DETERMINANTS OF THE OUTCOMES OF ACUTE KIDNEY INJURY IN NEONATES AT THE PAEDIATRIC UNIT OF KENYATTA NATIONAL HOSPITAL

By

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DECLARATION

This thesis is my own personal work and has not been submitted to any other institution for examination purposes or award of credit.

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To my family - for all the shared memories, love and inspiring words.

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ABBREVIATIONS AND ACRONYMS

AKI	Acute Kidney Injury
ATN	Acute Tubular Necrosis
BUN	Blood Urea Nitrogen
CHD	Congenital Heart Disease
CKD	Chronic Kidney Disease
ESKD	End Stage Kidney Disease
FGR	Fetal growth restriction
GFR	Glomerular Filtration Rate
HICs	High Income Countries
ICU	Intensive Care Unit
IMV	Invasive Mechanical Ventilation
IUGR	Intrauterine Growth Restriction
KDIGO	Kidney Disease: Improving Global Outcomes
KNH	Kenyatta National Hospital
LBW	Low Birth Weight
LMICs	Low and Middle Income Countries
MV	Mechanical Ventilation
NBU	Newborn Unit
NEC	Necrotizing Enterocolitis

NICU	Neonatal Intensive Care Unit
RDS	Respiratory Distress Syndrome
RRT	Renal Replacement Therapy
SCr	Serum Creatinine
SDGs	Sustainable Development Goals
SPSS	Statistical Package for Social Sciences
UO	Urine Output
UoN	University of Nairobi
US	United States

OPERATIONAL DEFINITION OF TERMS

Renal function related determinants - Refers to levels of serum creatinine and/or urine output and their influence on outcomes of acute kidney injury in neonates.

Neonate related determinants - Refers to attributes of an individual neonate that may influence outcomes of acute kidney injury.

Treatment related determinants - Refers to aspects of care offered to neonates with acute kidney injury that may influence outcomes of acute kidney injury among the neonates.

Outcomes of AKI - Refers to whether the neonate survived to hospital discharge following treatment at KNH or died from AKI in the hospital.

ABSTRACT

Background: Neonatal acute kidney injury (AKI) has become 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 as well as any combination thereof. However, there was dearth of local empirical data as to the predictors of outcomes of AKI among neonates, necessitating this study.

Objective: To assess the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

Methods: A retrospective study design was applied. As such, a retrospective desk review of the medical records of neonates aged 1 - 28 days treated with AKI at Kenyatta National Hospital's pediatric unit was carried out. A study sample of 141 neonates with AKI seen at Kenyatta National Hospital's pediatric unit between 1st January and 31st December, 2021 was used. The study utilized secondary data based on the study objectives which was collected using a Data Abstraction Form. The study data was analyzed through descriptive statistics using the Statistical Package for Social Sciences (SPSS, version 25). Logistic regression analysis was utilized to analyze the association between the study variables at 5% significance level. Results were presented in tables and figures.

Results: A total of 141 health records of neonates with acute kidney injury at KNH in 2021 were reviewed. 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 have a statistically significant association with outcomes of acute kidney injury in the neonates were serum creatinine (SCr) values (β = -1.792, p = .000) and urine output values (β = 1.720, p = .011). The treatment related factors found to be statistically associated with outcomes of AKI in the neonates were stage of the AKI (β = -1.014, p = .007); onset of AKI (β = 1.101, p = .022) and being mechanically ventilated (β = -3.788, p =.003). None of the neonate related variables was found to have a statistically significant association with outcomes of AKI in the neonates.

Conclusion: Serum creatinine and urine output levels were the renal function factors associated with outcomes of AKI in the neonates. Similarly, stage of the AKI, onset of AKI and being under mechanical ventilation were the treatment related factors associated with outcomes of AKI in the neonates.

Recommendation: Efforts are required on development of appropriate for policies, strategies and interventions aimed at reducing the burden of neonatal AKI and improving the outcomes of acute kidney injury in this highly vulnerable patient population.

CHAPTER ONE: INTRODUCTION

1.1 Background Information

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) (Askenazi, 2020). However, immediately after a kidney injury, BUN or creatinine levels may be normal, and the only sign of a kidney injury may be decreased urine production (Vincent, Murphy, Ross, Twombley, Harris-Haman & Zukowsky, 2020). Careful evaluation of the patient is important as rise in SCr or BUN levels could result from other causes and not necessarily renal injury (Levey & James, 2017). In neonates, AKI is defined as an increase in SCr of at least 0.3 mg/dL (≥26.5 µmol/l) within 48 hours or a decrease in urine output (UO) to less than 0.5 mL/kg/hour for ≥ 6 hours (Ostermann, Bellomo, Burdmann, … & Zarbock, 2020). 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 (Nada, Bonachea & Askenazi, 2017).

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 (Kavanaugh, Jetton & Kent, 2021). 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 (Mattoo, Martin, Stapleton & Kim, 2019; Starr, Charlton, Guillet, & Haver, 2021). 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 (Ueno, Shiokawa, Takahashi, & Kawan, 2020).

Evidence from existing literature indicates that AKI is associated with serious short-term outcomes in neonates which also translate into adverse long-term outcomes in their future lives (Askenazi, 2020). Ordinarily, the short-term outcomes of AKI in neonates can be thought of as those reflecting an acute deterioration in renal function per se. These include fluid overload, metabolic acidosis or electrolyte disorders and uremia (Kashani, Rosner, Haase, … & Wu, 2019). The most significant short-term outcome of AKI in neonates is mortality. Existing literature depicts mortality rates among neonates with AKI as ranging between 14 - 50%, with even higher death rates among neonates with oliguric AKI and those who suffer multi-organ failure. For those that survive, their renal function often does not return to that seen before AKI, with persisting renal dysfunction reducing their long-term survival (Kavanaugh et al., 2021; Doyle & Forni, 2016). Longer hospital stays and increased risk of in-hospital re-admission leading to significant healthcare costs constitute other immediate outcomes of AKI in neonates (Jetton, Guillet, Reidy, Tipple, … & Haver, 2017).

In the long-term, AKI in neonates is also linked to several adverse outcomes. Neonatal AKI has been shown to be a leading risk factor for the development of chronic kidney disease (CKD), end stage kidney disease (ESKD), pulmonary oedema as well as cardiovascular and cerebrovascular diseases (Shalaby, Sawan, Nawawi, Alsaedi, Al-Wassia & Kari, 2018; Harer, Selewsky, Kashani, & Askenazi, 2021; Starr et al., 2021). Further, it may also serve as a pathogenic factor in the development of other renal sequelae such as proteinuria, hyperkalemia, persistent microalbuminuria and hypertension further compounding the risk of adverse cardiovascular events over time (Nada et al., 2017). Neonates with AKI are also at increased risk of long-term mortality while a proportion of AKI survivors become dialysis dependent (Rangaswamy & Sud, 2018). The outcomes of acute kidney injury in neonates depend on various variables. These include the severity of renal failure, the need for renal replacement therapy (RRT), number of AKI episodes, age of the child, duration with AKI prior to therapeutic intervention and nature of the underlying disease (Gorga, Murphy & Selewski, 2018).

Evidence derived from empirical studies done on the outcomes of AKI in neonates indicate that increased infant mortality is observed among neonates with low gestational age, very low birth weight, bronchopulmonary dysplasia, antenatal steroid, high creatinine level, high blood urea nitrogen and potassium, low serum sodium level, anuria, dialysis and mechanical ventilation and hypotension requiring inotropic support (Gohiya, Nadkarni & Mishra, 2021). 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 (Luna, Akter, Jesmin, Haque, Uddin & Roy, 2021). Similarly, higher mortality rates among neonates with AKI have also been noted in neonates with congenital renal anomalies, those with ATN as well as those with other underlying comorbidities (Sethi, Bunchman, Chakraborty & Raina, 2021).

It is therefore clear that AKI in neonates leads to significant short and long term outcomes that require close attention. Often, three patterns are evident in prognosis of AKI in neonates based on the severity and duration of the insult. Following an acute injury, renal function returns close to its baseline value, remains stable for a variable period of time and then progress to CKD (subclinical CKD) (Bakr, Eid, Allam & Saleh, 2018), or the recovery in renal function may be only partial and result in 'established CKD'. In the latter situation, if the renal injury is severe and/or of considerable duration, it is likely to necessitate a permanent need for renal replacement therapy (RRT) from the outset. This increases the risk for poorer outcomes among neonates (Askenazi, 2020). One of the critical pillars for improving the outcomes of AKI in neonates is the identification of the determinants of AKI outcomes in this vulnerable population. However, there was paucity of empirical data on the determinants of the outcomes of acute kidney injury in neonates in the local context, a gap the current study has addressed.

1.2 Problem Statement

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 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 (Jetton et al., 2017; Gohiya et al., 2021). 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 (Starr, et al, 2021). This notwithstanding, in most low resource settings, Kenya included the determinants of the outcomes of acute kidney injury in this cohort remains unclear. There is need to elucidate on this aspect as AKI constitutes an important population admitted in pediatric units and has huge implications on the wellbeing of the patients, both in the short and long term (Askenazi, 2020).

Evidence drawn from mortality and morbidity reports in the Newborn Unit (NBU) of Kenyatta National Hospital indicated that AKI imposed a heavy disease burden particularly on critically ill neonates. In addition, a review of the hospital's Newborn Unit records indicated consistently higher mortality rates among neonates with AKI compared to those without AKI. The health records at KNH's NBU also showed that the burden of AKI as a cause of infant mortality at the facility was rising hence the need for greater focus on neonatal AKI (KNH Newborn Unit, 2021). The determinants of the outcomes of AKI among neonates at KNH had not been explored. Consequently, the current study evaluated the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

1.3 Study Justification

The rationale for this study was based on the appreciation that understanding the determinants of the outcomes of AKI in neonates constituted a critical pathway for gaining greater insights on the health condition and informing efforts towards improving treatment outcomes for this patient population. This would in turn help

ensure that more infants diagnosed with AKI survived into adulthood with minimal or lesser debilitating complications hence a better quality of life.

Insights on determinants of the outcomes of acute kidney injury in neonates at KNH were also critical in development of a clear roadmap for optimal resource allocation and improvement of clinical care practices at the facility with a view of eradicating or minimizing incidences of adverse outcomes in neonatal AKI patients.

Increased focus on neonatal AKI locally is vital, not only as a way of reducing its associated burden, but also as part of efforts for the realization of the SDGs and specifically SDG No. 3, which aims to end preventable deaths of neonates. It would also positively contribute to realization of Kenya's Vision 2030 health goals of a health population served by an equitable and affordable health care system of the highest possible standards for all.

Insights generated from this study may also be useful in supporting development of evidence-based treatment monitoring guidelines for use by neonatologists and paediatric nephrologists as they care for neonates with AKI in the future.

1.4 Research Questions

1. What were the renal function related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital?

2. What were the neonate related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital?

3. What were the treatment related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital?

1.5 Study Objectives

1.5.1 Broad Objective

To assess the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital

1.5.2 Specific Objectives

1. To establish the renal function related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

2. To establish the neonate related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

3. To assess the treatment related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

1.6 Research Hypothesis

The null hypothesis was that renal function, neonate and treatment related factors had no significant association with the outcomes of AKI in neonates at Kenyatta National Hospital.

1.7 Significance of the Study

The findings from this study would inform or influence policy review by shedding light on the determinants of the outcomes of AKI in neonates hence in turn inform development of appropriate AKI care policies and protocols for this population.

The findings from this study would also inform practice in the care of neonates with AKI with increased focus on better management of AKI in neonates with a view of improving care outcomes in this cohort.

The findings from this study would also inform education with insights generated from this study acting as a basis for formulation of training tools and guides to help nurses and other health care workers involved in the care of neonates diagnosed with AKI to better meet the various needs of this patient population.

Last but not least, the findings from this study would inform research, as this study adds to existing local literature on acute kidney injury in neonates, hence acting as a reference point and a basis for further research on the study subject among other scholars.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter presents a review of literature as guided by the study objectives. It therefore contains a review of empirical literature on the renal function, neonate and treatment related determinants of the outcomes of acute kidney injury in neonates. The chapter also includes a summary of the reviewed empirical literature and also presents the study's conceptual framework.

Relevant empirical studies were identified through searches in academic literature databases such as PubMed, MEDLINE, Embase, Cochrane Library, CINAHL and Google Scholar. Key words used in the searches included acute kidney injury or AKI, renal function, AKI in neonates or neonatal AKI, AKI risk factors, AKI outcomes and factors or determinants of AKI outcomes in neonates. Thirty two (32) studies were reviewed, twenty four (24) were from the developed countries in Europe and North America; 7 were from the developing countries in Asia, Latin America and Middle East and 3 were from the sub-Saharan region, though none had been done in Kenya. The reviewed studies were restricted to a period of not more than 5 years ago. These studies constitute this study's empirical literature review.

2.2 Renal Function Related Determinants of AKI Outcomes in Neonates

This section presents reviewed empirical literature on renal function related determinants of AKI outcomes in neonates. The renal function indicators discussed in this section are serum creatinine (SCr) and urine output (UO) and how their changes influence outcomes of acute kidney injury in neonates.

2.2.1 Serum Creatinine Level

Though not an ideal biomarker of AKI in pediatrics, for various reasons, serum creatinine remains a gold standard for diagnosis of AKI in neonates, as other novel biomarkers of AKI are still in development phases and are yet to be formally adopted. Reasons that make serum creatinine imperfect for AKI diagnosis in neonates includes newborn's SCr value initially reflects maternal creatinine; SCr is a measure of function

(not injury), and is a late marker of an acute injury or renal dysfunction; at lower GFR, serum Cr will overestimate renal function, owing to tubular secretion of Cr; SCr varies by muscle mass, hydration status, age, and gender in neonates; and bilirubin and certain medications can affect SCr measurement via the Jaffe method (Gorga et al., 2018; Askenazi, 2020). This notwithstanding, SCr level is a common measure of AKI in neonates as there are currently no better alternative measures. This is in line with the general consensus that an absolute increase in serum creatinine level reflects differing degrees of kidney dysfunction in neonates (Ostermann et al., 2020). Most of the empirical studies apply the KDIGO neonatal AKI definition of SCr rise ≥ 0.3 mg/dL within 48 hours or SCr rise of ≥ 1.5 from the previous lowest value within 7 days to qualify AKI in neonates (Nada et al., 2017). It is thus clear that despite its deficiencies, SCr level remains a key measure of acute kidney injury in the pediatric population.

Rises in serum creatinine levels have an effect on the outcome of acute kidney injury in neonates. In a study that sought to predict outcomes of acute kidney injury in neonates, AlGadeeb, Qaraqei, Faqeeh and Al-Matay (2021), observed differences in outcomes in this population based on their levels of serum creatinine. Poorer outcomes manifesting as increased mortality rates and longer durations of hospitalization were evident among neonates with SCr increase of ≥ 3 of the Baseline SCr or a SCr increase of ≥ 2.5 mg/dL (defined as Stage 3 AKI) compared to those with SCr increase of ≥ 1.5 to 1.9 of the Baseline SCr within a 7 day period. Hence, significant rises in serum creatinine levels portended poor outcomes of AKI in neonates (AlGadeeb et al., 2021). Similarly, in a study exploring outcomes of AKI in newborns in an Indian pediatric unit, serum creatinine increases of 3 or more of the Baseline SCr or SCr increase of ≥ 2.5 mg/dL above the Baseline SCr had a significant correlation with poor outcomes of acute kidney injury compared to more milder increases of serum creatinine such as serum creatinine of 0·3 mg/dl or more or 50% or more from the previous lowest value (Bansal, Nimbalkar, Kungwani, Patel, Sethi & Nimbalkar, 2017). This showed that greater increases in serum creatinine levels were significant predictors of poor outcomes of AKI in neonates.

Levels of serum creatinine are identified as an important biomarker of renal function in AKI diagnosis in neonates, with higher increases in SCr level associated with poor outcomes of AKI in this population. While evaluating outcomes of AKI in neonates and its associated clinical features, Gallo, de Bijl-Marcus, Alderliesten, Lilien and Groenendaa (2021), implicated higher increases in serum creatinine as leading to poorer outcomes of AKI in neonates relative to lower increases with neonates with SCr rises of 3 or more of the lowest prior SCr measurement reporting poorer outcomes compared to those with SCr rises of < 2 of the Baseline SCr measurement. Kupferman, Yitayew and Rastogi (2018), in a review of acute kidney injury in term neonates also observed that SCr changes had a major implication on neonatal AKI outcomes. Higher serum creatinine increases especially those beyond 3 or more above the Baseline SCr measurement portended greater risk of poor outcomes compared to milder increases such as those of < 2 of the Baseline SCr measurement, observations also echoed by Shalaby et al. (2018) and Pantoja-Gómez, Gomez, Realpe, and Calvache (2022). Changes in serum creatinine levels in neonates are therefore a useful determinant of outcomes of AKI in neonates.

2.2.2 Urine Output

Urine output is another important renal function biomarker considered an important determinant of outcomes of acute kidney injury in neonates. In neonates, based on the KDIGO neonatal AKI definition, acute kidney injury is defined as a decrease in urine output (UO) to less than 0.5 mL/kg/hour for 6 or more hours (Ostermann et al., 2020). Neonatal AKI based on urine output level is termed as either oliguric or nonoliguric, with oliguric AKI characterized by a urine output of less than 1 mL/kg per hour while urine flow rate above this level is termed nonoliguric AKI (Nada et al., 2017). Evidence suggests that poor outcomes of acute kidney injury in neonates correspond with lower UO levels. This was so reported in a review exploring outcomes of acute kidney injury in neonates born prematurely in which higher mortality rates and longer hospital stays, markers of poor AKI outcomes in neonates, were more evident in neonates with UO of <1 mL/kg per hour in the first week of life compared to those that had UO of greater than 1 mL/kg per hour in the first week of life, denoting that neonatal oliguric AKI

portended greater risk of poor outcomes compared to neonatal nonoliguric AKI (Timovska, Bojadzieva, Sofijanova, Shuperliska, Kirovski & Jordanova, 2021). In studies by Esezobor, Ladapo, Osinaike and Lesi, (2019) and Mwamanenge et al. (2020), neonates with UO levels of ≤ 0.3 mL/kg/hour for 6 or more hours had significantly higher odds of poor AKI outcome than those with UO of > 0.5 mL/kg/hour for ≥ 6 hours. Significant decreases in urine output were thus an important predictor of poor outcomes of AKI in neonates.

Urine output constitutes an important determinant of AKI outcomes in neonates. Studies by Lee, Chan, Lai, Hsu, Wu, Lim and Lien, (2017), Gallo et al. (2021) and AlGadeeb et al. (2021) offered evidence to the effect that neonates with urine output levels of less than or equal to 0.3 mL/kg per hour for 12 or more hours had significantly elevated risk of poor outcome including mortality compared to neonates with urine output level of > 0.5 mL/kg/hour. These studies concluded that decreases in urine output in neonates with AKI were a marker of deterioration of the neonates' health condition which in turn led to poor outcomes among these infants. Similarly, studies by Fan, Ye, Qian, Zhao, Zhang, Xue, … and Jiang (2019) and Pantoja-Gómez et al. (2022) also observed increased odds of poor outcomes of acute kidney injury in neonates with a urinary output of less than 1 mL/kg per h on postnatal days 2 - 7, compared to those with a or a urinary output of greater than 1 mL/kg per h over the said period, hence denoting that neonates with oliguric AKI had poor outcomes compared to those with nonoliguric AKI. This illustrates that decreased UO in neonates with AKI portends poor outcomes.

2.3 Neonate Related Determinants of AKI Outcomes in Neonates

This section highlights reviewed empirical literature on neonate related determinants of outcomes of acute kidney injury in neonates. The neonate related factors discussed include gestational age, birth weight, intrauterine growth restriction, Apgar score and comorbidities.

2.3.1 Gestational Age

One of the neonate related factors identified as being a significant determinant of acute kidney injury outcomes in neonates is gestational age with most of the studies done linking lower gestational age with poor outcomes that include increased mortality and longer hospital stays. For instance, in a single hospital study undertaken prospectively among neonates diagnosed with acute kidney injury, significantly higher mortality rates and longer hospital stays were observed among neonates with gestational age of < 32 weeks compared to those of gestational age ≥ 35 weeks. The study concluded that lower gestational age was a predictor of poor outcome in neonates with AKI (Shalaby et al., 2018). Similarly, in a US study that investigated risk of dying among neonates diagnosed with AKI receiving care in a NICU, the likelihood of dying among the surveyed neonates was positively associated with a gestational age of less than 32 weeks hence lower gestational age was cited as predictor of poor AKI outcome in neonates (Sanderson, Warady, Carey, Tolia, Boynton, Benjamin & Greenberg, 2022). It is possible that lower gestational age implies incomplete nephrogenesis or poor nephron development status in these neonates which predisposes them to poor AKI outcomes.

Prematurity, based on available empirical evidence, contributes to poor outcomes of AKI in neonates. In a cross-sectional study evaluating AKI outcomes among severely sick neonates in a tertiary care setting, neonates born prematurely were found to have statistically significant higher odds of dying from AKI compared to those born a term (Mwamanenge, Assenga, & Furia, 2020). Similarly, lower gestational age was found to significantly relate with poor outcomes (that is, neonatal mortality) in surveyed neonates in a study by Lee et al. (2017). Similar observations were made by Hu, Li, Chen, Chen, Li and Wang (2021) who also established a statistically significant association between lower gestational age marked by prematurity and poor outcome of AKI in neonates denoted by increased mortality risk. These studies therefore illustrate gestational age as being a major predictive factor of outcomes of AKI in neonates.

2.3.2 Birth Weight

Another neonate related factor associated with outcomes of acute kidney injury in neonates is birth weight with low birth weight reported as being a predictor of poor neonatal AKI outcomes. In a study evaluating risk factors for poor outcomes in severely ill neonates with AKI, low birth weight neonates were observed to have significantly higher odds for mortality compared to their normal birth weight counterparts. Consequently, it was concluded that low birth weight was a predictor of poor AKI outcome in critically sick neonates (Hu et al., 2021). Similarly, compared to normal birth weight neonates, low birth weight neonates had significantly higher odds of poor AKI outcome denoted by neonatal mortality as reported by Mwamanenge et al. (2020). Likewise, in a review of acute kidney injury outcomes among surveyed neonates, survival rates in low-birth-weight infants were significantly reduced compared to in the normal birth weight cohort (Lee et al., 2017). This therefore denoted that low birth weight was one of the neonate related attributes that led to poor outcomes of AKI among neonates.

Birth weight is an important variable in evaluation of acute kidney injury outcomes in neonates. For instance, while in general, AKI in neonates is an independent risk factor for poor outcome including neonatal mortality and longer hospitalizations, LBW infants were found to be at a significantly greater risk for these poor AKI outcomes compared to those born with normal weight, depicting the significance of birth weight in neonatal AKI outcomes (Jetton et al., 2017). Ademola, Asinobi, Ekpe, Adewuyi, Ayede, Ajayi, Raji and Samuel (2019) in a cross-sectional study on care outcomes of AKI among neonates observed differences in the outcomes on the basis of birth weight. Greater incidences of neonatal mortality and longer hospital stays were observed in the LBW neonate cohort compared to the normal birth weight cohort, hence LBW was reported as being a significant predictor of poor outcomes of AKI in neonates, sentiments also shared by Nandhagopal, Firdaus, Ali and Afzal (2020) and Perico, Askenazi, Cortinoris, and Remuzzi, (2018). The association of LBW with poor outcomes of acute kidney injury in neonates could possibly be due to its association with poor nephron development.

2.3.3 Intrauterine Growth Restriction

Fetal growth restriction (FGR), also referred to as intrauterine growth restriction (IUGR), which denotes a rate of growth of a fetus that is less than normal for the growth potential of the fetus (for that particular gestational age) is another neonate related factor linked to poor outcomes of AKI in neonates. According to a study by AlGadeeb et al. (2021) that looked at the outcomes of acute kidney injury in neonates and its associated factors, poor outcomes of AKI in neonates were found to be significantly correlated to fetal growth restriction. In the study, neonates that had IUGR were 3 times more likely to die when diagnosed with AKI compared to those without IUGR. Similarly, in a study evaluating factors that led to poor outcomes following AKI diagnosis among neonates, FGR was established as one of the gestational risk factors that contributed to elevated neonatal mortality rates among neonates with AKI (Perico et al., 2018). IUGR as a significant determinant of poor AKI outcomes in neonates was also reported in the study by Esezobor et al. (2019). This denotes that IUGR is a significant predictor of poor outcomes among neonates diagnosed with acute kidney injury.

2.3.4 Apgar Score

Another neonate related determinant of the outcomes of acute kidney injury in neonates is Apgar score which is a measure of a neonate's condition after birth. Apgar scores of ≥7 at 1 and 5 minutes after birth are considered re-assuring or normal, scores of 4 - 6 are considered moderately abnormal denoting that the newborn may require some assistance with breathing while scores of 0 - 3 are considered low denoting that the newborn is in a poor state and may require immediate medical attention (Santos, Vogt, Duarte, Pimenta, Madeira & Abreu, 2019). In an Indian study evaluating outcomes of acute kidney injury among in-hospital neonates born at term, significantly higher odds of poor outcome of AKI among the neonates, marked by longer hospitalization and higher mortality, were observed in neonates that registered poor Apgar score at the 5th minute compared to neonates that registered normal range of Apgar score in the 5th minute (Nandhagopal et al., 2020). Similar findings were reported by Stojanović, Barisic, Radovanovic, Bjelica, Milanovic and Doronjski (2017) who established a

statistically significant association between poor outcomes of AKI in neonates (in the form of higher mortality rate) with low or poor Apgar scores in the 1st and 5th minutes. This illustrates that low or poor Apgar scores among newborns are a leading determinant of poor outcome of acute kidney injury in this vulnerable population.

The essence of Apgar score is to assist the health care team determine whether a newborn requires any immediate medical attention or monitoring following birth. This is crucially important as it could help in timely interventions to address any medical conditions that could contribute to AKI incidences. In an exploration of the clinical profile and outcomes in neonates diagnosed with AKI, Bansal et al. (2017) established that low Apgar scores of below 4 at the first and fifth minutes had a significant correlation with poor AKI outcomes among the surveyed neonates. Similar findings were reported by Jetton et al. (2017) who also identified low Apgar scores as being a significant predictor of poor AKI outcomes in neonates, sentiments also shared by Harer et al. (2021). Similar observations were made by El-Badawy, Makar, Abdel-Razek and Abd Elaziz (2015) who also established a positive and significant association between poor outcomes of AKI in neonates, which included neonatal death and prolonged stays in hospital, and the surveyed neonates' low Apgar scores at the first and fifth minutes. This therefore depicted that low or poor Apgar scores among newborns contributed to poor outcomes of AKI during the neonatal period.

2.3.5 Comorbidities

Presence of comorbidities among newborns has also been linked with poor outcomes of acute kidney injury in neonates. Such comorbidities include bronchopulmonary dysplasia, patent ductus arteriosus, necrotizing enterocolitis (NEC), respiratory distress syndrome (RDS), perinatal asphyxia, congenital heart disease and sepsis. For instance, in a case control study on prognostic factors associated with outcomes of acute kidney injury in neonates, Bansal et al. (2017) identified sepsis and respiratory distress syndrome as contributing to poor outcomes of AKI in surveyed newborns. On their part, El-Badawy et al. (2015) also identified sepsis, NEC and perinatal asphyxia as leading predictors of poor acute kidney injury outcomes among neonates. Similar views were shared by Nada et al. (2017) who in a review of acute kidney injury in neonates

also identified comorbidities among neonates such as heart failure, sepsis, hypovolemia, asphyxia, RDS and congenital heart anomalies as leading contributors to poor AKI outcomes in the form of higher mortality and longer hospital stays in this population. This clearly shows that poor outcomes of AKI in neonates are partly attributable to neonatal comorbidities.

Evidence exists to the effect that neonatal comorbidities do affect outcomes of acute kidney injury among neonates. In a cross-sectional study comparing AKI outcomes among neonates with and without comorbidities, poor outcomes of AKI in the form of elevated mortalities were observed among neonates with various comorbidities (sepsis, RDS, asphyxia, congenital heart anomalies and renal venous thrombosis) compared to the control group. It was hence concluded that neonatal comorbidities were a significant determinant of poor AKI outcomes in neonates (Momtaz, Sabzehei, Rasuli, & Torabian, 2021). Similar views were shared by Perico et al. (2018) and Nandhagopal et al., (2020) who identified presence of comorbid sepsis, asphyxia and circulatory failure as leading to higher mortalities among neonates with AKI. Likewise, Hu et al. (2021) cited congenital heart disease, necrotizing enterocolitis, hyperbilirubinemia and sepsis while Kupferman et al. (2018) identified neonatal sepsis, perinatal asphyxia and cardiovascular or respiratory failure as major predictors of poor outcome of acute kidney injury in newborns during the neonatal period, an observation also shared by Lee et al. (2017). Other studies that identified neonatal comorbidities including perinatal asphyxia, sepsis, congenital heart disease [CHD], congenital urinary tract malformations and RDS as contributing to poor outcomes of AKI in neonates were those by Ghobrial et al. (2018), Mitharwal, Makwana, Mourya, Kumari and Ram (2020) and Gallo et al. (2021).

2.4 Treatment Related Determinants of AKI Outcomes in Neonates

This section presents reviewed empirical literature on treatment related determinants of outcomes of acute kidney injury in neonates. The treatment related factors explored included stage of the acute kidney injury, time of AKI onset, need for mechanical ventilation, need for dialysis and exposure to nephrotoxins.

2.4.1 Stage of Acute Kidney Injury

One of the treatment related factors that impact outcomes of acute kidney injury in neonates is the stage of AKI which is an indicator of the severity of AKI. Acute kidney injury is classified into 3 stages based on the diagnostic and classification criteria of the Kidney Disease: Improving Global Outcomes (KDIGO) modified for newborns. Stage 1 is marked by SCr increase of ≥0.3 mg/dL within 48 hours or SCr increase of ≥ 1.5 to 1.9 of the Baseline SCr within 7 days or urine output of < 0.5 mL/kg/h for 6-12 hours. Stage 2 is marked by SCr increase of ≥ 2 to 2.9 of the Baseline SCr or urine output of < 0.5 mL/kg/h for 12 or more hours. Stage 3 is marked by SCr increase of ≥ 3 of the Baseline SCr or SCr level of ≥ 2.5 mg/dL or receipt of dialysis or urine output of < 0.3 mL/kg/h for 24 or more hours or anuria for ≥12 hours. Baseline SCr is defined as the lowest previous SCr value (Jetton et al., 2017; Nada et al., 2017; Ostermann et al., 2020). In a multiple center study conducted prospectively among newborns aged 2 - 28 days of life, significantly higher mortality rates were reported among neonates with severe AKI (stages 2 & 3) compared to those with mild AKI (stage 1) as reported by Pantoja-Gómez et al. (2022). Similarly, studies by Fan et al. (2019) and AlGadeeb et al. (2021), also established higher mortality rates and longer hospital stays among neonates with Stage 2 and 3 AKI compared to those with Stage 1 AKI. This showed that the likelihood of poor outcomes of AKI in neonates increased with greater severity of the condition marked by Stages 2 and 3 AKI.

Severity of acute kidney injury has significant implications on outcomes of AKI in neonates with greater potential of poor outcome as one moves from Stage 1 to Stage 3 of the illness. In a single center prospective study undertaken to evaluate the outcomes of AKI in preterm newborns, neonates diagnosed with Stage 2 and 3 AKI had significantly higher odds of poor outcomes (dying or being in the hospital for longer) compared to those diagnosed with Stage 1 of the condition (Timovska et al., 2021). Similarly, there were significant differences in recorded mortality rates among surveyed neonates on the basis of severity of AKI with more deaths happening among neonates with Stage 3 AKI compared to those with Stage 1 AKI in studies by Katariya and Pandya (2019) and Ramesh (2018). Positive association of advanced stage of AKI with

poor outcomes including neonatal mortality, longer hospital stays and complications was also cited by Bansal et al. (2017) and Hu et al. (2021). From this, it is safe to say that poor outcomes of AKI in neonates correlate with the severity of the condition.

2.4.2 Time of AKI Onset

Time of AKI onset is another treatment related determinant that is associated with outcomes of acute kidney injury in neonates. Prevailing evidence suggests that late onset of neonatal AKI correlates with poor patient care outcomes while early onset of neonatal acute kidney injury correlates with better patient care outcomes (Kupferman et al., 2018). Among the adverse patient care outcomes associated with AKI in neonates include increased length of mechanical ventilation, prolonged length of stay, and rise in mortality (Gohiya et al., 2021). In this study, early onset of AKI in neonates denotes AKI in neonates that occur within the first 7 days of life from birth while late onset of AKI in neonates denotes AKI in neonates that occur after the first 7 days of the neonate's life from birth. This is as applied in studies by Bansal et al. (2017), Mattoo et al. (2019) and Perazzo et al. (2020).

In a study evaluating treatment outcomes among hospitalized term neonates diagnosed with AKI, the odds of positive care outcomes were found to significantly relate with early onset of the condition while late onset of AKI was found to strongly correlate with poor treatment outcomes and particularly neonatal mortality (Nandhagopal et al., 2020). Similarly, in a multi-center study undertaken prospectively in a cohort of neonates with acute kidney injury, better care outcomes were evident among neonates diagnosed with early onset AKI while poor outcomes in the form of neonatal mortality were evident among neonates diagnosed with late AKI onset (Pantoja-Gómez et al., 2022). Similar findings were reported by Ramesh (2018) who also noted that late onset of acute kidney injury in newborns increased the risk of poor outcomes significantly while early onset correlated to more positive outcomes. It is thus clear from these studies that time of AKI onset was a critical factor with significant influence on the outcomes of AKI in neonates.

Late onset of acute kidney injury in neonates is acknowledged as one of the attributes that significantly increases the burden of neonatal AKI across the globe. In a review exploring variables associated with improved outcomes of acute kidney injury in neonates, Vincent et al. (2020) identified early onset of AKI in neonates as being paramount as they observed that late onset of AKI was a leading contributor to poor care outcomes of AKI in this vulnerable population. Similar sentiments were espoused by Starr et al. (2021) who noted that diagnosis of early onset neonatal acute kidney injury tended to be associated with more positive care outcomes in both LMICs and HICs compared to dealing with late onset AKI. Mattoo et al. (2019) and Jetton et al. (2017) did also identify late onset AKI as a leading predictor of poor treatment outcomes of AKI in pediatric patients. Hence, it's clear that time of onset of AKI is a major predictor of pediatric patients care outcomes.

2.4.3 Need for Mechanical Ventilation

Need for mechanical ventilation is another treatment related factor identified as influencing the outcomes of acute kidney injury in neonates. This is especially evident in neonatal critical care settings. In a review of diagnostic and treatment challenges for neonates diagnosed with acute kidney injury, Bakr et al. (2018) observed significant differences in outcomes among neonates with AKI on the basis of need for mechanical ventilation. Neonates with AKI who were invasively intubated experienced greater odds of poor outcomes compared to the non-intubated group. In a review of risk factors and outcomes of acute kidney injury in neonates, poor outcome scores were evident among neonates who underwent invasive mechanical ventilation (IMV) compared to the group who underwent non-invasive mechanical ventilation and both groups had higher odds of poor AKI outcome when compared to neonates that did not require any form of mechanical ventilation (MV) (AlGadeeb et al., 2021). Similar views were espoused by Kavanaugh et al. (2021) who also reported that need for mechanical ventilation in neonates with AKI significantly raised their odds for poor outcome which they attributed to MV related complications such as severe nosocomial infection and hemodynamic instability. This therefore illustrates that need for MV may portend poor

outcome in neonates with AKI especially when compared to neonates not in need of intubation.

Need for mechanical ventilation is an indicator of possible deterioration of a patient's health condition which could possibly explain the higher incidence of poor outcomes of AKI in neonates requiring MV. This was so reported by Doyle and Forni (2016) who identified increased risk of mortality in mechanically ventilated neonates under treatment for AKI compared to the non-intubated cohort. Similarly, in studies by Lee et al. (2017) and Esezobor et al. (2019), neonates in need of invasive intubation were generally diagnosed to be sicker compared to the group not requiring MV. Similarly, the care outcomes in the MV group of neonatal AKI patients were much worse that the neonatal AKI group not in need of MV. Need for mechanical ventilation was also identified as a significant predictor of poor outcomes among newborns undergoing treatment for AKI according to studies by Mitharwal et al. (2020) and Sanderson et al. (2022). Need for MV is thus an attribute of treatment that may occasion poor outcomes of acute kidney injury in newborns within the neonatal period.

2.4.4 Need for Dialysis

Need for dialysis is another treatment related factor that has been highlighted as impacting outcomes of acute kidney injury in neonates. It is observed that neonates with AKI in need of dialysis have inferior outcomes compared to those not requiring any dialysis as a form of treatment. Shalaby et al. (2018) in a cross-sectional study exploring the outcomes of AKI in neonates observed that neonates in need of dialysis as the treatment mode for the AKI had greater odds of poor outcomes compared to the AKI cohort that did not require undergoing any form of dialysis. Similarly, in a review of outcomes of acute kidney injury in hospitalized term neonates, poor outcome scores were observed among neonates treated using various forms of dialysis when compared to neonates who were treated using non-dialysis therapies (Nandhagopal et al., 2020). According to reviews by Fan et al. (2019), Mitharwal et al. (2020) and Bansal et al. (2017), neonates with AKI with a need for dialysis had significantly raised odds for poor outcome compared to the non-dialysis group. This therefore illustrated that need for dialysis may portend poor outcome in neonates with AKI.

Need for dialysis is a significant indicator of possible deterioration of the neonates' renal function and possible advanced status of the AKI which could explain the poor prognosis recorded. Ghobrial et al. (2018) in a review of risk factors for poor outcomes among neonates diagnosed with acute kidney injury did identify need for dialysis as one of the predictive factors for poor outcomes in newborns with AKI during the neonatal period. Studies by Katariya and Pandya (2019) and Momtaz et al. (2021) did also report higher odds of poor outcomes among neonates designated as requiring dialysis as a primary medical intervention compared to neonates that did not require undergoing dialysis for treatment, sentiments also shared by Stojanović et al. (2020) and Pantoja-Gómez et al. (2022). Need for dialysis was thus an attribute of treatment found to relate with poor outcomes of acute kidney injury in neonates in the neonatal period.

2.4.5 Exposure to Nephrotoxins

Another treatment related factor identified as influencing outcomes of acute kidney injury in neonates is exposure to nephrotoxins and which is linked to poor AKI outcomes in neonates. As espoused by Sethi et al. (2021), exposure to nephrotoxins remains one of the leading factors associated not only with increased risk of acute kidney injury in neonates but also increased likelihood of poor AKI outcomes in this cohort. Similar position was espoused by Nada et al. (2017) who also identified exposure to nephrotoxins as a significant determinant of poor outcomes of acute kidney injury in neonates. In a review of outcomes of acute kidney injury in neonates based on data derived from multiple care centres, Jetton et al. (2017) did also establish that neonates exposed to treatments that contained nephrotoxins had an increased likelihood of poor outcomes of AKI compared to those not exposed to nephrotoxins. The higher poor outcomes in neonates with AKI exposed to nephrotoxins could be attributable to the delicate state of the neonates' urinary tract system during the early days of life. Due care is thus needed to ensure that treatments offered to neonates with AKI do not contain nephrotoxins as this increases risk of poor care outcome.

2.5 Summary of Literature Review

Evidence from the reviewed empirical studies indicated that neonatal AKI was a health condition with significant adverse short-term and long-term outcomes and hence deserves greater attention. In addition, it was also evident from the reviewed empirical literature that there was a wide range of renal function, neonate and treatment related determinants of outcomes of acute kidney injury in neonates across the diverse pediatric care settings. However, the reviewed empirical studies were largely done in other countries whose healthcare settings and systems likely differed from that of Kenya. It was thus important to appraise their findings in the local context. Consequently, this study sought to assess the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

2.6 Conceptual Framework

The conceptual framework is a visual representation showing how the study variables relate and provides a quick glimpse of the study's key variables (Mugenda & Mugenda, 2003). Renal function, neonate and treatment related determinants constituted the study's predictor variables while AKI outcome(s) in neonates was the study's dependent variable. The intervening variables were resource allocation and staffing levels while the outcome variable was institution of measures to improve neonatal AKI outcomes. Figure 2.1 depicts the conceptual framework.

Independent variables

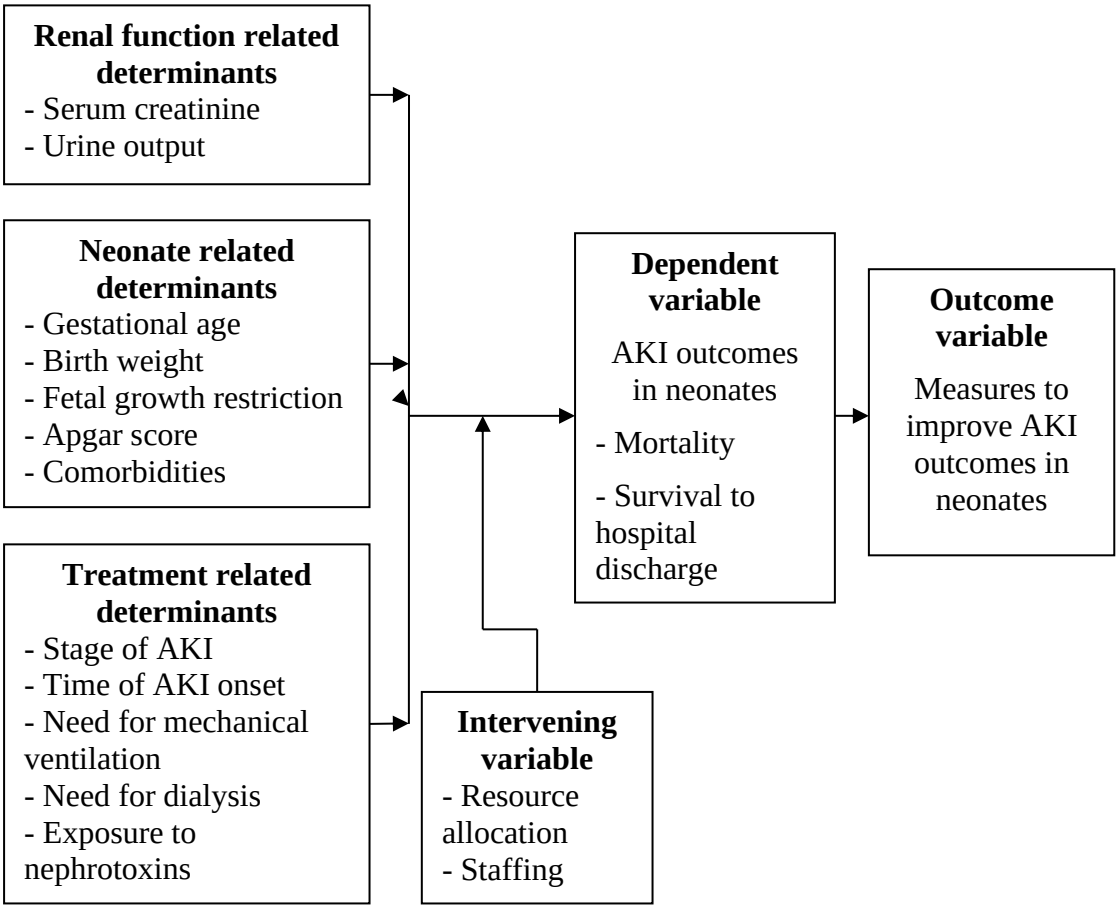

Figure 2.1: Conceptual framework

Source: Researcher, 2023

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Introduction

This chapter contains a description of the methods or procedures applied to realize this study's objectives. The chapter thus covers the following aspects: the study design, study area, study population, inclusion and exclusion criteria, sample size and sampling method, data collection tools and procedures, pretesting of tools, data analysis, ethical considerations, study limitations as well as the study findings dissemination plan.

3.2 Study Design

This study adopted a retrospective study design. As such, a retrospective desk review of the medical records of neonates aged 1-28 days treated with acute kidney injury at Kenyatta National Hospital's pediatric unit was carried out. Data from the neonates' medical records was abstracted and reviewed. This enabled the researcher to identify the patterns of care outcomes and associated factors during the neonatal period among this cohort.

3.3 Study Area

This empirical research study was carried out in Kenyatta National Hospital. Kenyatta National Hospital (KNH) is Kenya's largest public referral hospital, located about four kilometers from the Nairobi city center, off Ngong road along Hospital Road. The current bed capacity of the hospital is about 2,000. The facility offers a wide range of specialized in and out-patient health care services. The specialized health-care services provided at KNH include radiotherapy, heart surgery, neurosurgery, oncology, diabetic, renal dialysis and kidney transplant operations, plastic and reconstructive surgery, orthopedic surgery and burns management among others. The hospital also facilitates medical training and research and participates in national healthcare planning.

In KNH, neonatal patients presenting with various health conditions are cared for in the Pediatric Unit. Thus, neonates with AKI are managed and cared for within the hospital's Pediatric Unit and thereafter their treatment records are transferred to the Records Department upon their discharge, referral back to another hospital for continued care

or upon their demise. The Records Department at KNH thus provided a good platform for evaluating the health records of neonates with AKI treated in the hospital on a retrospective basis.

3.4 Study Population

The study population was neonates diagnosed with AKI admitted to the Pediatric Unit of Kenyatta National Hospital between 1st January and 31st December, 2021 - being the period for which the most recent data on the study subject was available. Existing hospital records indicated that the hospital handled 250 neonatal AKI cases in 2021 (KNH Pediatric Unit Records, 2021). Data was retrieved from the medical records of these pediatric patients.

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion Criteria

The study included all health records of neonatal patients aged 1 - 28 days with acute kidney injury seen in KNH's Pediatric Unit between 1st January and 31st December, 2021. The study only included cases in which neonatal AKI was the primary diagnosis and the reason for which the neonate was under treatment. Included health records were also only for neonates that were born in a hospital.

3.5.2 Exclusion Criteria

The study excluded AKI neonatal health records that missed crucial data required for the success of this research work. Such data included serum creatinine and urine output levels, the child's gestational age, birth weight, Apgar scores (at minutes 1 and 5), comorbidities (if any), stage of the neonatal AKI, time of the AKI diagnosis, intubation of the neonate and patient treatment outcomes.

Patients' reports in which the AKI was incidental (not the primary diagnosis) were also excluded given that the other diagnoses, apart from AKI, could also have influenced the treatment outcomes of such neonates while the current study's focus was only on the outcomes of AKI among neonates.

3.6 Sample Size Determination

Fishers *et al*. (1998) formula was applied in determining this study's sample size as follows;

$n = [z^2pq/d^2]$

Where;

n = desired sample size (if the population was greater than 10,000).

Z = standard normal deviation at the required confidence interval, 95%. In this case, it was 1.96

p = the proportion of the population with desired characteristics. The prevalence of AKI in neonates, as reported in the largest study to date - the AWAKEN study was 30% (Jetton et al., 2017), hence p = 0.3.

q = (1 - p) = 1 - 0.3 = 0.7

d = the level of significance, set as 0.05.

Hence, $n= (1.96^2 \times 0.3 \times 0.7) / 0.05^2$

n = 322.7 hence approximately 323

Given that the population for the study (that is, 250) was less than 10,000, the sample size was moderated for using the Finite Population Correction formula as recommended by Fishers *et al*. (1998) as follows;

$n_f = n / [1 + n/N]$

Where n_f = desired sample size when the total population was less than 10,000

n = estimated sample size when the total population (N) was greater or equal to 10,000

N = estimated total population

Therefore, 323 / (1 + [323/250]) = 323/2.292 = 141

Hence, the study sample size comprised of 141 health records of neonates with AKI seen in the Pediatric Unit of Kenyatta National Hospital between 1st January and 31st December, 2021.

3.7 Sampling Method

All the 141 health records of neonates with AKI were selected as the study units using convenience sampling technique. As such all the health records of the targeted neonate patients that met the inclusion criteria were included till the study sample was achieved. This sampling method was adopted as it is cost-effective, efficient and simple to implement.

3.8 Data Collection Instruments and Procedures

Data on care outcomes and associated factors for the study population was obtained from the health records of the targeted patient group within the hospital's Registry. The data was obtained using a Data Abstraction Form (Appendix 2) created based on reviews of relevant literature and on the basis of data needed to achieve the study objectives. Abstraction involves direct matching of information found in the record to the data element required for the study. The information that was collected 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 in the hospital.

The principal investigator was aided by 2 research assistants in the data collection exercise. The 2 research assistants were Final Year Bachelor of Science in Nursing students at the University of Nairobi. Their role in the data collection was aiding the principal researcher in retrieving the required data from the neonates' health records at KNH's registry and recording it in the study's data abstraction forms. A three step process was utilized in data collection. First, correct identification of the patients' records. This was guided by the study's inclusion and exclusion criteria which were

adhered to in identifying appropriate health records for use in the study. Once identified, the health records were retrieved for thorough scrutiny. This was then followed by data abstraction in which eligible health records of the neonates were scanned for the required study data using the Data Abstraction Form. Health records found to miss crucial data items were excluded from the final set of records applied in this study. The 2 research assistants received training from the principal investigator on the study's purpose, its objectives, nature of data being sought, how to utilize the study's data abstraction form in retrieval of required data and on proper recording and organization of the retrieved data.

To ensure the safety of the patients' records, the required data from the patients' health records was extracted by the research team (principal researcher and the research assistants) within the confines of the hospital's registry. This ensured that the patients' records were immediately returned to their designated section after extracting the required information and hence ensuring that the records did not leave the safety of the hospital's Registry.

3.9 Pre-testing of Tools

Pretesting of the data abstraction form was carried out at Mbagathi District Hospital where 14 data abstraction forms (representing 10% of the study sample size) were used. Pretesting was carried out to refine the data collecting tool. Upon pretesting, the indicators for AKI outcomes, neonate related as well as treatment related determinants were further refined to make them specific.

3.10 Data Storage

The raw data in form of the completed data abstraction forms was kept in a safe under lock and key and was accessible to the authorized persons only. The processed data was stored in a flash disk as well as in the principal investigator's personal computer in a password protected folder which was accessible to the principal investigator only. This helped ensure safety of the data.

3.11 Data Management and Analysis

The study data was analyzed using both descriptive and inferential statistics. The analysis of the study data was done using the Statistical Package for Social Sciences (SPSS version 25.0). Data on the neonates' demographic characteristics, outcomes of AKI in the neonates and the respective indicators for renal function related, neonate related and treatment related determinants were analyzed descriptively using percentages and frequencies. 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. For regression analysis, p values of less than 0.05 denoted that a statistically significant association existed between the variables and vice-versa. Results of the study were presented in tables, graphs and charts.

3.12 Ethical Considerations

The study's ethical clearance was offered by the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee (Ref: KNH-ERC/A/12). The approval to conduct the study at Kenyatta National Hospital was also sought from relevant authorities at the hospital. In addition, appropriate authorization, to access patients' health records of targeted participants who met the inclusion criteria, was issued by the Head of the Pediatric Unit and the Officer-In-Charge of the Records Department at Kenyatta National Hospital (Ref: KNH/PAEDS-HOD/48 Vol. II). The study data was processed confidentially, anonymously and securely and was used for the purposes of the study only and due care was observed to safeguard the integrity of the patients' records during data extraction. No personal or identifying information relating to the neonates was included in the data abstraction forms and codes were applied for each health record to protect the identity of the neonates whose records were utilized. To ensure the safety of the patients' records, the researcher extracted the required information from the patients' health records within the confines of the hospital's Registry, hence ensuring that the records did not leave the safety of the hospital's Registry.

3.13 Limitations of the Study

The study utilized secondary data and therefore heavily relied on the integrity of health records maintained by KNH on neonates treated for AKI. Health records of eligible neonate patients missing important data were excluded via data cleaning. In addition, perspectives of the caregivers of the neonates and health care professionals who served these patients, on the study subject, did not form part of the study.

3.14 Dissemination of Study Findings

The study findings shall be disseminated through presenting a copy of the final thesis report to the University of Nairobi's Department of Nursing Sciences, to UoN's Library and to Kenyatta National Hospital. The findings shall also be shared via presentations in organized workshops and conferences and be published in a relevant peer-reviewed journal.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter presents the study results as set out in the research methodology. The results are on the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital. In total, 141 health records of neonates with AKI seen in the Pediatric Unit of Kenyatta National Hospital between 1st January and 31st December, 2021 were reviewed. Results are outlined in line with the study objectives.

4.2 Demographic Characteristics of the Neonates

The neonates' demographic attributes which included their gender, age at admission, birth weight, how they were delivered and point at which the AKI was diagnosed were probed. About two-thirds (67.4%, n = 95) of the neonates were diagnosed with AKI after the first week of their birth. Results on the neonates' demographic qualities are as shown in Table 4.1.

Table 4.1: Demographic characteristics of the neonates

Attribute		Frequency	Percentage
Gender	Male	63	44.7
	Female	78	55.3
	Total	**141**	**100.0**
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
	Total	**141**	**100.0**
Birth weight	< 2,500g	13	9.2
	2,500g - 4,000g	123	87.2
	> 4,000g	5	3.5
	Total	**141**	**100.0**
Manner in which they delivered	Vaginal birth	92	65.2
	Caesarean section (CS)	49	34.8
	Total	**141**	**100.0**

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
	Total	**141**	**100.0**

4.3 Treatment Outcomes of AKI among the Neonates

The study evaluated the treatment outcomes of acute kidney injury (AKI) in neonates admitted at KNH's paediatric unit during the period January 1st to 31st December, 2021. 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.

4.4 Renal Function Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

The first objective of the study sought to establish the renal function related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

Two variables were assessed. These are the neonates' serum creatinine (SCr) and urine output values at admission. Results are as presented in the following sub-sections.

4.4.1 Serum Creatinine

Serum creatinine values at admission were classified into two categories, on the basis of the standardized definition of the Kidney Disease: Improving Global Outcomes (KDIGO) AKI working group (KDIGO Clinical Practice Guideline for Acute Kidney Injury, 2012) as it is considered to offer a more appropriate classification or categorization of neonatal AKI based on the serum creatinine level (Gohiya et al., 2022).

The two categories are 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. This classification is deemed important as SCr increase of 3 times or more of the Baseline SCr value represent more severe AKI

disease status and possible worse prognosis than SCr increase of less than 3 times of the Baseline SCr value (Kidney International, 2012). Results on the neonates' serum creatinine levels are depicted in Table 4.2.

Table 4.2: Neonates' serum creatinine values on admission

SCr values on admission	Frequency	Percentage
SCr increase of < 3 x Baseline SCr value	49	34.8
SCr increase of ≥ 3 x Baseline SCr value	92	65.2
Total	**141**	**100.0**

4.4.2 Urine Output

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 standardized definition of the Kidney Disease: Improving Global Outcomes (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. This classification is deemed important as urine output of < 0.5 mL/kg/h for more than 12 hours represents more severe AKI disease status and possible worse prognosis than urine output of < 0.5 mL/kg/h occurring for 6 - 12 hours (Kidney International, 2012). Results on the neonates' urine output levels are illustrated in Table 4.3.

Table 4.3: 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
Total		**141**	**100.0**

4.5 Neonate Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

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

4.5.1 Gestational Age at Birth of the Neonates

Results on the neonates' gestational age at birth showed that majority (96.5%, n = 136) were born at term while the remaining (3.5%, n = 5) were born prematurely.

4.5.2 Birth Weight of the Neonates

Results on the neonate's birth weight showed that most had normal birth weight (2,500g - 4,000g), as is illustrated in Figure 4.3.

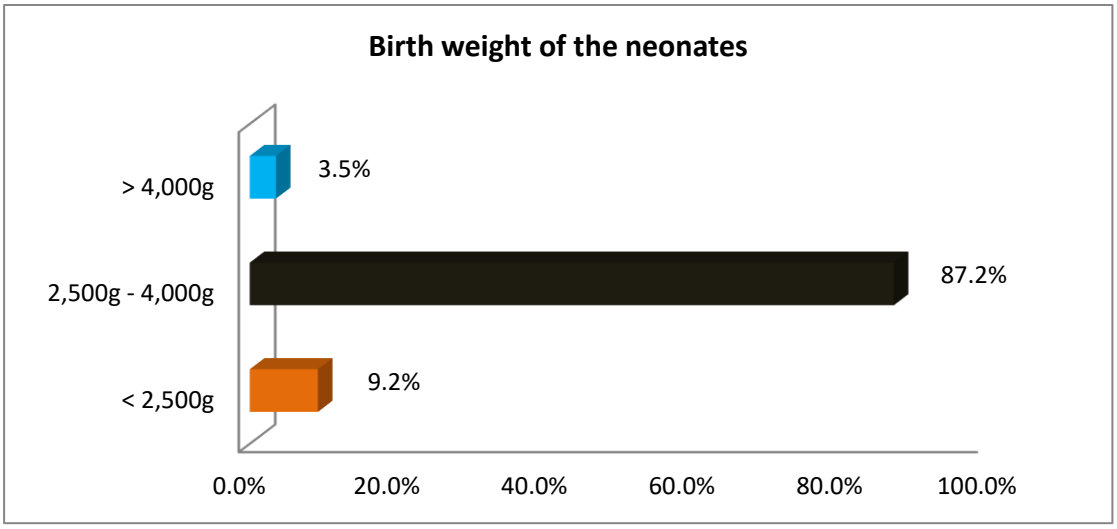

Figure 4.1: Birth weight of the neonates

4.5.3 Fetal Growth Restriction in the Neonates

The study evaluated whether any of the newborns had suffered from fetal growth restriction (FGR). From the findings, almost all (99.3%, n = 140) of the neonates did not suffer from fetal growth restriction. Only 1 of the neonates had suffered FGR.

4.5.4 Apgar Scores of the Neonates

The neonates' Apgar scores at minute 1 and minute 5 were analysed. Results indicated that majority of the neonates had Apgar scores of 7 or more at both minute intervals as is demonstrated in Table 4.4.

Table 4.4: Apgar scores of the neonates at minute 1 and 5

	Minute 1		**Minute 5**	
Apgar score	**Frequency**	**Percentage**	**Frequency**	**Percentage**
0 - 3	1	0.7	0	0.0
4 - 6	5	3.5	3	2.1
≥ 7	135	95.7	138	97.9
Total	**141**	**100.0**	**141**	**100.0**

4.5.5 Comorbidities in the Neonates

Comorbidities referred to other health conditions that the neonates were diagnosed with, in addition to the primary diagnosis of AKI. This was evaluated through checking the neonates' health records for other incidental diagnosis made on the neonate apart from the AKI diagnosis. Results indicated that majority (90.1%, n = 127) of the neonates did not have comorbidities.

Of the 14 neonates with comorbidities, the comorbidities listed included congenital polycystic kidney disease (n = 2), congenital cardiac abnormalities (n = 4), neonatal sepsis (n = 8).

4.6 Treatment Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

The third objective of the study sought to assess the treatment related determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital. 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 are presented in subsequent sub-sections.

4.6.1 Stage of the AKI

According to the KDIGO Clinical Practice Guideline for Acute Kidney Injury, 2012 non-extreme oliguria (urine output of < 0.5 mL/kg/h for 6 - 12 hours) represents Stage 1 AKI while extreme oliguria comprises of Stage 2 AKI marked by urine output of < 0.5 mL/kg/h for > 12 hours and Stage 3 AKI marked by urine output of < 0.3 mL/kg/h for ≥ 24 hours or anuria for ≥12 hours. Results showed that most of the neonates had Stage 3 AKI. This is demonstrated in Figure 4.2.

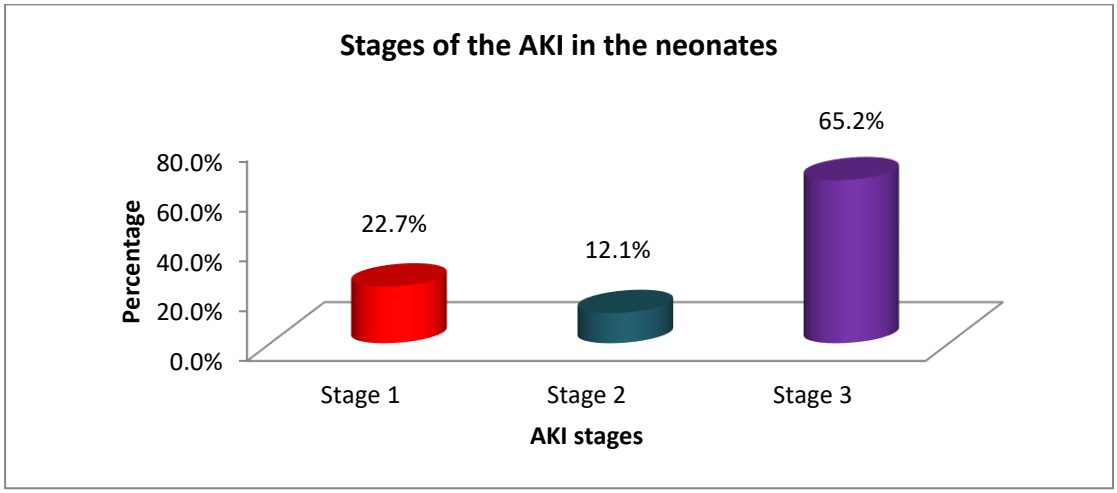

Figure 4.2: Stage of the AKI in the neonates

4.6.2 Onset of AKI

The study evaluated the onset of AKI in the neonates which denoted point at which the AKI was diagnosed. Results were grouped into two categories - early onset AKI for AKI diagnosed within the first 7 days after birth and late onset AKI for AKI diagnosed after the first 7 days after birth. Results indicated that most (67.4%, n = 95) of the neonates had late onset AKI while 32.6% (n = 46) had early onset AKI.

4.6.3 Mechanical Ventilation of the Neonates

As to whether the neonates had been mechanically ventilated. Results indicated that majority (90.1%, n=127) of the neonates were not mechanically ventilated while only a small proportion (9.9%, n = 14) had been mechanically ventilated.

4.6.4 Dialysis of the Neonates

In relation to the neonates' treatment, the study examined whether the neonates were dialysed and if so the form of dialysis received. Results showed that peritoneal dialysis was performed on slightly over half (53.9%, n = 76) of the neonates, as is illustrated in Table 4.5.

Table 4.5: Dialysis of the neonates

Attribute		**Frequency**	**Percentage**
Neonate dialysed?	Yes	76	53.9
	No	65	46.1
	Total	**141**	**100.0**
If yes, kind of dialysis (n = 76)	Peritoneal dialysis	76	100.0
If yes, duration of the dialysis (n = 76)	24 hours or less	16	21.1
	More than 1 day	60	78.9
	Total	**76**	**100.0**

4.6.5 Exposure to Nephrotoxins and Outcome of AKI in Neonates

The study also evaluated whether the neonates were exposed to nephrotoxins. The key finding was that most (62.4%, n = 88) of the neonates were not exposed to nephrotoxins. However, 37.6% (n = 53) of the neonates were exposed to nephrotoxins.

4.7 Associations of the various Determinants with Outcomes of Acute Kidney Injury in Neonates

To ascertain the association between the various renal function, neonate and treatment related determinants as predictor variables and outcomes of acute kidney injury in neonates as the explained variable, logistic regression analysis was applied at a significance level of 5%. Results of the logistic regression analysis are hereby illustrated.

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 is 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 4.6.

Table 4.6: 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^2 and the Nagelkerke R^2 values denote that the model

predicted 34.5% and 47% of the changes in the study's dependent variable, respectively (Table 4.7).

Table 4.7: Model summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	126.960[a]	.345	.470

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

Further, Table 4.8 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.

Table 4.8: The model's predictive accuracy

Classification Table[a]

			Predicted		
			Patient's treatment outcomes		Percentage Correct
	Observed		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

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 (β = -1.792, df = 1, p = .000); urine output values (β = 1.720, df = 1, p = .011); stage of the AKI (β = -1.014, df = 1, p = .007); onset of AKI (β = 1.101, df = 1, p = .022) and whether the neonate was mechanically ventilated (β = -3.788, df = 1, p = .003). The results are demonstrated in Table 4.9.

Table 4.9: Model coefficients results

		β	S.E.	Wald	df	Sig.	Exp(β)
Step 1[a]	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	.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.

CHAPTER FIVE: DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter presents discussion of findings, conclusions and recommendations of the study in line with the study objectives. The study evaluated the determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital.

5.2 Discussion of Findings

5.2.1 Demographic Characteristics of the Neonates

Health records reviewed were of male and female neonates who underwent treatment for acute kidney injury at KNH in 2021. Most were aged 1 - 21 days at admission, were of normal birth weight and were born through vaginal birth. The neonates had either early onset AKI (neonatal AKI that occurred within the first 7 days after birth) or late onset AKI (neonatal AKI that occurred after the first 7 days after birth) with most having late onset AKI. Similar demographic attributes were observed in studies carried out by Kupferman et al. (2018) and Nandhagopal et al. (2020) in which assessed pediatric patients were male and female neonates with acute kidney injury, a significant proportion of whom had normal birth weight and were delivered through vaginal birth. Similarly, in studies by Ramesh et al. (2018), Ghobrial et al. (2018) and Pantoja-Gómez et al. (2022), the study subjects were neonates admitted for AKI treatment most of whom were born vaginally, had normal birth weight and were admitted in hospital while aged three weeks or younger. In all these studies, the neonates were diagnosed with early or late onset AKI as is in the current study.

5.2.2 Renal Function Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

The researcher assessed the neonates' serum creatinine and urine output values at admission.

According to the findings, most of the neonates had a serum creatinine increase of 3 times or more of their Baseline SCr value (the lowest previous SCr value) at admission. This depicted that a significant proportion of the neonates were admitted with severe acute kidney injury as the Kidney Disease: Improving Global Outcomes (KDIGO) AKI working group Clinical Practice Guideline for Acute Kidney Injury classifies a SCr increase of 3 times or more of the Baseline SCr value as the most severe form of neonatal AKI. Further, a statistically significant association was established between serum creatinine values and the outcome of AKI in the neonates as denoted by logistic regression p value of .000. The negative beta coefficient ($\beta = -1.792$) signified an inverse relationship between changes in serum creatinine values and outcomes of AKI in neonates while the Exp(β) 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 while low levels of serum creatinine were predictors of positive outcome of AKI in neonates.

Similar findings were reported by Pantoja-Gómez et al. (2022) who in a multi-facility study probing neonatal AKI outcomes and related factors 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. (2017) 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 of less than 2 times the Baseline SCr value. Similar views were espoused by AlGadeeb et al. (2021) who in a study on neonatal AKI observed differences in outcomes of AKI in this patient population based on their levels of serum creatinine. According to their study, poor outcome manifested as increased mortality rates were evident among neonates with SCr increase of ≥ 3 of the Baseline SCr compared to neonates with SCr increase of ≥ 1.5 to 1.9 of the Baseline SCr within a 7 day period. Other studies that also linked greater increases in serum creatinine levels with poor outcomes of AKI in neonates were those by Shalaby et al. (2018) and Gallo

et al. (2021). It is therefore evident that significant increases in serum creatinine levels were a notable predictor of poor outcomes of AKI in neonates.

On the urine output values at admission, this study 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 in line with the classification given in the 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury (Kidney International, 2012). Further, a statistically significant association was established between urine output values and the outcome of AKI in the neonates as denoted by logistic regression p value of .011. The positive beta coefficient ($\beta = 1.720$) signified a positive relationship between urine output values and outcomes of AKI in neonates while the Exp(β) 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.

The findings were in agreement with those of Timovska et al. (2021) who in a study of AKI outcomes in neonates 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 postnatal week. Similar observations were made by Fan et al. (2019) and Pantoja-Gómez et al. (2022) who noted increased odds of poor outcomes of acute kidney injury in neonates with a urinary 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. (2019) and Mwamanenge et al. (2020). It is therefore evident that lower UO levels constitute a notable determinant of poor outcomes of acute kidney injury in neonates.

5.2.3 Neonate Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

The gestational age at birth of the neonates was evaluated. The study results indicated that majority of the neonates were born at term. Based on the logistic regression findings, 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(β) value of .593. Hence, in this study, gestational age at birth was not a significant determining factor of outcomes of AKI in neonates. The findings were in contrast with those of Lee et al. (2017) and Shalaby et al. (2018) as well as those of Mwamanenge et al. (2020), Hu et al. (2021) and Sanderson et al. (2022) who 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. These 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 the current study could be due to the proportion of neonates born prematurely in the study group being few or good/effective management of prematurity cases.

The neonates' birth weight was evaluated. Results indicated that most of the neonates had normal birth weight (2,500g - 4,000g). Further, the association between birth weight and outcomes of acute kidney injury in the neonates was found to be statistically significant as denoted by logistic regression p value of .100. the birth weight's coefficient of -1.196 signified that the association between birth weight and outcomes of AKI in neonates was negative while an Exp(β) value of .302 denoted low odds of the neonates living relative to dying on the basis of their birth weight. Hence, in this study, birth weight was not a notable predictor of outcomes of acute kidney injury in neonates. In contrast, reviews by Lee et al. (2017) and Hu et al. (2021) 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., (2017), Ademola et al. (2019)

and Nandhagopal et al. (2020). They attributed the identified link to possible poor nephron development in the low birth weight neonates as most are often born preterm. In the current study, the low proportion of low birth weight neonates or their effective management/care could be the reason behind the reported findings.

The neonates' Apgar scores at minute 1 and minute 5 were assessed. Results of the study showed that a significant proportion of the neonates had Apgar scores of 7 or more at both minute intervals. This signified that most of the neonates were well or in good health at and following birth. Further, the association between the neonates' Apgar scores at minute 5 and the outcomes of acute kidney injury in the neonates was found not to be statistically significant as denoted by logistic regression p value of .151. The 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 while the odds of the neonates living relative to dying based on their Apgar score at minute 5 was low as depicted by the Exp(β) value of .131. Hence, in this 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. (2020) and Stojanović et al. (2017). Jetton et al. (2017) and Harer et al. (2021) also reported the association between Apgar scores at minute 5 and outcomes of AKI in neonates as being significant. Current study's findings are attributed to most of the neonates registering high Apgar scores in both minute intervals implying that they were in good health after birth.

The researcher examined whether the neonates had comorbidities. According to the findings, the bulk of the neonates did not have comorbidities. The association between having comorbidities and outcomes of acute kidney injury in neonates was found not to be statistically significant as denoted by logistic regression p value of .153. The beta coefficient value of -1.100 depicted that the relationship between comorbidities and the outcomes of AKI in neonates was negative. The odds of living relative to dying on the basis of comorbidities was low as denoted by an Exp(β) value of .333. Hence, in this study, comorbidities were not a major determinant of outcomes of AKI among the

neonates. In contrast, studies by Bansal et al. (2017) and Momtaz et al. (2021) 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. (2018), Nandhagopal et al. (2020) and Gallo et al. (2021) who also identified neonatal comorbidities as being leading contributors of adverse outcomes of AKI in neonates. Not many of the neonates, in the current study, had comorbidities which could possibly explain the reported lack of association finding.

5.2.4 Treatment Related Determinants of the Outcomes of Acute Kidney Injury in Neonates

The stage of the AKI in the neonates at diagnosis was evaluated. Results indicated that most of the neonates had Stage 3 AKI marked by urine output of < 0.3 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 association was established between the stage of AKI and outcomes of acute kidney injury among the neonates as denoted by logistic regression p value of .007. Beta coefficient value of -1.014 denoted that the relationship between stage of AKI and outcomes of AKI in neonates was negative while the Exp(β) value of 2.755 signified increased odds of living relative to dying with relation to the stage of AKI that the neonate had. The findings implied that stage of AKI was a significant determinant of outcomes of acute kidney injury in neonates. Similarly, in studies by Katariya and Pandya (2019) and Ramesh (2018), 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. (2017), Fan et al. (2019) and AlGadeeb et al. (2021) with increased odds of neonates dying with advanced stages of AKI. It is safe therefore to say that outcomes of AKI in neonates correlate with severity of the AKI as denoted by its stage.

On onset of AKI (or the point at which the AKI was diagnosed), results of the study indicated 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 Exp(β) value of 3.008. It is thus implied that onset of AKI affected the outcomes of acute kidney injury in neonates. Ramesh (2018) and Nandhagopal et al. (2020) made similar observation that outcomes of AKI were significantly influenced by onset of AKI. Similarly, Mattoo et al. (2019), Vincent et al. (2020) and Starr et al. (2021) 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. It can therefore be said that onset of AKI was a significant determinant of the outcomes of AKI in neonates.

The researcher also assessed whether the neonates were mechanically ventilated. Results indicated that majority of the neonates were not mechanically ventilated. In addition, the association between need for mechanical ventilation and outcomes of acute kidney injury in the neonates was found to be statistically significant as denoted by logistic regression p value of .003. The association between mechanical ventilation and outcomes of AKI in neonates was negative as depicted by the Beta coefficient value of -3.788. However, the odds of living relative to dying on the basis of mechanical ventilation were low as depicted by an Exp(β) value of .023. Based on these findings, it is clear that being mechanically ventilated had notable effect on the outcomes of AKI among the neonates. Bakr et al. (2018) and AlGadeeb et al. (2021) 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. (2019), Kavanaugh et al. (2021) and Sanderson et al. (2022). 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. In the current study, the negative influence of mechanical ventilation on outcomes of AKI in neonates is attributed to possible compromised respiratory function and potential complications of mechanical ventilation in this vulnerable cohort.

The researcher also assessed whether the neonates were dialysed. Results indicated that slightly above half of the neonates received peritoneal dialysed largely on more than a day. The remaining did not undergo dialysis. However, the study found no statistically significant association between neonatal dialysis and outcomes of acute kidney injury among the neonates as denoted by logistic regression p value of .340 with the beta coefficient value of .506 denoting that the association between neonatal dialysis and outcomes of AKI in neonates was positive. The likelihood of neonates living relative to dying based on whether they underwent dialysis was at 1.659. The findings illustrated that neonatal dialysis was not a leading determinant of outcomes of acute kidney injury among the neonates. The findings were in contrast with those of Shalaby et al. (2018), Katariya and Pandya (2019) and Momtaz et al. (2021) who identified neonatal dialysis as being a leading predictive factor for poor outcomes of AKI in neonates during the neonatal period, sentiments also shared by Stojanović et al. (2020) and Pantoja-Gómez et al. (2022). It is thus possible that the need for dialysis could be a predictor of poor outcomes of AKI in neonates though this was not the case in the current study.

The researcher also assessed whether the neonates were exposed to nephrotoxins. Results of the study 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 not to be statistically significant as denoted by logistic regression p value of .987. The association between the two was also weak as depicted by beta coefficient value of .007. The odds of the neonates living relative to dying based on exposure to nephrotoxins was also relatively low as depicted by an Exp(β) value of 1.008. The findings depict that exposure to nephrotoxins was not a leading predictor of outcomes of acute kidney injury in neonates in the study area. This could possibly be attributed to protocols in place to safeguard neonates with AKI against exposure to nephrotoxins at KNH. The findings agreed with those of Kupferman et al. (2018) and Luna et al. (2021) who 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. (2021), Jetton et al. (2017) and Nada et al.

(2017) 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.

5.3 Conclusions

Based on the findings of the study, the researcher drew the following conclusions:

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 urine output levels at admission constituted the renal function related determinants significantly associated with poor outcome of AKI in the neonates and vice-versa.

The treatment related variables identified as having a notable association with poor outcome of acute kidney injury in neonates in the hospital included advanced stage of the AKI, late onset of AKI and being mechanically ventilated.

None of the neonate related attributes was established to have a significant association with the outcomes of AKI in neonates in the hospital.

5.4 Recommendations

5.4.1 Recommendations for Practice

The renal health care team should utilize existing evidence-based monitoring guidelines to enhance their care for patients with AKI in the hospital's pediatric care settings. In addition, the renal health care team 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.

5.4.2 Recommendations for Policy

There is need for policies, strategies and interventions including treatment related aimed at preventing AKI and reducing the burden of AKI in newborns and vulnerable infants at Kenyatta National Hospital. The policies, strategies and interventions should also aim to improve the outcomes of acute kidney injury in this highly vulnerable patient population.

5.4.3 Recommendations for Research

An investigation on the long term outcomes of neonatal acute kidney injury through follow up of the patients after discharge from the hospital would equally be informative especially with respect to gaining greater understanding of the condition and its long term sequelae.

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APPENDICES

Appendix 1: Introduction Letter

Janeth Ijai Inima,
P.O. Box 813-00100,
Nairobi.
Cell: 0722550 051
17th May 2022.

To The Director,
Medical Research Center,
Kenyatta National Hospital,
Nairobi.

Dear Sir/Madam,

RE: <u>Authority To Carry Out A Research Study at KNH</u>

I am Janeth Ijai Inima, a student at the Department of Nursing Sciences, Faculty of Health Sciences - University of Nairobi, Registration Number: H56/37647/2020. I am undertaking Masters of Science in Nephrology Nursing studies at the university. I am undertaking a research study entitled "determinants of the outcomes of acute kidney injury in neonates at the Paediatric Unit of Kenyatta National Hospital", as a requirement in partial fulfillment for the award of the said degree.

I hereby request your permission to conduct data collection within the Records Department/pediatric unit registry from the health records of neonates with acute kidney injury for the period January 1 to December 31, 2021.

Attached, find the copy of ERC approval letter. Thank you.

Yours faithfully,

Janeth Ijai Inima.

Appendix 2: Data Abstraction Form

	Neonate's demographic characteristics		
1.	Gender	Male [ ]	Female [ ]
2.	Age (in days)		
3.	Age at admission (in days)		
4.	Birth weight		
5.	Delivered in which way?	Vaginal birth [ ]	CS delivery [ ]
6.	Point at which the AKI was diagnosed	Within the first 7 days after birth	After the first 7 days after birth
	* Within the first 7 days after birth denotes early onset neonatal AKI * After the first 7 days after birth denotes late onset neonatal AKI		
	Determinants of the outcomes of AKI in neonates		
	Renal function related determinants		
		Value at admission	
7.	Serum creatinine		
8.	Urine output		
	*Value at admission is used as KNH being a referral institution also receives cases from other hospitals; hence not all neonates admitted in its Peadiatric Unit were born at the hospital. Further, neonate's SCr and urine output values at birth often reflect those of their mothers and neonate's SCr and urine output values change over time.		
	Neonate related determinants		
9.	Gestational age at birth Whether the neonate was born at term?	Yes	
		No	
	If no, indicate the gestational age recorded		
10.	Birth weight		

	Indicate the infant's birth weight?		
11.	Whether the newborn suffered from fetal growth restriction?	Yes	
		No	
12.	The newborn's Apgar score	At minute 1	
		At minute 5	
13.	Whether the newborn had any comorbidities?	Yes	
		No	
	If yes, indicate which ones?		
	Treatment related determinants		
14.	Stage of the AKI at diagnosis? [Based on KDIGO's classification criterion]	Stage 1	
		Stage 2	
		Stage 3	
15.	Whether the newborn was mechanically ventilated or intubated?	Yes	
		No	
	If yes, type of mechanical ventilation?	Noninvasive	
		Invasive	
	If yes, duration of the intubation ……		
16.	Whether the newborn was dialysed?	Yes	
		No	
	If yes, which kind of dialysis did he/she undergo?		
	Duration of the dialysis		
17.	Newborn exposed to nephrotoxins	Yes	
		No	
	If yes, indicate the type?		
	Patient's treatment outcomes		
18.	Positive outcome (patient discharged from hospital following treatment)		
19.	Poor outcome (patient died in the hospital)		

End

Appendix 3: Letter to KNH-UoN Ethical and Research Committee

Janeth Ijai Inima,

Reg. No. H56/37647/2020,

Department of Nursing Sciences,

Faculty of Health Sciences,

University of Nairobi.

The Secretary,

KNH/UoN - Ethics and Research Committee,

P.O. Box 20723-00202,

Nairobi.

Dear Sir/Madam,

RE: <u>Review of my Research Protocol entitled 'determinants of the outcomes of acute kidney injury in neonates at the Paediatric Unit of Kenyatta National Hospital'</u>

My name is Janeth Ijai Inima a master's student at the University of Nairobi's Department of Nursing Sciences undertaking a Masters of Science Degree in Nephrology Nursing. I am hereby requesting for your review and approval of my research protocol entitled "determinants of the outcomes of acute kidney injury in neonates at the paediatric unit of Kenyatta National Hospital", as a requirement in partial fulfillment for the award of the said degree.

Thank you in advance

Yours faithfully,

Janeth Ijai Inima.

Appendix 4: Approval Letter from KNH-UoN ERC

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/12

12th January 2023

Janeth Ijai Inima
Reg.No.H56/37647/2020
Dept. of Nursing Sciences
Faculty of Health sciences
University of Nairobi

Dear Janeth,

RESEARCH PROPOSAL: DETERMINANTS OF THE OUTCOME OF ACUTE KIDNEY INJURY IN NEONATES AT THE PAEDIATRIC UNIT OF KENYATTA NATIONAL HOSPITAL (P455/05/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P455/05/2022.** The approval period is 12th January 2023 – 11th January 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Assistant Director, Health Information Dept., KNH
The Chairperson, KNH- UoN ERC
The Chair, Dept. of Nursing Sciences, UoN
Supervisors: Dr. Dorcas Maina, Dept. of Nursing Sciences, UoN
Ms. Hannah Inyama, Dept. of Nursing Sciences, UoN

Appendix 5: Approval for Data Collection from Kenyatta National Hospital

KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723, 00202 Nairobi

Tel.: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/PAEDS-HOD/48 Vol.II

Date: 30th January 2023

Janeth Ijai Inima
Reg. No.H56/3747/2020
Department of Nursing Sciences
Faculty of Health Sciences
University of Nairobi

Dear Janeth,

RE: AUTHORITY TO COLLECT DATA IN PAEDIATRICS DEPARTMENT

Following approval of your Research proposal by the KNH/UON-Ethics & Research Committee and subsequent filing of the Study Registration Certificate, this is to inform you that authority has been granted to collect data in ***Paediatrics Department*** on your study titled ***"Determinants of the outcome of Acute Kidney Injury in Neonates at the Paediatric unit of Kenyatta National Hospital"***.

Kindly liaise with the Assistant Chief Nurse Incharge, Paediatric Specialized unit for facilitation.

You will also be required to submit a report of your study findings to the office of the HOD, Paediatrics - KNH after completion of your study.

Dr. Mukokinya Kailemia
Ag. HOD, Paediatrics

Cc. ACN Incharge, PSU

Appendix 6: Study Registration Certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   JANETH IJAI INIMA
2. Email address: ijais72@gmail.com Tel No. 0722550051
3. Contact person (if different from PI) –
4. Email address: – Tel No. –
5. Study Title
   DETERMINANTS OF THE OUTCOME OF ACUTE KIDNEY INJURY IN NEONATES AT THE PAEDIATRIC UNIT OF KENYATTA NATIONAL HOSPITAL
6. Department where the study will be conducted PAEDIATRICS
   (Please attach copy of Abstract)
7. Endorsed by Research Cordinator of Department where study will be conducted.

   Name: ..... Signature ..... Date .....
8. Endorsed by KNH Head of Department where study will be conducted.

   Name: DR. MUKOKINYA KAILEMIA (Ag HOD) Signature ..... Date 27/1/2023
9. KNH UoN Ethics Research Committee approved study number P455/05/2022
   (Please attach copy of ERC approval)
10. I JANETH IJAI INIMA commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.

    Signature ..... Date 27/1/2023
11. Study Registration number (Dept/Number/Year) Paediatrics /370 /2023
    (To be completed by Medical Research Department)
12. Research and Program Stamp _____

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.

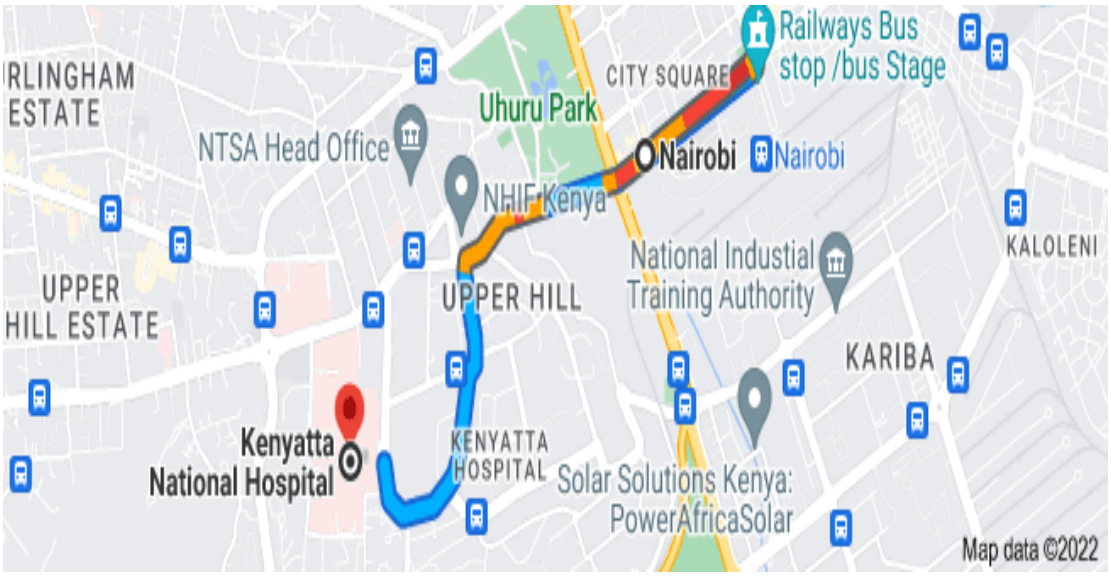
Appendix 7: Work Plan

Activity	2022						2023		
	Jul	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**
Development of the concept									
Proposal writing and presentation									
Submitting the proposal to ERC									
Pretesting the study tool									
Collecting the study data									
Data analysis, report writing and corrections									
Defense of the project									

Appendix 8: Budget

Component	Description	Item	Quantity	Unit Cost (Ksh)	Total (Ksh)
Literature Review	Literature search	Airtime Internet	6 Months 6 Months	1,000/Month 2,500/Month	6,000 15,000
	Stationery	Laptop	1	60,000	60,000
		External Hard Disc	1	7,000	7,000
		Pens, Pencils, Eraser, Folders	10	@ 100	1,000
Proposal	Related costs	Plain paper Printing Photocopying Binding	2 reams 1 Draft 2 Drafts 3 Drafts	@650 @750 @250 @100	1,300 750 500 300
Approval	KNH Data ERC		1 1	@500 @ 2,000	500 2,000
Research Phase	Pretesting of questionnaire	Printing	245	@ 20	4,900
	Study tool	Printing, photocopy	4,900	@5	24,500
	Data collection	Research Assistants	2	@ 10,000	20,000
	Data Processing and analysis	Statistician	1	@ 40,000	40,000
Report Phase	Final Report	Printing Photocopying Binding	1 copy 4 copies 5 copies	@ 1,000 @ 500 @ 100	1,000 2,000 500
Publishing					30,000
Sub Total					**217,250**
Contingencies	10% of sub-totals				**21,725**
Grand Total					**238,975**

Appendix 9: Map of the Study Area



Appendix 10: plagiarism

Determinants Of The Outcomes Of Acute Kidney Injury In Neonates At The Paediatric Unit Of Kenyatta National Hospital

ORIGINALITY REPORT

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