicate probability of AKI at <20%,
- Score of 38-42 will indicate 20- <40% probability of AKI
- Score 43-48 will indicate 40-<60%probability of AKI
- Score of 49-53% will indicate at 60-<80% probability of AKI
- Score of >54 at >80% probability of AKI.

Data management and analysis:

The data from the present study was systematically collected and compiled in Microsoft Excel, then statistically analysed using the Statistical Package for the Social Sciences (SPSS) 26 to draw relevant conclusions. Categorical data was presented as numbers and percentages, while parametric data was presented as mean ± standard deviation (SD). The student's t-test was used to analyse continuous variables. Categorical data was analysed using the Chi-square test or Fisher's exact test, as appropriate. A significance level of $p<0.05$ was considered significant, and $p<0.001$ was considered highly significant.

Results

Out of 127 neonates, 26% neonates had AKI (n = 33) at 7 days post admission in the NICU. STARZ score was used to predict the risk of AKI during any time post 12 hours admission, 69.3% neonates had score more than 31.5 which falls in high risk for acute kidney injury (Table-4). In this high-risk group, 33(37.5%)

had acute kidney injury during the stay. The probability of acute kidney injury was divided according to the score, 33.9% neonates had probability less than 20% with score of less than 37, 17.3% neonates 20-40% with score 38-42, 16.5% had 40-60% with score 43-48, 7.1% score 49-53 had 60-80% and 25.2% neonates had more than 80% with score of above 54(Table-5).

The neonates who had AKI were observed to have, higher serum creatinine (1.11±0.44 vs 0.82±0.28; p value <0.001) during the first 24h of admission. Likewise, the p value was statistically significant in the neonates with following risk factors, extremely preterm (87.5%, p value <0.001), the neonates who received positive pressure ventilation (PPV) in the delivery room[31.8%(21); p value 0.035], had sepsis during NICU stay 38.1%(16; p value <0.028), significant cardiac disease (51.6% ; p value <0.001), required mechanical ventilation (40.3%; p value <0.001), longer duration of mechanical ventilation in AKI neonates with mean duration of 7.61±4.39 vs 3.93±2.88 in non-AKI, use of nephrotoxic drugs(35.2%; p value 0.034); use of furosemide (78.6%; p value <0.001), use of inotropes(45.2%; p value <0.001), more mean duration of inotrope use (4.36±2.48, p value <0.001) than the non-AKI group, duration in NICU stay: 16.18±11.86 days in AKI vs 13.67±9.49 in non-AKI with p value not significant. Among the various maternal risk factors studied oligohydramnios was the main risk factor associated with neonatal AKI (57.1%, p value <0.008).(Table-3)

Acute kidney injury was classified according to the modified KDIGO criteria and out of 33 neonates, 21(63.6%) stage 1 AKI, 7(21.1%) had stage 2 AKI and 5(15.1%) had stage 3 AKI(Table-6). In AKI group, 21(63.6%) had mortality and 12(36.3%) were discharged (Table-7)**.** In AKI group, maximum mortality was seen in stage 3 AKI in 80% neonates (Table 8)

Table 1. STARZ scoring model

Variables		Assigned Score
Age at entry in NICU (hours)	<25.5	6
	≥25.5	0
PPV in the delivery room	Yes	7
	No	0
Gestational age (weeks)	<28	7
	≥28	0
Sepsis (during the NICU stay)	Yes	6
	No	0
Significant cardiac disease	Yes	10
	No	0
Urine output^ (ml/kg/hr)	<1.32	7
	≥1.32	0
Serum creatinine^(mg/dl)	≥0.98	20
	<0.98	0
Use of nephrotoxic drugs	Yes	11
	No	0
Use of furosemide	Yes	9
	No	0
Use of Inotropes	Yes	17
	No	0

^ First 12 hour post admission in NICU, PPV, positive pressure ventilation; NICU- neonatal intensive care unit; hr-hour; ml- millilitre; Kg- kilogram; mg- milligram; dl- decilitre, Nephrotoxic drugs included vancomycin or colistin or amphotericin B. Significant cardiac disease included hemodynamically significant patent ductus arteriosus, persistent pulmonary hypertension of the newborn, and other congenital heart disease. Inotropes included dopamine or dobutamine or epinephrine or norepinephrine

Table 2. Demographic variables (n=127)

Variables	**No.**	**Percent**
Male	76	59.8%
Female	51	40.2%
Inborn	99	78.0%
Out born	28	22.0%
Lower Segment Caesarean Section (LSCS)	92	72.4%
Normal Vaginal Delivery	35	27.6%
Primigravida	58	45.6%
Multigravida	69	54.4%

Table 3. Maternal and neonatal risk factors associated with AKI

Risk factors	AKI present(n)	AKI absent(n)	P -value
Maternal risk factors			
1. Oligohydraminos	8(57%)	6(43%)	0.008
2. Maternal diabetes	1(16.7%)	5(83.3%)	0.593
3. PIH	4(20%)	16(80%)	0.506
4. Hypothyroidism	7(64%)	4(36%)	0.003
Neonatal risk factors			
1. Gestational age			
Extremely preterm(<28weeks)	7(87.5%)	1(12.5%)	<0.001
2. Resuscitation in delivery room	27(32%)	58(68%)	0.035
3. Mechanical ventilation during NICU	31(40%)	46(60%)	<0.001
4. Perinatal asphyxia	19(41.3%)	27(58.7%)	0.003
5. Significant cardiac disease	16(52%)	15(48%)	<0.001
6. Nephrotoxic drugs use	19(35.2%)	35(64.8%)	0.034
7. Furosemide use	11(79%)	3(21%)	<0.001
8. Inotrope use	28(45%)	34(55%)	<0.001
9. Sepsis	16(38%)	26(62%)	0.028
10. APGAR at 1min	5.5(5-7)	6(5-7)	0.018
11. APGAR at 5 min	7.5(6.75-8)	8(7-9)	0.021

Table 4. Association of STARZ criteria with AKI (n=127)

Item	**AKI Present**		**AKI Absent**		**Total**	**P value**
Risk of AKI	**Number**	**Percent**	**Number**	**Percent**		
High risk (>31.5)	33	37.5%	55	62.5%	88	<0.001
Low risk (<31.5)	0	0.0%	39	100.0%	39	

Table 5. Association of STARZ criteria with AKI in predicting AKI (n=127)

Item	**AKI Present**		**AKI Absent**		**Total**	**P value**
RISK OF AKI	**Number**	**Percent**	**Number**	**Percent**		
<20%	0	0.0%	43	100.0%	43	<0.001
20-40%	3	13.6%	19	86.4%	22	
40-60%	4	19.0%	17	81.0%	21	
60-80%	2	22.2%	7	77.8%	9	
>80%	24	75.0%	8	25.0%	32	

Table 6. Staging of AKI according to the KDIGO criteria (n=33)

Stage of AKI (KDIGO classification)	**No.**	**Percent**
Stage-1	21	63.6%
Stage-2	7	21.1%
Stage-3	5	15.1%
Total	33	100

Table 7. Association of acute kidney injury with the outcome of admitted neonates (N=127)

Item	**AKI Present(n=33)**		**AKI Absent(n=94)**		**Total**	**P value**
	Number	**Percent**	**Number**	**Percent**		
No. of Deaths	21	75.0%	7	25.0%	28	<0.001
No. of Discharges	12	12.1%	87	87.9%	99	

Table 8. Incidence of mortality in various stages of AKI (According to modified KDIGO classification)

Stage of AKI	Mortality	Total	Percent
Stage-1	14	21	66.6%
Stage-2	3	7	42%
Stage-3	4	5	80%

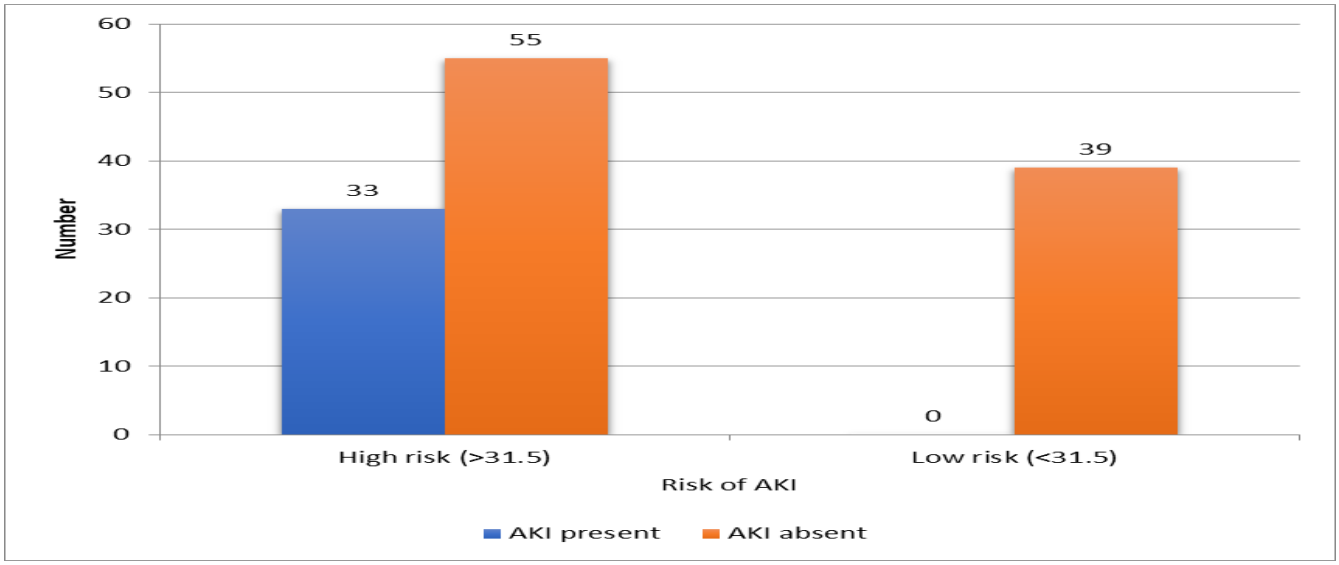

Figure (1): Association of STARZ criteria with AKI

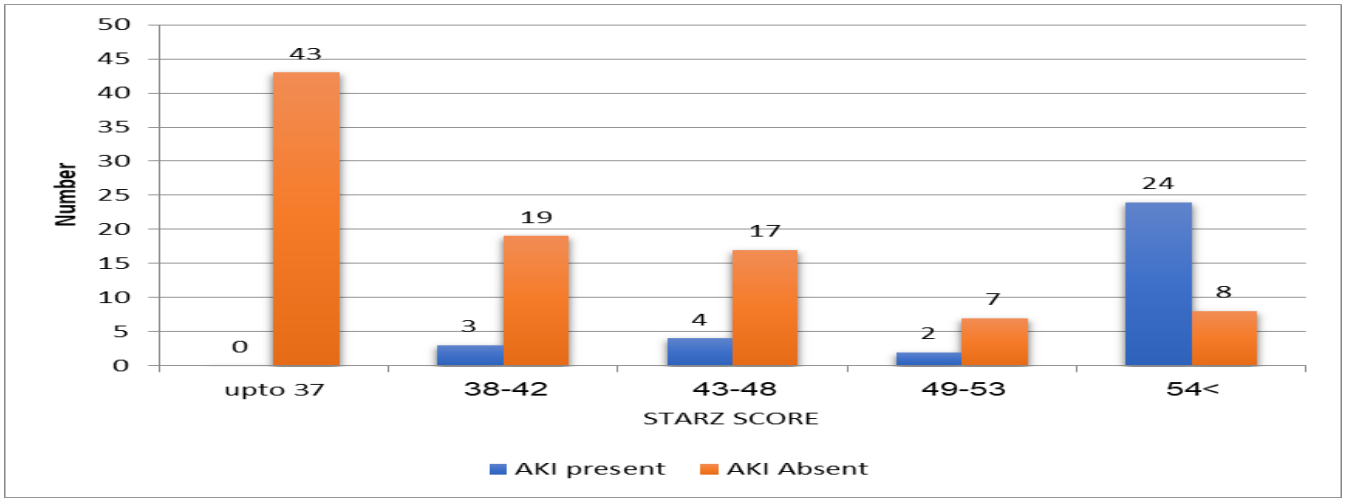

Figure (2): Association of STARZ criteria with AKI in predicting the incidence of AKI during the course of hospitalization

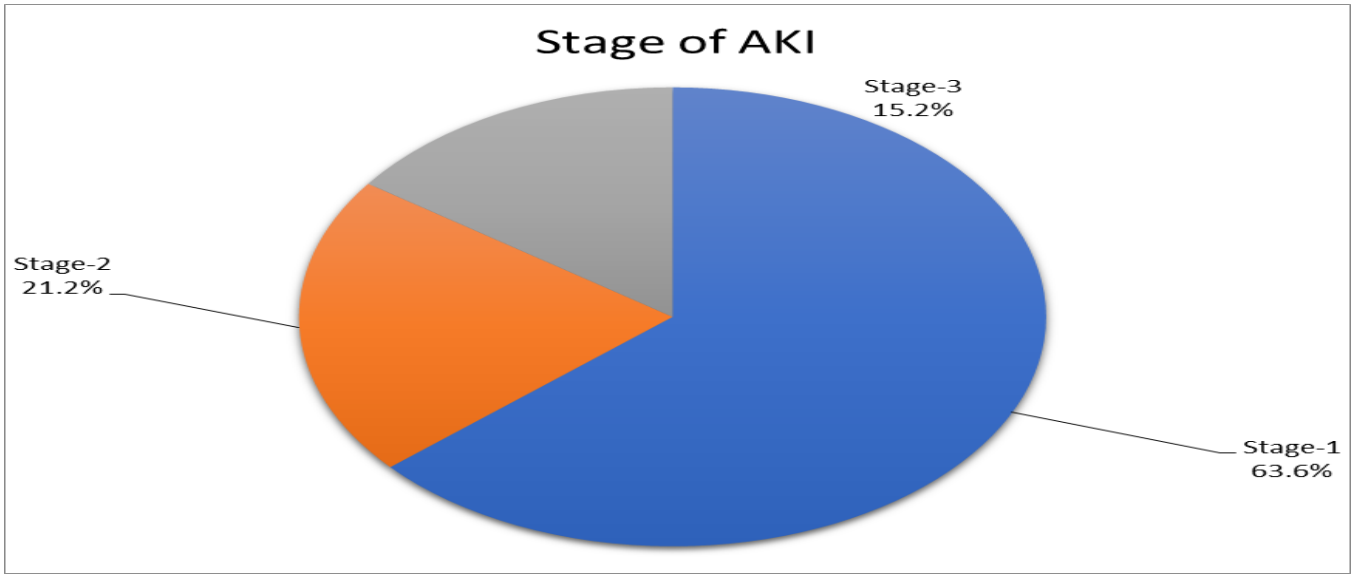

Figure (3): Staging of AKI defined according to the KDIGO classification (N=33)

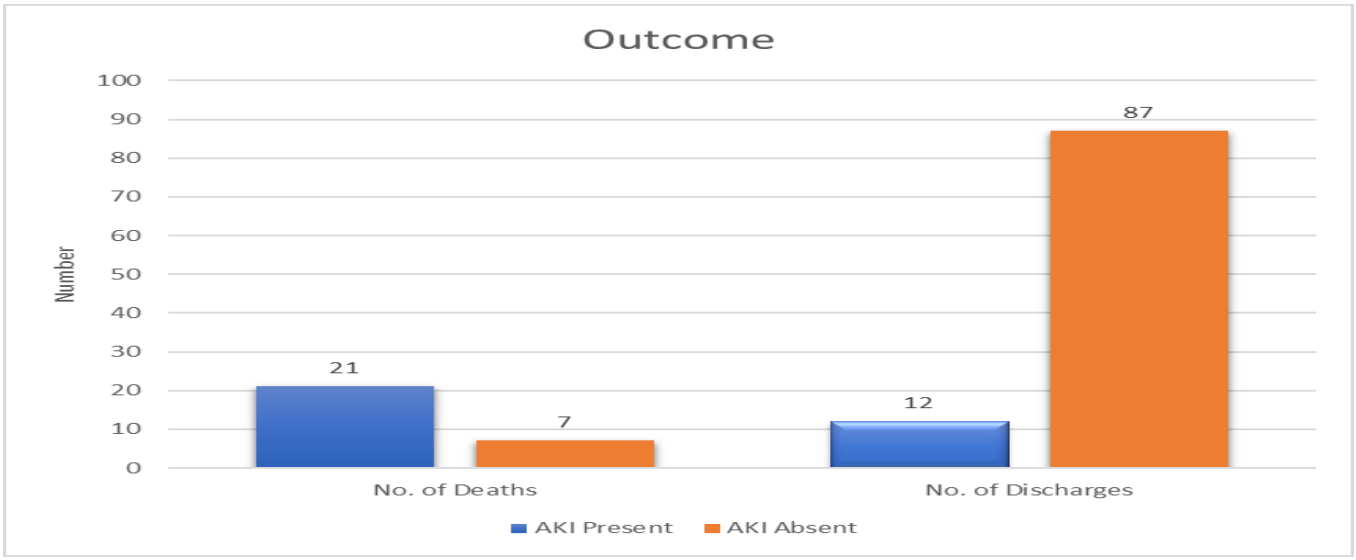

Figure (4): Association of acute kidney injury with the outcome of admitted neonates (N=127)

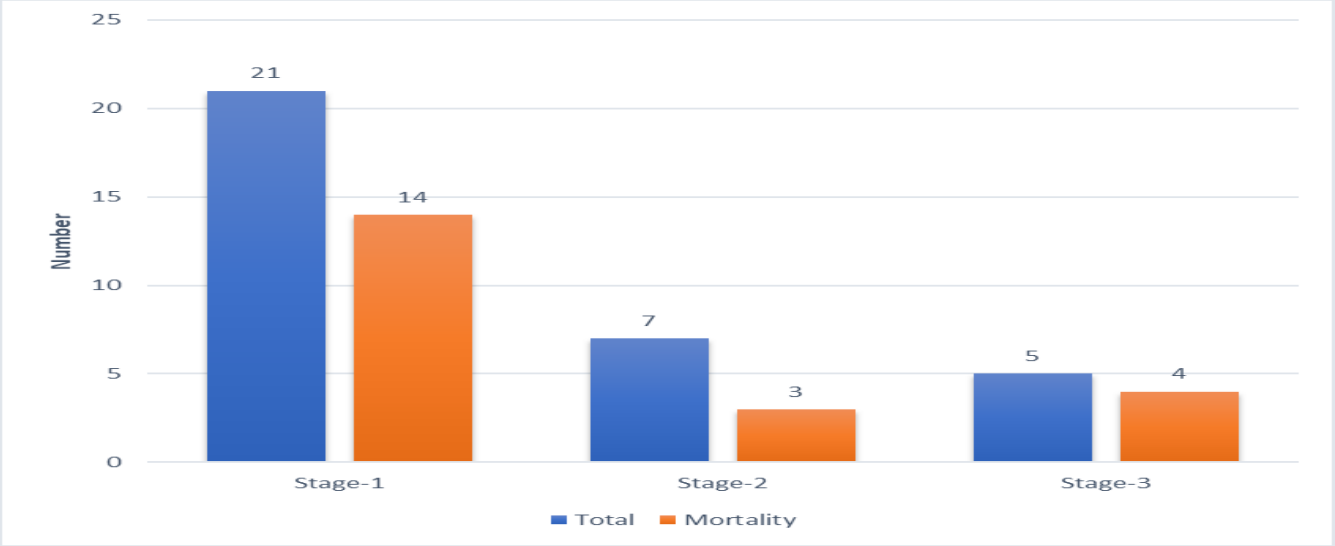

Figure (5): Incidence of mortality in various stages of AKI (according to modified KIDGO classification)

Discussion

In our study, the incidence of AKI was maximum in extremely preterm (87.5%, p value -0.001) The AWAKEN study found that the incidence of AKI varied similarly by gestational age group, with the oldest newborns (>36 weeks) and youngest neonates (22-29 weeks) having the greatest rates.2 Carmody J et al [19]. also found the incidence of AKI more in preterm population

The incidence of AKI in our study was 26%. A prospective observational study conducted at Sardar Patel Medical College, Bikaner by N. Nagaraj et al [19] incidence of AKI was 12% in hospitalized preterm neonates. The incidence of AKI in neonates enrolled in the AWAKEN study was 30 %. [2] AKI in neonates is predisposed to develop due to a variety of etiological factors; specific risk factors for AKI are present in sick neonates admitted to the NICU and may be related to immature renal physiology, maternal environment, perinatal events, and iatrogenic insults.

Incidence of AKI was low in the neonates born to mothers with pregnancy induced hypertension (20%). Similar results were seen in a study done by Kolarkal et al. [10] & Lee et al. [20] In our study, incidence of AKI was significantly higher in the neonates born to mothers with oligohydramnios (p-value - 0.008). Similar results were seen in AWAKEN study with higher incidence of acute kidney injury in neonates born to mothers with oligohydramnios with p value 0.005. [21] In our study, 27 (31.8%) neonates requiring positive pressure resuscitation in delivery room had AKI with p value of 0.035. It was further observed that the neonates with low APGAR score at 5 min had higher incidence of AKI with p value significant (0.021). Similar results were seen in a study conducted by Cataldi L et al. [22] Furthermore, in neonates with AKI, 19 (35.1%) cases were exposed to nephrotoxic drugs($p<0.034$). Neonates in the 48-bed level IV NICU at Children's Hospital of Alabama were tested for high-risk nephrotoxic medication exposure in one prospective quality improvement initiative (three nephrotoxic medications within 24 hours or 4 calendar days of an intravenous [IV] aminoglycoside). [23]

In our study, significant cardiac disease in 16 (51.6%) neonates had AKI, and most common cardiac disease was patent duct arteriosus in 13(41.9%) of the neonates. In a study conducted by Majed B et al [24], it was seen that moderate-to-large PDA was strongly associated with all stages of AKI in preterm infants $\leq$ 28 weeks of gestational age. In another study conducted by Cataladi et al [22] it was seen that patent ductus arteriosus (PDA) were diagnosed in a significantly greater percentage of preterm infants with Acute Renal Failure

Another factor in contributing to the neonatal acute kidney injury was inotropic use, 26(45.1%) neonates on inotropic support developed AKI, as compared to 5(7.7%) cases in non-ionotropic usage group (p value <0.001)

and the duration of inotropic use in neonates with acute kidney injury was more. In a study conducted by Mathur et al [25] the association of AKI with shock and inotropes was higher seen in 27 % of the neonates with p value significant. (<0.001)

Limitations

Sample size was small. Fluid therapy and usage of aminoglycosides (amikacin, gentamicin) were not compared in the AKI and non-AKI group separately, although they were administered according to the standard treatment guidelines of NICU.

Conclusions

STARZ score was simple and easy to predict the risk of AKI in neonates during anytime post 12 hours admission in NICU. Neonates in the high-risk group having high probability score were vigilantly monitored and appropriate actions were taken. In our study, 26% of the neonates had AKI of varied stages according to KDIGO classification. Neonates in AKI group had more mortality in comparison to non-AKI group. Neonates with stage 1 and 2 AKI were more in number and had less mortality in comparison to the neonates with stage 3 AKI.

Data Availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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Author's contributions

Dr. Ekamjot Kaur- Collection of Data, carried out the study and funding of the study. Dr. Preeti Malhotra- Designing and coordinated the implementation of the study. Dr. Naresh Kumar- Drafting and revision of the manuscript.

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Conflict of interest

We declared no conflict of interest concerning the study.

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