

# Determinants of the Outcomes of Acute Kidney Injury in Neonates at Kenyatta National Hospital's Paediatric Unit

Janeth Ijai Inima<sup>1\*</sup>, Dorcas Maina<sup>2</sup>, Hannah Inyama<sup>3</sup>

<sup>1,2,3</sup>Department of Nursing Sciences, University of Nairobi, Nairobi, Kenya

**Abstract:** **Background:** Neonatal acute kidney injury [AKI] is a significant health concern across the globe due to its rising incidence and association with adverse outcomes. AKI in neonates is often multifactorial and may result from prenatal, perinatal or postnatal insults or any combination thereof. An understanding of the predictors of outcomes of AKI among neonates is therefore essential. **Objective:** To assess the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital. **Methods:** We conducted a retrospective study involving a retrospective desk review of the medical records of neonates aged 1-28 days treated with AKI at Kenyatta National Hospital's pediatric unit. Medical records of 141 neonates with AKI seen in the hospital between 1st January and 31st December, 2021 were examined with data retrieved using a Data Abstraction Form. Data were analyzed through descriptive statistics while logistic regression analysis was utilized to analyze the association between the study variables at 5% significance level. **Results:** From the results, 62.4% [n = 88] of the neonates lived following treatment while 37.6% [n = 53] died. The renal function related factors found to be significant predictors of outcomes of AKI in the neonates were serum creatinine [SCr] values [ $\beta = -1.792$ ,  $p = .000$ ] and urine output values [ $\beta = 1.720$ ,  $p = .011$ ]. The treatment related factors that were significant predictors of outcomes of AKI in the neonates were stage of the AKI [ $\beta = -1.014$ ,  $p = .007$ ]; onset of AKI [ $\beta = 1.101$ ,  $p = .022$ ] and being mechanically ventilated [ $\beta = -3.788$ ,  $p = .003$ ]. Neonate related variables were, however, found not to be significant predictors of outcomes of neonatal AKI. **Conclusion:** Outcomes of AKI in neonates were largely influenced by various renal function and treatment related factors. **Recommendation:** Focus is required on efforts needed to improve outcomes of AKI in this vulnerable patient population.

**Keywords:** Acute kidney injury, mortality, neonate, serum creatinine, survival to hospital discharge, urine output.

## 1. Introduction

Acute kidney injury [AKI] is defined as an abrupt or rapid decline in renal filtration function. It is usually marked by a rise in serum creatinine [SCr] concentration or by azotemia [a rise in blood urea nitrogen [BUN] concentration] [1]. Careful evaluation of the patient is however important as rise in SCr or BUN levels could result from other causes and not necessarily renal injury [2]. In neonates, AKI is defined as an increase in SCr of at least 0.3 mg/dL [ $\geq 26.5 \mu\text{mol/l}$ ] within 48 hours or a decrease in urine output [UO] to less than 0.5 mL/kg/hour for  $\geq$

6 hours [3]. It is classified as either oliguric or nonoliguric. Oliguric AKI is characterized by a urine output of less than 1 mL/kg per hour in infants while urine flow rate above this level is termed nonoliguric AKI [4].

The exact incidence of AKI in neonates is unknown. However, available data suggests an incidence of 6 - 30% for ICU-admitted neonates, and 3 - 5% for neonates in non ICU settings, globally, with high associated mortality and morbidity [5]. The clinical presentation of AKI in neonates includes oliguria, systemic hypertension, cardiac arrhythmia, evidence of fluid overload or dehydration, decreased activity, hypotension, seizures, vomiting, abdominal pain, and anorexia [6].

In neonates, the causes of AKI are multifactorial and are classified as pre-renal, intrinsic [renal] and post-renal. Pre-renal AKI mainly results from hypoperfusion or ischemia. Intrinsic/renal AKI occurs when there is injury to the renal glomeruli, tubules, interstitium, or vessels such as from parenchyma damage, acute tubular necrosis [ATN], infections such as pyelonephritis, vascular insults and exposure to nephrotoxins. Post-renal AKI results from obstruction of the urinary tract system mainly from congenital malformations or anomalies of the urinary tract and obstructive nephropathy [7], [8].

In general, infants with prerenal acute kidney injury who receive prompt treatment for renal hypoperfusion have an excellent prognosis. Infants with post-renal acute kidney injury related to congenital urinary tract obstruction have a variable outcome which depends on the degree of associated renal dysplasia. Infants with intrinsic acute kidney injury have significant risks of morbidity and mortality [9]. Similarly, higher mortality rates among neonates with AKI have also been noted in neonates with low gestational age, very low birth weight, congenital renal anomalies, those requiring dialysis and mechanical ventilation, those with hypotension requiring inotropic support and those with underlying comorbidities [10], [11], [12].

Evidence from nephrology and critical care communities across the world, in the last decade, consistently shows that acute kidney injury [AKI] in neonates portends poor short-term

\*Corresponding author: [janethinima@gmail.com](mailto:janethinima@gmail.com)

and long-term outcomes independent of severity of illness. The evidence is clear that neonates with AKI have increased rates of mortality and longer hospital stays compared to those without AKI [10], [12]. They are also at increased risk of adverse long-term outcomes including acquiring CKD, ESKD and cardiovascular and cerebrovascular diseases with their associated adverse effects on health-related outcomes [8]. This notwithstanding, in most low resource settings, Kenya included the determinants of the outcomes of acute kidney injury in this cohort remains unclear. We therefore examined the determinants of the outcomes of AKI in neonates at the paediatric unit in Kenya's largest public referral hospital.

## 2. Methods

### A. Study Design

We adopted a retrospective study design by performing a retrospective desk review of the medical records of neonates with acute kidney injury at Kenyatta National Hospital's pediatric unit. This allowed us to gain insights on the patterns of care outcomes and associated factors in this patient cohort.

### B. Study Area

We undertook the study at the Kenyatta National Hospital's [KNH] Pediatric Unit. KNH is the country's largest public referral hospital with about 2,000 beds. It offers specialized in and out-patient services in a wide range of medical specialties. It also facilitates medical training and research and supports national healthcare planning. Neonatal patients presenting with various health conditions are cared for in the hospital's pediatric unit. Medical records of these patients are thereafter transferred to the Records Department.

### C. Study Population and Sample

Neonates diagnosed with AKI admitted to the Pediatric Unit of Kenyatta National Hospital between 1st January and 31st December, 2021 constituted the study population. A study sample of 141 neonates with AKI was selected using convenience sampling technique and hence their health records were evaluated. Health records included were those for neonates aged 1 - 28 days with neonatal AKI as the primary

diagnosis and the reason for their admission and having been born in a hospital. Patients' reports in which the AKI was incidental [not the primary diagnosis] and those missing crucial data required for the study were excluded.

### D. Data Management

We collected data using a Data Abstraction Form. The information sought included the patients' treatment outcomes as well as on select renal function, neonate and treatment related factors associated with the AKI outcomes in the study units. The study's primary outcome was death of the neonate from AKI occurring in the hospital or neonate's survival to hospital-discharge following treatment. Two well trained research assistants supported the principal investigator in the data collection exercise. We pre-tested the study tool at Mbagathi District Hospital. Retrieval of data was conducted within the confines of the hospital's registry to safeguard safety of the patients' health records. The study data was described using various descriptive statistics. Logistic regression analysis was then applied to determine the association between the predictor variables [renal function related, neonate related and treatment related determinants] and the dependent variable [treatment outcomes of AKI among the neonates] at 5% significance level. Analysis was performed using SPSS version 25.

### E. Ethical Considerations

The KNH-UoN ERC approved the study [Ref: KNH-ERC/A/12] while permission to undertake the study at KNH pediatric unit was granted by the hospital's administration with appropriate authorizations to access the targeted patients' health records also sought from relevant authorities in the hospital. Research permit was issued by NACOSTI. Obtained data were processed and reported anonymously. Safety of the patients' health records and retrieved data were also observed.

## 3. Results

### A. Demographic Characteristics of the Neonates

The demographic profile of the neonates was sought. Results demonstrated that majority of the neonates were of normal birth weight [2,500g - 4,000g], most were delivered through vaginal

Table 1  
Demographic characteristics of the neonates

Attribute		Frequency	Percentage
Gender	Male	63	44.7
	Female	78	55.3
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Age at admission	1 - 7 days	52	36.9
	8 - 14 days	59	41.8
	15 - 21 days	24	17.0
	22 - 28 days	6	4.3
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Birth weight	< 2,500g	13	9.2
	2,500g - 4,000g	123	87.2
	> 4,000g	5	3.5
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Manner in which they delivered	Vaginal birth	92	65.2
	Caesarean section [CS]	49	34.8
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Point at which the AKI was diagnosed	Within the first 7 days after birth	46	32.6
	After the first 7 days after birth	95	67.4
	<b>Total</b>	<b>141</b>	<b>100.0</b>

Table 2  
Neonates' serum creatinine values on admission

SCr values on admission	Frequency	Percentage
SCr increase of $< 3 \times$ Baseline SCr value	49	34.8
SCr increase of $\geq 3 \times$ Baseline SCr value	92	65.2
<b>Total</b>	<b>141</b>	<b>100.0</b>

Table 3  
Urine output values among the neonates

Urine output values	Frequency	Percentage
Non-extreme oliguria $< 0.5$ mL/kg/h for 6 - 12 hours	32	22.7
Extreme oliguria $< 0.5$ mL/kg/h for $> 12$ hours	109	77.3
<b>Total</b>	<b>141</b>	<b>100.0</b>

Table 4  
Neonate related factors

		Frequency	Percentage
Gestational age at birth	Term	136	96.5
	Preterm	5	3.5
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Birth weight	$< 2,500$ g	13	9.2
	2,500g - 4,000g	123	87.2
	$> 4,000$ g	5	3.5
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Suffered from fetal growth restriction	Yes	1	0.7
	No	140	99.3
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Apgar scores Minute 1	0 - 3	1	0.7
	4 - 6	5	3.5
	$\geq 7$	135	95.7
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Minute 5	0 - 3	0	0.0
	4 - 6	3	2.1
	$\geq 7$	138	97.9
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Had comorbidities	Yes	14	9.9
	No	127	90.1
	<b>Total</b>	<b>141</b>	<b>100.0</b>

birth and a considerable proportion of them were diagnosed with AKI after the first week of their birth. Results are summarized in Table 1.

#### B. Treatment Outcomes of AKI Among the Neonates

We evaluated the treatment outcomes of acute kidney injury [AKI] in neonates at KNH's pediatric unit for the study period. From the findings, 62.4% [n = 88] of the neonates survived to hospital discharge following treatment at KNH while 37.6% [n = 53] died from AKI in the hospital.

#### C. Renal Function Related Factors

We sought to establish the renal function related determinants of the outcomes of acute kidney injury in neonates at Kenyatta National Hospital's paediatric unit. In this regard, we assessed the neonates' serum creatinine [SCr] and urine output values at admission.

Serum creatinine values at admission were classified into two categories, on the basis of the kidney disease: Improving Global Outcomes [KDIGO] AKI working group [KDIGO Clinical Practice Guideline for Acute Kidney Injury, 2012] [Gohiya et al., 2022]. The two categories were neonates with SCr increase of 3 times or more of the Baseline SCr value [that is, the lowest previous SCr value] and neonates with SCr increase of less than 3 times of the Baseline SCr value. Results on the neonates' serum creatinine levels are depicted in Table 2.

Urine output values, recorded at point of admission and at

point intervals of 6 hours, 12 hours and 24 hours after admission, were classified on the basis of the KDIGO AKI working group [KDIGO Clinical Practice Guideline for Acute Kidney Injury, 2012] as either '*extreme oliguria*' denoting neonates with less than 0.5 mL/kg/h for more than 12 hours or '*non-extreme oliguria*' denoting neonates with urine output of less than 0.5 mL/kg/h for 6 - 12 hours. Results on the neonates' urine output levels are illustrated in Table 3.

#### D. Neonate Related Factors

We sought to establish the neonate related determinants of the outcomes of acute kidney injury in neonates at Kenyatta National Hospital's paediatric unit. The neonate related variables probed included gestational age at birth, birth weight, fetal growth restriction, Apgar scores at minutes 1 and 5, and comorbidities.

Results indicated that majority of the neonates were born at term [96.5%, n = 136]; had normal birth weight [2,500g - 4,000g] [87.2%, n = 123]; did not suffer from fetal growth restriction [99.3%, n = 140] and had no comorbidities [90.1%, n = 127]. In addition, majority of the neonates had Apgar scores of 7 or more at both minute intervals, as is illustrated in Table 4.

#### E. Treatment Related Factors

We sought to assess the treatment related determinants of the outcomes of acute kidney injury in neonates at Kenyatta

Table 5  
Neonate related factors

		Frequency	Percentage
Stage of the AKI	Stage 1 [urine output of <0.5 mL/kg/h for 6 - 12 hours]	32	22.7
	Stage 2 [urine output of <0.5 mL/kg/h for > 12 hours]	17	12.1
	Stage 3 [urine output of <0.3 mL/kg/h for $\geq$ 24 hours or anuria for $\geq$ 12 hours]	92	65.2
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Onset of AKI	Early onset AKI [AKI diagnosed within the first 7 days after birth]	46	32.6
	Late onset AKI [AKI diagnosed after the first 7 days after birth]	95	67.4
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Whether the neonate was mechanically ventilated	Yes	14	9.9
	No	127	90.1
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Whether the neonate was dialysed	Yes	76	53.9
	No	65	46.1
	<b>Total</b>	<b>141</b>	<b>100.0</b>
Neonate exposed to nephrotoxins	Yes	53	37.6
	No	88	62.4
	<b>Total</b>	<b>141</b>	<b>100.0</b>

Table 7  
Model summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	126.960 <sup>a</sup>	.345	.470

a. Estimation terminated at iteration number 20 because maximum iterations has been reached.

Table 8  
The model's predictive accuracy

Classification Table <sup>a</sup>					
Observed			Predicted		Percentage Correct
			Patient's treatment outcomes		
			Positive outcome	Poor outcome	
Step 1	Patient's treatment outcomes	Neonate lived	82	6	93.2
		Neonate died	21	32	60.4
Overall Percentage					80.9

a. The cut value is .500

National Hospital's paediatric unit. The treatment related variables probed included stage of the AKI, onset of AKI, whether the neonates were mechanically ventilated, whether the neonates were dialysed and whether the neonates were exposed to nephrotoxins.

Results indicated that most of the neonates had Stage 3 AKI [65.2%, n = 92]; had late onset AKI [67.4%, n = 95] and were not mechanically ventilated [90.1%, n=127]. Results also showed that slightly over half [53.9%, n = 76] underwent dialysis and most [62.4%, n = 88] of the neonates were not exposed to nephrotoxins as depicted in Table 5.

#### F. Associations of the Various Determinants with Outcomes of Acute Kidney Injury in Neonates

We utilized logistic regression analysis, at 5% significance level, to ascertain the association between the predictor variables [renal function, neonate and treatment related factors and the explained variable [outcomes of acute kidney injury in neonates]. Results of the logistic regression analysis are hereby described.

Omnibus tests of model coefficients is a test of the null hypothesis that adding the predictor variables to the model has not significantly increased our ability to predict the study's dependent variable [outcomes of AKI in neonates]. This null hypothesis was however rejected as the test yielded significance values of .000 implying that addition of the study's predictor variables to the logistic regression model notably increased our ability to predict the study's dependent variable. Results appear in Table 6.

Table 6  
Omnibus tests of model coefficients

		Chi-square	df	Sig.
Step 1	Step	59.728	12	.000
	Block	59.728	12	.000
	Model	59.728	12	.000

Model summary results depict that the -2 Log Likelihood statistic is 126.96 which denotes that the adopted logistic regression model fairly predicts the outcomes of AKI in neonates. The Cox & Snell R<sup>2</sup> and the Nagelkerke R<sup>2</sup> values denote that the model predicted 34.5% and 47% of the changes in the study's dependent variable, respectively [Table 7].

Further, Table 8 shows that the logistic regression model has an overall success rate of 80.9% in correctly matching predicted events with the observed events. This meant that the model has an aggregate 80.9% ability of correctly predicting the outcome of AKI in neonates, signifying good predictive accuracy.

From the model coefficient results table, the predictor variables found to have a statistically significant association with the outcomes of acute kidney injury in neonates were serum creatinine values [ $\beta$  = -1.792, df = 1, p = .000]; urine output values [ $\beta$  = 1.720, df = 1, p = .011]; stage of the AKI [ $\beta$  = -1.014, df = 1, p = .007]; onset of AKI [ $\beta$  = 1.101, df = 1, p = .022] and whether the neonate was mechanically ventilated [ $\beta$  = -3.788, df = 1, p = .003]. The results are demonstrated in Table 9.

## 4. Discussion

We established that most of the neonates had a serum

Table 9  
Model coefficients results

		$\beta$	S.E.	Wald	df	Sig.	Exp[ $\beta$ ]
Step <sup>a</sup> 1	Serum creatinine	-1.792	.458	15.277	1	.000	6.000
	Urine output	1.720	.678	6.445	1	.011	5.585
	Gestational age	-.522	1.683	.096	1	.756	.593
	Birth weight	-1.196	.727	2.707	1	.100	.302
	Fetal growth restriction	-.543	1.751	1.751	1	.186	.581
	Apgar scores at minute 5	-2.036	1.417	2.065	1	.151	.131
	Having comorbidities	-1.100	.770	2.042	1	.153	.333
	Stage of the AKI	-1.014	.375	7.306	1	.007	2.755
	Onset of AKI	1.101	.567	4.776	1	.022	3.008
	Mechanical ventilation	-3.788	1.268	8.929	1	.003	.023
	Being dialysed	.506	.531	.910	1	.340	1.659
	Exposure to nephrotoxins	.007	.476	.000	1	.987	1.008
	Constant	2.215	4.244	4.244	1	.019	3.417

a. Variable[s] entered on step 1: serum creatinine, urine output, gestational age, birth weight, fetal growth restriction, Apgar scores at minute 5, comorbidities, stage of the AKI, onset of AKI, mechanical ventilation, being dialysed, exposure to nephrotoxins.

creatinine increase of 3 times or more of their Baseline SCr value [the lowest previous SCr value] at admission. Serum creatinine values at admission were found to have an inverse relationship with outcomes of AKI in neonates which was statistically significant as denoted by logistic regression beta coefficient value of -1.792 and p value of .000. The Exp[ $\beta$ ] value of 6 signified that the odds of a neonate living significantly increased with every unit decline in serum creatinine values and vice-versa. The findings therefore illustrated that high serum creatinine levels were a significant predictor of poor outcome of AKI in neonates and vice-versa. Likewise, Pantoja-Gómez et al. [13] in a multi-facility study in Colombia also identified increases in SCr values of 3 or more above the Baseline SCr measurement as portending greater risk of poor outcome compared to lower increases in SCr values. Bansal et al. [14] in a study performed in India made similar observations with serum creatinine increases of 3 or more times above the Baseline SCr found to have a significant correlation with poor outcomes of neonatal acute kidney injury compared to milder increases of serum creatinine such as those of less than 2 times the Baseline SCr value. AlGadeeb et al. [15] also observed that poor outcome manifested as increased mortality was evident among neonates with SCr increase of  $\geq 3$  of the Baseline SCr compared to neonates with SCr increase of  $\geq 1.5$  to 1.9 of the Baseline SCr within a 7 day period, an observation also echoed by Shalaby et al. [16] and Gallo et al. [17] clearly signifying that significant increases in serum creatinine levels were a notable predictor of poor outcomes of AKI in neonates.

We also established that a significant proportion of the neonates suffered from extreme oliguria marked by urine output of less than 0.5 mL/kg/h for more than 12 hours at admission. Further, a statistically significant positive association was also established between urine output values and the outcome of AKI in the neonates as denoted by logistic regression beta coefficient value of 1.720 and p value of .011 which signified a positive relationship between urine output values at admission and outcomes of AKI in neonates. The Exp[ $\beta$ ] value of 5.585 signified that the odds of a neonate living significantly increased with every unit increase in urine output level and vice-versa.

The findings therefore illustrated that urine output values were a significant predictor of outcomes of AKI in neonates. Similarly, in a study of AKI outcomes in neonates, Timovska

et al. [18] also concluded that neonatal oliguric AKI marked by urine output of <1 mL/kg per hour portended greater risk of poor outcomes compared to neonatal nonoliguric AKI denoted by urine output of >1 mL/kg per hour in the first weeks after birth. Fan et al. [19] and Pantoja-Gómez et al. [13] also noted increased odds of poor outcomes of acute kidney injury in neonates with urine output of less than 1 mL/kg per h on postnatal days 2 - 7 compared to those with urinary output of greater than 1 mL/kg per h over the said period. Low urine output levels were also cited as significant predictors of poor outcomes of AKI in neonates in studies by Esezobor et al. [20] and Mwamanenge et al. [21] signifying that lower UO levels constituted a notable determinant of poor outcomes of acute kidney injury in neonates.

Further, we established that majority of the neonates were born at term and that no statistically significant association was established between the neonates' gestational age at birth and outcomes of acute kidney injury in the neonates as denoted by p value of .756. The odds of the neonates living relative to dying based on their gestational age at birth was also low as depicted by an Exp[ $\beta$ ] value of .593. Hence, in our study, gestational age at birth was not a significant determining factor of outcomes of AKI in neonates. In contrast, studies by Lee et al. [22] and Shalaby et al. [16] as well as those of Mwamanenge et al. [21], Hu et al. [23] and Sanderson et al. [24] [2022] all established a significant relationship between neonates' gestational age at birth and outcomes of AKI in neonates with prematurity identified as a significant predictor of poor outcomes of AKI in neonates. The cited studies attributed the increased odds of poor neonatal AKI outcomes in preterm neonates to possible incomplete or poor nephrogenesis. The lack of association between gestational age at birth and neonatal AKI outcomes in our study could be due to the small proportion of preterm neonates in the study group or effective management of prematurity cases.

Results of our study also indicated that most of the neonates had normal birth weight [2,500g - 4,000g]. A logistic regression beta coefficient value of -1.196 signified that the association between birth weight and outcomes of AKI in neonates was negative though a p value of .100 signified that the association between birth weight and outcomes of acute kidney injury in the neonates was not statistically significant. Further, an Exp[ $\beta$ ] value of .302 denoted low odds of the neonates dying relative

to living on the basis of their birth weight. Hence, in our study, birth weight was not a notable predictor of outcomes of acute kidney injury in neonates. In contrast, reviews by Lee et al. [22] and Hu et al. [23] reported low birth weight as being a significant determinant of poor outcomes of acute kidney injury in neonates, an observation also echoed by Jetton et al. [10], Ademola et al. [25] and Nandhagopal et al. [26]. They attributed the identified link to possible poor nephron development in the low birth weight neonates as most are often born preterm. The low proportion of low birth weight neonates or their effective management/care could be the reason behind the no association findings in our study.

Results of our study also showed that a significant proportion of the neonates had Apgar scores of 7 or more at both minute intervals [at minute 1 and minute 5] signifying that most of the neonates were well or in good health at and following birth. The logistic regression beta coefficient value of -2.036 signified that the association between the Apgar score at minute 5 and the outcomes of AKI in neonates was negative. However, the association between the neonates' Apgar scores at minute 5 and the outcomes of acute kidney injury in the neonates was not statistically significant as denoted by logistic regression p value of .151. Hence, in our study, the neonates' Apgar score at minute 5 was not a significant predictor of outcomes of AKI among the neonates. In contrast, neonates with Apgar scores of below 7 in the 5th minute were found to have greater odds of poor outcomes of AKI compared to those who had Apgar scores of 7 or more at minute 5 as reported by Nandhagopal et al. [26] and Stojanović et al. [27]. Jetton et al. [10] and Harer et al. [28] also reported the association between Apgar scores at minute 5 and outcomes of AKI in neonates as being significant. We attribute our contrasting findings to the high Apgar scores in both minute intervals implying that the surveyed neonates were in good health after birth.

We also established that the bulk of the neonates, in our study, did not have comorbidities. The association between comorbidities and outcomes of acute kidney injury in neonates was negative as signified by beta coefficient value of -1.100; however, the relationship was not statistically significant as denoted by logistic regression p value of .153. The odds of living relative to dying on the basis of comorbidities was low as denoted by an  $\text{Exp}[\beta]$  value of .333. Hence, in our study, comorbidities were not a major determinant of outcomes of AKI among the neonates. In contrast, studies by Bansal et al. [14] and Momtaz et al. [29] identified neonatal comorbidities as being a significant determinant of poor outcomes of AKI in neonates. Similar views were shared in studies by Perico et al. [30] and Gallo et al. [17] who also identified neonatal comorbidities as being leading contributors of adverse outcomes of AKI in neonates. We therefore attribute our contrasting findings to the low number of neonates that had comorbidities in our study group.

We also established that most of the neonates had Stage 3 AKI marked by urine output of  $< 0.3 \text{ mL/kg/h}$  for  $\geq 24$  hours or anuria for  $\geq 12$  hours as per the 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury. In addition, a statistically significant negative association was established between the

stage of AKI and outcomes of acute kidney injury among the neonates as denoted by logistic regression beta coefficient value of -1.014 and p value of .007 while the  $\text{Exp}[\beta]$  value of 2.755 signified increased odds of poor outcome of AKI in the neonates with relation to advancing stage of the AKI. Hence, stage of AKI was a significant determinant of outcomes of acute kidney injury in neonates. Similarly, in studies by Katariya and Pandya [31] and Ramesh [32], neonatal AKI outcomes were found to be significantly influenced by the neonates' stage of AKI. Notable associations of stage of AKI with outcomes of AKI in neonates were also reported in studies by Bansal et al. [14], Fan et al. [19] and AlGadeeb et al. [15] with increased odds of neonates dying with advanced stages of AKI. It was therefore safe to say that poor outcomes of AKI in neonates correlated with increased severity of the AKI as denoted by its stage.

We further established that most of the neonates were diagnosed with late onset AKI - AKI diagnosed after the first 7 days after birth. Further, the association between onset of AKI and outcomes of acute kidney injury in the neonates was established to be statistically significant as denoted by logistic regression p value of .022. Diagnosis with late onset AKI increased odds of the neonates dying from the AKI compared to an early onset AKI diagnosis as depicted by an  $\text{Exp}[\beta]$  value of 3.008, which implied that onset of AKI affected outcomes of acute kidney injury in neonates. Ramesh [32] and Nandhagopal et al. [26] made similar observation that outcomes of AKI were significantly influenced by onset of AKI. Similarly, Mattoo et al. [7], Vincent et al. [33] and Starr et al. [8] did also point that outcomes of AKI in neonates were influenced by onset of AKI with late onset of AKI portending adverse outcomes of AKI in neonates relative to early onset of AKI. Onset of AKI was therefore a significant determinant of the outcomes of AKI in neonates.

From the results, majority of the neonates were not mechanically ventilated. We also established that a statistically significant negative association existed between need for mechanical ventilation and outcomes of acute kidney injury in the neonates as depicted by logistic regression beta coefficient value of -3.788 and p value of .003. However, the odds of living relative to dying on the basis of mechanical ventilation were low as depicted by an  $\text{Exp}[\beta]$  value of .023. Based on the findings, it was clear that being mechanically ventilated had adverse effect on the outcomes of AKI among the neonates. Bakr et al. [34] and AlGadeeb et al. [15] made similar observations noting that mechanical ventilation had significant influence on the outcomes of AKI in neonates and correlated more with adverse neonatal AKI outcomes, sentiments also shared by Esezobor et al. [20], Kavanaugh et al. [5] and Sanderson et al. [24]. In these studies, the higher odds of poor neonatal AKI outcome in mechanically ventilated neonates was attributed to MV related complications such as severe nosocomial infection and hemodynamic instability. We attribute the negative influence of mechanical ventilation on outcomes of AKI in neonates to possible compromised respiratory function and potential complications of mechanical ventilation in this vulnerable cohort.

Results of the study also indicated that slightly above half of the neonates underwent peritoneal dialysis largely on more than a day while the remaining did not undergo dialysis. However, the association between neonatal dialysis and outcomes of acute kidney injury in the neonates was not statistically significant as denoted by logistic regression p value of .340 though a beta coefficient value of .506 denoted that the association was positive. The likelihood of neonates living relative to dying based on whether they underwent dialysis was at 1.659. Hence, in our study, neonatal dialysis was not a leading determinant of outcomes of acute kidney injury among the neonates. In contrast studies by Shalaby et al. [16], Katariya and Pandya [31] and Momtaz et al. [29] all identified neonatal dialysis as being a leading predictive factor for poor outcomes of AKI in neonates during the neonatal period, an observation also echoed by Stojanović et al. [27] and Pantoja-Gómez et al. [13].

Results of the study also indicated that most of the neonates were not exposed to nephrotoxins. The association between exposure to nephrotoxins and outcomes of acute kidney injury among the neonates was found to be weak and not statistically significant as denoted by logistic regression beta coefficient value of .007 and p value of .987. In addition, the odds of the neonates living relative to dying based on exposure to nephrotoxins was also relatively low as depicted by an Exp[B] value of 1.008. Hence, exposure to nephrotoxins was not a leading predictor of outcomes of acute kidney injury in neonates in our study which could possibly be attributed to protocols put in place to safeguard neonates with AKI against exposure to nephrotoxins at the study area. Likewise, studies by Kupferman et al. [35] and Luna et al. [9] also did not identify a significant relationship between exposure to nephrotoxins and outcomes of acute kidney injury among surveyed neonates, which they attributed to existence of strict protocols aimed at safeguarding against exposure to nephrotoxins among admitted AKI neonatal patients. In contrast, though, studies by Sethi et al. [11], Jetton et al. [10] and Nada et al. [4] identified exposure to nephrotoxins as being a leading determinant of outcomes of acute kidney injury in affected neonates. Hence, it is plausible to say that exposure to nephrotoxins would be a risk factor for poor outcomes of acute kidney injury in neonates in settings with poor or inadequate control measures.

## 5. Conclusion

Outcomes of acute kidney injury in neonates at KNH in 2021 were either positive [where the neonates lived or survived to hospital discharge following treatment] or poor [where the neonates died from the illness]. High serum creatinine and low urine output levels at admission, advanced stage of the AKI, late onset of AKI and being mechanically ventilated correlated with poor outcome of acute kidney injury in neonates in the hospital.

## 6. Recommendations

Renal health care team at KNH should make timely therapeutic efforts aimed at preventing progression of AKI in neonates to help improve neonatal AKI outcomes. For the

hospital records keepers, continued review of documented data on the outcomes of AKI in neonates at KNH is necessary to establish prognostic factors and to help the health care team identify priority areas of concern that merit immediate action so as to improve treatment outcomes of this cohort and hence reduce the burden of AKI in neonates in the hospital. There is also need for policies, strategies and interventions aimed at improving the outcomes of acute kidney injury in this highly vulnerable patient population in the hospital. A follow up on the long-term outcomes of neonatal acute kidney injury post-discharge is also required for a deeper understanding of the condition and its long-term sequelae.

*Study Limitation:* Views of health care practitioners on the study subject were not evaluated.

## References

- [1] Askenazi, D. J. (2020). AWAKEN-ing a new frontier in neonatal nephrology. *Frontiers in Pediatrics*, 8, 21.
- [2] Levey, A. S., & James, M. T. (2017). Acute kidney injury. *Annals of internal medicine*, 167(9), ITC66-ITC80.
- [3] Ostermann, M., Bellomo, R., Burdmann, E. A., Doi, K., Endre, Z. H., Goldstein, S. L., & Zarbock, A. (2020). Controversies in acute kidney injury: conclusions from a kidney disease: Improving Global Outcomes (KDIGO) Conference. *Kidney international*, 98(2), 294-309.
- [4] Nada, A., Bonachea, E. M., & Askenazi, D. J. (2017, April). Acute kidney injury in the fetus and neonate. In *Seminars in Fetal and Neonatal Medicine*, Vol. 22, No. 2, pp. 90-97, WB Saunders.
- [5] Kavanaugh, K. J., Jetton, J. G., & Kent, A. L. (2021). Neonatal acute kidney injury: Understanding of the impact on the smallest patients. *Critical Care Clinics*, 37(2), 349-363.
- [6] Ueno, K., Shiokawa, N., Takahashi, Y., Nakae, K., Kawamura, J., Imoto, Y., & Kawano, Y. (2020). Kidney disease: improving global outcomes in neonates with acute kidney injury after cardiac surgery. *Clinical and Experimental Nephrology*, 24(2), 167-173.
- [7] Mattoo, T. K., Martin, R., Stapleton, F. B., & Kim, M. S. (2019). Neonatal acute kidney injury: pathogenesis, etiology, clinical presentation and diagnosis. *UpToDate*, 20, 1-26.
- [8] Starr, M. C., Charlton, J. R., Guillet, R., Reidy, K., Tipple, T. E., Jetton, J. G., ... & Harer, M. W. (2021). Advances in neonatal acute kidney injury. *Pediatrics*, 148(5), e2021051220.
- [9] Luna, S. A., Akter, S., Jesmin, T., Haque, S. S., Uddin, G. M., & Roy, R. R. (2021). Risk Factors and Primary Diseases Responsible for Acute Kidney Injury among Neonates. *Journal*
- [10] Jetton, J. G., Boohaker, L. J., Sethi, S. K., Wazir, S., Rohatgi, S., Soranno, D. E., & Wintermark, P. (2017). Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study. *The lancet child & adolescent health*, 1(3), 184-194.
- [11] Sethi, S. K., Bunchman, T., Chakraborty, R., & Raina, R. (2021). Pediatric acute kidney injury: New advances in the last decade. *Kidney Research and Clinical Practice*, 40(1), 40-51.
- [12] Gohiya, P., Nadkarni, J., & Mishra, M. (2022). Study of neonatal acute kidney injury based on KDIGO criteria. *Pediatrics & Neonatology*, 63(1), 66-70.
- [13] Pantoja-Gómez, O. C., Realpe, S., Cabra-Bautista, G., Restrepo, J. M., Prado, O. L., Velasco, A. M., & Calvache, J. A. (2022). Clinical course of neonatal acute kidney injury: multi-center prospective cohort study. *BMC pediatrics*, 22(1), 1-7.
- [14] Bansal, S. C., Nimbalkar, A. S., Kungwani, A. R., Patel, D. V., Sethi, A. R., & Nimbalkar, S. M. (2017). Clinical profile and outcome of newborns with acute kidney injury in a level 3 neonatal unit in Western India. *Journal of Clinical and Diagnostic Research: JCDR*, 11(3), SC01-SC04.
- [15] AlGadeeb, K., Qaraqei, M., Algadeeb, R., Faqeehi, H., & Al-Matary, A. (2021). Prediction of risk factors and outcomes of neonatal acute kidney injury. *Journal of Nephrology*, 34(5), 1659-1668.
- [16] Shalaby, M. A., Sawan, Z. A., Nawawi, E., Alsaedi, S., Al-Wassia, H., & Kari, J. A. (2018). Incidence, risk factors, and outcome of neonatal acute kidney injury: a prospective cohort study. *Pediatric Nephrology*, 33(9), 1617-1624.

- [17] Gallo, D., de Bijl-Marcus, K. A., Alderliesten, T., Lilien, M., & Groenendaal, F. (2021). Early acute kidney injury in preterm and term neonates: Incidence, outcome, and associated clinical features. *Neonatology*, 118(2), 174-179.
- [18] Timovska, S. N., Bojadzieva, S., Sofijanovska, A., Shuperliska, E., Kirovski, I., & Jordanova, O. (2021). Incidence, risk factors and outcomes of acute kidney injury in preterm newborns. *Journal of Morphological Sciences*, 4(1), 40-45.
- [19] Fan, Y., Ye, J., Qian, L., Zhao, R., Zhang, N., Xue, L., & Jiang, L. (2019). Risk factors and outcomes of acute kidney injury in ventilated newborns. *Renal Failure*, 41(1), 995-1000.
- [20] Esezobor, C. I., Ladapo, T. A., Osinaike, B., & Lesi, F. E. A. (2019). Paediatric acute kidney injury in a tertiary hospital in Nigeria: prevalence, causes and mortality rate. *PloS one*, 7(12), e51229.
- [21] Mwamanenge, N. A., Assenga, E., & Furia, F. F. (2020). Acute kidney injury among critically ill neonates in a tertiary hospital in Tanzania; Prevalence, risk factors and outcome. *Plos one*, 15(2), e0229074.
- [22] Lee, C. C., Chan, O. W., Lai, M. Y., Hsu, K. H., Wu, T. W., Lim, W. H., & Lien, R. (2017). Incidence and outcomes of acute kidney injury in extremely-low-birth-weight infants. *PLoS One*, 12(11), e0187764.
- [23] Hu, Q., Li, S. J., Chen, Q. L., Chen, H., Li, Q., & Wang, M. (2021). Risk Factors for Acute Kidney Injury in Critically Ill Neonates: A Systematic Review and Meta-Analysis. *Frontiers in Pediatrics*, 660(3), 507-515.
- [24] Sanderson, K. R., Warady, B., Carey, W., Tolia, V., Boynton, M. H., Benjamin, D. K., & Greenberg, R. G. (2022). Mortality Risk Factors among Infants Receiving Dialysis in the Neonatal Intensive Care Unit. *The Journal of pediatrics*, 242, 159-165.
- [25] Ademola, A. D., Asinobi, A. O., Ekpe-Adewuyi, E., Ayede, A. I., Ajayi, S. O., Raji, Y. R., & Samuel, S. M. (2019). Acute kidney injury among paediatric emergency room admissions in a tertiary hospital in South West Nigeria: a cohort study. *Clinical Kidney Journal*, 12(4), 521-526.
- [26] Nandhagopal, N., Firdaus, U., Ali, S. M., & Afzal, K. (2020). Incidence, risk factors, and outcome of acute kidney injury in hospitalized term newborns. *Journal of Clinical Neonatology*, 9(2), 121-124.
- [27] Stojanović, V., Barišić, N., Radovanović, T., Bjelica, M., Milanović, B., & Doronjski, A. (2017). Acute kidney injury in premature newborns—definition, etiology, and outcome. *Pediatric nephrology*, 32(10), 1963-1970.
- [28] Harer, M. W., Selewski, D. T., Kashani, K., Basu, R. K., Gist, K. M., Jetton, J. G., & Askenazi, D. J. (2021). Improving the quality of neonatal acute kidney injury care: neonatal-specific response to the 22nd Acute Disease Quality Initiative (ADQI) conference. *Journal of Perinatology*, 41(2), 185-195.
- [29] Momtaz, H. E., Sabzehei, M. K., Rasuli, B., & Torabian, S. (2021). The main etiologies of acute kidney injury in the newborns hospitalized in the neonatal intensive care unit. *Journal of Clinical Neonatology*, 3(2), 99-102.
- [30] Perico, N., Askenazi, D., Cortinovis, M., & Remuzzi, G. (2018). Maternal and environmental risk factors for neonatal AKI and its long-term consequences. *Nature Reviews Nephrology*, 14(11), 688-703.
- [31] Katariya, K. L., & Pandya, N. K. (2019). Clinical profile of neonates with acute renal injury in neonatal intensive care unit at GMERS Medical College and General Hospital, Gotri, Vadodara, Gujarat, India. *International Journal of Contemporary Pediatrics*, 6(3), 1136-1142.
- [32] Ramesh, S. (2018). Predisposing factors and outcome of acute kidney injury in neonates. *Indian Journal of Child Health*, 5(1), 46-49.
- [33] Vincent, K., Murphy, H. J., Ross, J. R., Twombly, K. E., Harris-Haman, P. A., & Zukowsky, K. (2020). Acute kidney injury guidelines are associated with improved recognition and follow-up for neonatal patients. *Advances in Neonatal Care*, 20(4), 269-275.
- [34] Bakr, A., Eid, R., Allam, N. A., & Saleh, H. (2018). Neonatal acute kidney injury: diagnostic and therapeutic challenges. *Journal of Nephrology Research*, 4(1), 130-134.
- [35] Kupferman, J. C., Yitayew, M., & Rastogi, S. (2018). Acute kidney injury in term neonates. *Current Treatment Options in Pediatrics*, 4(3), 386-403.