UNIVERSITY OF NAIROBI, COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

CLINICAL PROFILE AND SHORT-TERM OUTCOMES OF PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING HAEMODIALYSIS AT THE KENYATTA NATIONAL HOSPITAL

DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE.

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DECLARATION

This dissertation is my original work and has not been presented for a degree in any other University

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LIST OF ABBREVIATIONS AND ACRONYMS

ACE	Angiotensin converting enzyme
ACE-I	Angiotensin converting enzyme inhibitors
ADQI	Acute dialysis quality initiative
AKI	Acute kidney injury
AKI-D	Acute kidney injury requiring haemodialysis
AKIKI	Artificial kidney initiation in kidney injury
AKIN	Acute kidney injury network
ARBs	Angiotensin receptor blockers
CAD	Coronary artery disease
CHF	Congestive heart failure
CKD	Chronic kidney disease
CRRT	Continuous renal replacement therapy
ELAIN	Early versus late initiation of renal replacement
eGFR	Estimated glomerular filtration rate
GFR	Glomerular filtration rate
HD	Haemodialysis
ICU	Intensive care unit
IHD	Intermittent haemodialysis
KDIGO	Kidney disease improving global outcomes
KNH	Kenyatta National Hospital
KRT	Kidney replacement therapy
MAKE	Major adverse kidney event
MES	Managed equipment service
RCT	Randomized control trial
RIFLE	Risk, injury, failure, loss of kidney function, end stage kidney disease
START	Standard versus accelerated initiation of renal replacement

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ABSTRACT

Background: Acute Kidney Injury requiring haemodialysis (AKI-D) is associated with in-hospital morbidity, mortality and health care cost The few studies done in Africa on AKI-D patients show a high mortality rate of between 34% to 54%. Furthermore, it increases the future risk of major adverse kidney events (MAKEs), including chronic kidney disease (CKD), end-stage kidney disease (ESKD) and death.

Objectives: To determine the clinical presentation and 90-day outcomes of haemodialysis-treated AKI patients at Kenyatta National Hospital (KNH).

Methods: A retrospective cohort study that evaluated the clinical presentation and outcomes of haemodialysis-treated AKI adult patients at Kenyatta National Hospital from January 2020 to December 2021. Categorical data such as sex, ward versus ICU admission, baseline eGFR, aetiology, and outcomes were summarised using frequency tables and corresponding percentages. Continuous variables such as age and time to haemodialysis were summarized using mean and the corresponding standard deviation or median and the corresponding inter quartile range (IQR). Association analysis was carried out using logistic regression.

Results: Out of the 144 enrolled patients, median age was 33 (IQR 27–47) years. Females accounted for 68.1%. Fifty-three percent were admitted into the various Intensive Care Units (ICU). Obstetric conditions (46.5%) and Infections (36.1%) were the most frequent comorbidities. Hyperkalaemia (58%) and clinical complications of uremia (41%) were top indications for haemodialysis. Full recovery was observed in 52 (36.1%) of the cohort, while 20 (13.9%) had partial recovery and 22 (15.3%) became dialysis dependent. Mortality rate was 34.7% at 90-days. On multivariate analysis severe metabolic acidosis (aOR = 2.4, 95% CI 1.1-5.2, $P = 0.026$) and volume overload (aOR = 3.0, 95% CI 1.2–7.1, $P = 0.015$) were significantly associated with mortality. Obstetric complications were significantly associated with survival (aOR = 0.3, 95% CI 0.1–0.8, $P = 0.012$).

Conclusion: AKI requiring haemodialysis mainly affects the young adults at KNH with pregnancy-related conditions and infections being the most common comorbidities. AKI-D has a high mortality rate at KNH. Even though half of the patients recovered their kidney functions, a significant number had partial recovery of renal functions with some being dialysis dependent at 90 days.

1.0 CHAPTER ONE: INTRODUCTION

Acute kidney injury (AKI) is a clinical syndrome characterized by prompt decline of kidney function. One out of five hospitalized patients suffer from AKI with approximately 1% to 2% of them requiring kidney replacement therapy (KRT) (1–3). At discharge 30% of those requiring KRT will need to continue with haemodialysis as outpatient.

The incidence of AKI and its severe form requiring dialysis (AKI-D) has been on the rise over the years (4). Most of the research data on AKI-D comes from advanced world settings with varying results. In the United States, the incidence of AKI-D increased by more than two-fold from 2000 to 2009 (5). A retrospective population-based research among critically ill in Canada, found that there was a fourfold increase in AKI-D from 0.8 to 3% between 1996 and 2010 (6).

Little is known about AKI requiring dialysis in resource limited settings especially in Africa where kidney replacement therapy (KRT) is limited. Patients with AKI from low-income countries are quite different from the developed world in that they are often younger, have less comorbidities and have a high burden of infectious disease which leads to a difference in disease outcomes (7,8). Emem-Chioma *et al.* in a study done in a teaching hospital in Nigeria found the prevalence of dialysis-treated AKI was 1.0% of medical admissions, 8.4% of all kidney failure cases, and 51.2% of AKI patients (9).

The possible outcomes of AKI patients treated with dialysis include: - dialysis independence (partial or complete kidney recovery), end stage kidney disease (failure to recover in 90 days), or death. This study aims to assess these outcomes over 90 days in haemodialysis treated AKI patients at Kenyatta National Hospital (KNH). The 90-day is an important time point because it is the defined time when many patients with AKI still on dialysis treatment are considered to have reached end stage kidney disease (ESKD) (10).

The Kenyan Government recently made deliberate efforts to increase the renal dialysis equipment in level 5 hospitals and 2 national hospitals through the managed equipment service (MES) project. This is one of the many measures taken in order to attain Universal Health Coverage (UHC) in Kenya by the year 2030. The number of haemodialysis treated-AKI patients is set to increase with the availability of more dialysis equipment; therefore, knowing their outcomes and clinical profiles is important for purposes of planning and improving their overall management during follow up.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1 Definition and staging of AKI

The Kidney Disease Improving Global Outcome (KDIGO) guidelines developed in 2012 define AKI as increase in serum creatinine (sCr) by 0.3 mg/dl (≥26.5 μmol/l) within 48 hours; or an increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the preceding 7 days; or a urine volume <0.5 ml/kg/h for 6 hours. In the same guidelines the term acute kidney disease (AKD) was proposed to define a period between seven to ninety days in AKI patients whom kidney recovery is still ongoing(11).

KDIGO classification of AKI merged the Risk, Injury, Failure, Loss and End-stage renal disease (RIFLE), 2004 and the AKI Network (AKIN), 2007 classifications with the aim of unifying the definition of AKI (12). The National Institute for Health Care and Excellence systemic review of the KDIGO, RIFLE and AKIN definitions found that they do not differ significantly in their performance (13). The new definitions of AKI which entirely use serum creatinine and urine output to stage AKI have revolutionised both research and routine clinical practice (12).

The last decade has seen an explosion of research on novel biomarkers of AKI (14,15). These biomarkers are compounds released into the blood and urine by injured glomeruli and tubules and it is believed that quantification of these compounds reflects the degree of injury to the kidneys (15). The biomarkers of AKI have the capability to recognise patients who are going to develop AKI early compared to serum creatinine and urine output; henceforth have the potential of reducing severe AKI requiring dialysis (14). Currently over 15 different biomarkers have been investigated but none has been universally accepted for routine use in clinical practise; with some getting approval in certain countries in Europe, USA and Japan (15). Use of these biomarkers for research and clinical practice is yet to be explored by many African countries including Kenya. Some of the examples of these biomarkers according to Kashani *et al.* include neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1), liver-type fatty acid-binding protein, interleukin 18 (lL-18), insulin-like growth factor-binding protein 7, tissue inhibitor of metalloproteinase 2 (TIMP-2), calprotectin, urine angiotensinogen (AGT), and urine microRNA (14).

AKI has been staged by KDIGO in terms of severity into stage 1 to 3 with AKI requiring dialysis (AKI-D) falling directly under stage 3 (4,11). The staging is as shown below:

Table 1: Staging of AKI as per the KDIGO

STAGE OF AKI	PARAMETERS
Stage 1	-Serum creatinine 1.5-1.9 times above baseline within 7 days, or -A rise in serum creatinine of 26.5µmol/l (0.3 mg/dl) or more within 48 hours, or -A urine output of less than 0.5ml/kg/hour for 6-12 hours
Stage 2	-Serum creatinine 2-2.9 times above baseline, or -A urine output of less than 0.5ml/kg/hour for 12 hours
Stage 3	-Serum creatinine 3 times of the baseline, or -Increase in creatinine above 353.6µmol/l (4mg/dl), or -Initiation of dialysis, or -Urine output of less than 0.3ml/kg/hour for more than 24 hours, or -Anuria for more than 12 hours

2.2 Aetiologies of AKI

Makris *et al.* classified AKI into three groups based on aetiologies which includes pre-renal AKI, acute post-renal obstructive nephropathy and intrinsic acute kidney diseases (16). In their study they noted many patients with AKI have mixed aetiologies where the presence of sepsis, ischemia and nephrotoxicity often co-exist and complicate recognition and treatment. Whatever the aetiologies of AKI are, the presentations are those of fluid, electrolytes, blood urea nitrogen as well as acid-base disorders among others.

The Aetiologies are as summarized in table 2:

Table 2: Aetiology of AKI according to Makris et al.

Category	**Abnormality**	**Possible causes**
Prerenal (Renal hypoperfusion)	Hypovolemia	Haemorrhage Volume depletion - vomiting, diarrhoea Renal fluid loss (over-diuresis) Third space (burns, peritonitis, muscle trauma)
	Impaired cardiac function	Congestive heart failure Acute myocardial infarction Massive pulmonary embolism
	Systemic vasodilatation	Anti-hypertensive medications Gram negative bacteraemia (Sepsis) Cirrhosis Anaphylaxis
	Increased vascular resistance	Anaesthesia Surgery Hepatorenal syndrome NSAID medications Drugs that cause renal vasoconstriction (i.e., cyclosporine
Intrinsic	Tubular	Renal ischaemia (*Shock, complications of surgery, haemorrhage, trauma, bacteraemia, pancreatitis, pregnancy*) Nephrotoxic drugs (*Antibiotics, antineoplastic drugs, contrast media, organic solvents, anaesthetic drugs, heavy metals*) Endogenous toxins (*myoglobin, haemoglobin, uric acid)* All pre-renal causes
	Glomerular	Acute post-infectious glomerulonephritis Lupus nephritis IgA glomerulonephritis Infective endocarditis Goodpasture syndrome Wegener disease
	Interstitium	Infections (*bacterial, viral*) Medications (*Antibiotics, diuretics, NSAIDs, and many more drugs*)
	Vascular	Large vessels (*Bilateral renal artery stenosis, bilateral renal vein thrombosis*) Small vessels (*Vasculitis, malignant hypertension, atherosclerotic or thrombotic emboli, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura*)
Postrenal	Extrarenal obstruction	Prostate hypertrophy Improperly placed catheter Bladder, prostate or cervical cancer Retroperitoneal fibrosis
	Intrarenal obstruction	Nephrolithiasis Blood clots Papillary necrosis Urethral stricture

2.3 Dialytic modalities

2.3.1 Indications for haemodialysis

One to two percent of hospitalised patients will develop severe AKI requiring KRT (3). Among ICU patients the figure is much higher at 13% (14,15). The available dialytic treatment modalities of AKI include haemodialysis (HD) and peritoneal dialysis (PD). The HD can be continuous or intermittent. No one set of criteria exists to guide such interventions. The traditional indications for haemodialysis in AKI patients include symptomatic uremic manifestations (encephalopathy, pericarditis, convulsions, bleeding), fluid overload resistant to diuretic agents, intractable hyperkalaemia and severe metabolic acidosis (17).

The Acute kidney injury network (AKIN) has published guidelines in an effort to offer some objective guidance (17). The guidelines broadly classify the indications as absolute and relative. Each absolute indication merits dialysis by itself whereas, relative indications require assessment of the entire clinical scenario before making a decision to initiate dialysis. The indications are summarized in table 3:

Table 3: Indications for dialysis as per Acute Renal Failure Trial Network

Indication	Parameter	Relative/Absolute
Metabolic abnormality	*BUN >76 mg/dL (27.1 mmol/L)	Relative
	BUN >100 mg/dL (35.7 mmol/L)	Absolute
	Hyperkalaemia >6 mEq/L	Relative
	Hyperkalaemia >6 mEq/L with ECG changes	Absolute
	Dysnatremia	Relative
Acidosis	pH > 7.15	Relative
	pH < 7.15	Absolute
	Lactic acidosis related to Metformin use	Absolute
Anuria/oliguria	Urine output <0.5 mL/kg/h × 6 h	Relative
	Urine output <0.5 mL/kg/h × 12 h	Relative
	Urine output <0.3 mL/kg/h × 24 h	Relative
	Anuria × 12 hours	Relative
Fluid overload	Diuretic sensitive	Relative
	Diuretic resistant	Absolute

*Symptomatic uremia (encephalopathy, pericarditis, convulsions, bleeding) is an absolute indication

2.3.2 Choice of dialytic treatment modality

Intermittent haemodialysis (IHD) is the most commonly used form of KRT in majority of patients with AKI-D and can also be utilized in the ICU for more stable patients (18). Continuous renal replacement therapy (CRRT) is less strenuous to the hemodynamics of the patient and hence is often utilized for unstable critically ill patients that need fluid and or solute removal due to AKI (4). Peritoneal dialysis is rarely used in adult patients with AKI requiring haemodialysis. On the issue regarding the initial choice of KRT, Schneider *et al.* evaluated 23 studies (7 randomised control trials and 16 observational studies) of patients with AKI-D and noted that randomised control trials (RCT) failed to demonstrate any difference in outcomes interrelated to the primary choice of KRT modality (18). The observational studies they evaluated suggested there was a higher rate of kidney recovery among patients initially started on CRRT compared to IHD.

2.3.3 Early versus late initiation of KRT

The optimal time to start kidney replacement therapy (KRT) in patients with AKI is still contentious. Two randomized control trials (RCT), the Early Versus Late Initiation of renal replacement (ELAIN) trial and the Artificial Kidney Initiation in Kidney Injury (AKIKI) trial which reported explicitly on the issue of the timing of initiation gave conflicting results creating further confusion (19). ELAIN trial was a single-center study and resolved that early KRT also translated into better kidney recovery whereas the AKIKI trial which was a multicenter trial found no significant difference in the primary outcome between the early and delayed KRT (20,21).

The STARRT-AKI trial (Standard versus accelerated Initiation of renal replacement therapy in AKI trial) which is RCT done in 2020 among critically ill patients with AKI found that an accelerated KRT strategy was not associated with low risk of death at 90 days (22). More recently (2021), the AKIKI 2 trial was published and the authors concluded that in severe AKI (stage 3 patients with oliguria for more than 72 h or blood urea nitrogen concentration higher than 112 mg/dL) and no absolute indication for KRT, extended delaying of KRT initiation did not confer additional benefit and was associated with potential harm (23). A meta-analysis of 9 randomized trials done after year 2002 including both ELAIN and AKIKI found no substantial difference in timing of KRT initiation on clinical outcomes(21).

2.4 Outcomes

Patients who survive the short-term implications of AKI are known as "survivors". There is no agreement with regard to the time frame as to when a patient who experiences an episode of AKI

is declared a "survivor". Wald *et al.* in their review of care of an AKI survivor define an "AKI survivor" as a patient who achieves some degree of comprehensive clinical stability subsequent to the acute illness that led to his or her AKI (24). This includes those discharged from hospital and those with partial kidney recovery.

The possible outcomes of AKI "survivor" treated with dialysis include: - dialysis independence (partial or complete kidney recovery), end stage kidney disease (failure to recover in 90 days) or death (Mortality). This major adverse kidney events (MAKE) are clinically important endpoints in all subjects enrolled in AKI clinical trials and research (25). Frederic T. and colleagues in their review of clinical trial endpoints in AKI suggested adaptation of the MAKE composite assessed at 90 days after AKI (MAKE90) ; and they noted that it will advance our capacity to understand and treat AKI (26). This study aims to look at AKI-D outcomes over 90 days.

In a study done by Lorien *et al.* (2019) involving a large cohort of over 9000 patients with AKI requiring outpatient dialysis; observed the following outcomes at 90 days: 36% of patients recovered kidney function, 37 % transitioned to ESKD, 10% died and 10% had persistent AKI (CKD) (27).Pajewski *et al.* in their study done also in developed found overall, 43% of patients became dialysis independent by 90 days, with 16% fully recovering to previous baseline kidney function, 45-49% transitioned to ESKD and 9% died (3).

Hickson *et al.* in their study done at the Mayo Clinic observed that 21% of patients became dialysis independence within 6 months after AKI-D (28). Recovery most often occurred within the first 3 months of KRT initiation. Baseline kidney impairment (eGFR <30 mL/min) and CHF were associated with reduced chances of renal recovery in their research. Gautam and colleagues in their study done in a dialysis facility at University of Virginia observed that 42.0% achieved dialysis independence within 90 days, 48.7% transitioned to ESKD, while 9.2% died (29). It is of note that the above 3 studies were done with cohorts ranging 100-300 (3,28,29).

A prospective study done by Rathore and colleagues via telephone survey found that at 90 days post-HD initiation, 57% (n=91) of patients were declared ESKD and 43% were dialysis-independent (30). Another recent prospective study done in India by Jaryal *et al* found Overall, 39% regained serum creatinine in the normal range at 3 months, 36.7% died, 14.1% reached chronic kidney disease (CKD), 7.8% lost to follow-up, and 2.3% had reached end-stage renal disease (31). A study done in Taiwan by Wu *et al.* on long term outcomes of AKI-D found that 41.3% patients died from hospitalization to 90 days after discharge with 23.2% of those who survived to 90 days being weaned from acute dialysis (32).

Studies done on AKI-D in Africa are few and have mostly looked at mortality as an outcome. Arthur *et al.* in their study in Uganda found a mortality of 52.5 % (33). Emem-Chioma *et al.* in their study done in Nigeria found that out of the 62 patients with AKI-D, 29 (46.8%) became stable enough to be discharged from the hospital, 27 (43.5%) died in hospital while 6 (9.7%) were lost to follow up (9). Another study done by Igiraneza *et al.* in Rwanda observed a mortality rate of 34.1 % (34).

Tayabeli *et al.* in 2017, did a longitudinal study at the KNH (main public referral hospital in Kenya) to determine the point prevalence in 3 months' time of AKI with follow up of the patients to record their outcomes over 2 weeks at KNH. Their study found that the overall mortality associated with community acquired-AKI was 16.9% and of note it worsened with increasing severity. At 2 weeks (end of the study) 53.1% had not recovered from AKI, 18.6% recovered fully while 28,3% had partial recovery (35).

AKI-D is also a common cause of increased length of hospital stay and readmissions (33). A study done by Pascal *et al.* found that increased severity of AKI was associated with an increasing length of hospital stay for patients (36). Additionally, AKI especially the severe form has the potential of causing harm to other organ systems with multiple consequences; increased cardiac events like congestive heart failure (CHF), coronary artery disease (CAD) and stroke as well as catheter-related infections (4,37,38).

2.5 Comorbidities and risk factors

Some of the risk factors of developing CKD, ESKD or death after AKI is influenced by patient demographics, comorbidities and the degree of renal injury and recovery (39–44). Some of the comorbidities and their relationship with AKI and AKI-D are discussed below:

2.5.1 Prior AKI

Prior AKI increases the future risk of developing a new episode of kidney injury among AKI-D survivors (4). Gautam *et al.* observed that AKI-D patients with previous AKI were 75% more likely not to recovery as compared to those without a history of previous AKI (29). Siew *et al.* found that twenty five percent of AKI survivors have recurrent AKI which is another intermediate outcome that can threaten recovery and contribute to faster declines in kidney function (45). Traditional factors like CKD, diabetes and AKI-related factors (*e.g.*, severity) were risks for AKI recurrence in their study.

2.5.2 Chronic Kidney Disease (CKD)

Resent research and systemic review show that AKI and CKD are interrelated. Wald *et al.* observed that AKI-D survivors who recover in the short-term are 3 times more likely to progress to chronic dialysis as compared to matched patients who did not get AKI (24,46). Chawla and colleagues examined kidney outcomes after AKI more comprehensively by assessing major adverse kidney events (MAKE) which were defined as the composite of death, dialysis and a sustained decline in estimated glomerular filtration rate of 25% (24,47). They found that patients admitted with an AKI episode had a more than two-fold adjusted risk of a MAKE in comparison to referent group with a myocardial infarction. Additionally, Coca *et al.* in their met analysis of CKD after AKI found similar results (37).

Wald and colleagues advise that we must consider important caveats when analysing the relationship between AKI and CKD because they share common risk factors such as diabetes and cardiovascular disease which may confound their interconnection. Furthermore they noted that, AKI survivors are exposed to intervening event like episodes of heart failure and recurrent sepsis which might be the "true" mediators of CKD given the lengthy interval time between AKI and subsequent development of CKD (24).

2.5.3 Cardiovascular diseases

Patients with cardiovascular diseases particularly chronic hypertension and heart failure are frequently susceptible to getting episodes of AKI.(4). Furthermore, these comorbidities negatively affect recovery from AKI and increase the risk of death (4,48). Gautam *et al.* noted that patients with AKI-D who had congestive heart failure were 69% less likely to recover (29). Bucaloiu and colleagues in their study found that hypertensive patients who get AKI are at also at increased risk of for developing stage 4 CKD (49). Other studies done show changes in serum creatine after a myocardial infarction episode is associated with high risk of developing ESKD and mortality (42,43). Moreover, AKI can worsen the cardiovascular outcomes in patients with myocardial infarction.

2.5.4 Diabetes mellitus

Diabetes affects severity of AKI and is common in dialysis requiring AKI patients (50). In a recent study done in the United States, Harding *et al.* noted that the AKI-D patients with diabetes were 5 times more likely to be hospitalised compared with adults without diabetes (51). Diabetes Mellitus plays a major role both in the development of CKD and AKI (4). Simona and colleagues

noted that patients with diabetes with either normal kidney function or CKD at baseline have higher chances of developing both new and recurrent AKI compared with non-diabetic CKD controls (52). Thakar *et al.* in their study observed that each AKI episode in diabetes doubles the risk for CKD progression and development of advanced stage 4 CKD (53). The large-scale study done by Chawla and colleagues also showed similar results (47).

2.5 Obstetric complications

Pregnancy-related AKI especially the severe form is associated with significant morbidity and mortality in young and healthy women more so in the developing world (54). Hildebrand *et al.* in their study conducted in Canada found the maternal mortality after pregnancy-associated AKI-D was 4%, with 4% of survivors requiring to continue with dialysis after delivery (55). This is low compared to studies done in Africa.

Igiraneza *et al.* in their study in Rwanda found that obstetric complications were the second most common comorbidities of AKI-D at 26.9% (34). These comprised of conditions such as post-caesarean section peritonitis, post and antepartum haemorrhage, septic abortion, preeclampsia, and eclampsia. Kivai *et al.* in their study done in KNH found that AKI-D occurs in 28.8% of pregnant women with majority still requiring dialysis at discharge (56). In their study the predominant obstetric condition associated with AKI in pregnancy were hypertensive disorders (pre-eclampsia, eclampsia and HEELP syndrome) at 80.3%.

2.5.6 Infectious disease

Infectious diseases are major contributors to the development of major adverse kidney events after haemodialysis-treated AKI in Africa (9,33,34). Emem-Chioma *et al.* in their study done in Nigeria found sepsis as the leading medical etiology at 22.7% (9).

A study done by Arthur K *et al.* in Uganda to determine the clinical characteristics and 30-day outcome of intermittent Haemodialysis for AKI in an African ICU found similar results (33). Igiraneza *et al.* in their study in Rwanda observed that acute infections were common comorbidities observed in AKI-D patients. This included malaria at 12.2%, pneumonia at 3.6%, and sepsis at 3.6% (34).

2.5.7 Covid-19

The world is currently witnessing the COVID-19 pandemic which is an infectious disease caused by the novel coronavirus SARS-CoV-2. Covid-19 is a multisystem disease involving many organs including the kidneys. One out of three hospitalized patients with COVID-19 infection

end up developing AKI with the rates varying based on geography (4).

A recent multicenter study done by Moledina *et al.* found that COVID-19 patients have a higher rate of AKI across all the stage as compared to those without COVID-19 (57). They found the rate to be more than twice in AKI-D patients. Dursavula and colleagues from their experience in Seattle noted that 5% of Covid-19 patients will eventually require dialysis, often around the second week of infection (58). Observations in KNH medical wards and the Infectious disease unit has shown that some of the patients with severe Covid-19 end up developing AKI-D.

2.5.8 Other comorbidities

Patients with malignancy have increased risk for AKI and worse outcomes. Silver *et al.* found malignancy to be a major comorbid in patients with AKI and their related death was as common as cardiovascular death (44). Abudayyeh *et al.* in a recent study observed that that receiving KRT in the ICU was not associated with better survival in patients with stage IV cancer (59). Wang and colleagues observed that patients who underwent dialysis after surgery may have higher rates of mortality and failure to recover kidney function as compared to the non-dialysis cohort cohort(60). Furthermore, Nadkarni *et al.* in their study found that there is growing burden of AKI-D in non-renal solid organ transplant recipients and emphasized the need to develop strategies to reduce the risk of AKI (61).

2.6 Nephrology follow up

Given the short- and long-term effects of AKI-D, the process of care for the "survivor" is very important and there is need for involvement of a nephrologist in the follow up. The KDIGO AKI 2012 guidelines recommend that kidney function be checked in 90 days after an AKI episode in order to ascertain whether CKD or ESKD can be formally diagnosed (11). Review of multiple studies has shown that there is a gap between these guidelines recommendation and what essentially happens (62).

A study done by Siew *et al.* on US veterans AKI survivors showed that the cumulative incidence of nephrology referral before dying, initiating dialysis or experiencing an improvement in kidney function was 8.5% and severity did not affect referral rate (63). Another done by Harel *et al.* in Ontario Canada involving AKI-D patients found that only 41% saw a nephrologist during the 90 days after discharge. A more recent one done by Wu *et al.* involving AKI-D "survivors" found that only 37.3 % were followed up by nephrologist (64).

"The who to follow, when to conduct follow up visit, how to effectively deliver care and what

interventions to implement is still a matter of ongoing research"(65). Various models have and are still being developed to address these issues. Javier *et al.* in a recently published article reviewed some of the models and are of the opinion that we should start using the models already developed to strengthen clinical trials and ultimately care of AKI "survivor" (65).

Some of the interventions that can better patient centred outcome include monitoring of the volume status and introduction of cardio protective drugs like angiotensin converting enzyme (ACE) inhibitors and angiotensin receptors blockers (ARBS) (65). Recent studies have shown the benefit of using ACE inhibitors and ARBS during AKI recovery and have recommended their use by nephrologist with cautious monitoring of renal specific complications (66,67). Additionally, patients who remain dialysis-dependent will need to be educated on the available KRT modalities, plan for long-term vascular access and referral for kidney transplantation evaluation. Conversely, for patients who recover, measures to ensure avoidance of a new episode of kidney injury need to be implemented. This involves avoidance of kidney insults such as hypotensive episodes on dialysis and nephrotoxic drugs ; close monitoring of residual kidney function ; and nephrology outpatient follow up once off dialysis (4)

2.7 Justification

The International Society of Nephrology (ISN) has made AKI a priority issue and come up with a 0 by 25 initiative (no deaths by 2025) which is a few years from now (68). Despite this efforts AKI especially the severe form requiring KRT, still has a high mortality and is associated with long term multisystem complications. The few studies done in Africa on haemodialysis treated AKI patients show a high mortality rate of between 34% to 54% (9,33,34). Were *et al.* in a study done locally on AKI patients at KNH found a mortality of 40.4% with those with bleeding diathesis, pulmonary edema and hyperkalaemia (all indications for dialysis) associated with increased mortality(69). Currently no study has been done of AKI-D patients in our set up. Therefore, this study will help fill the gap and add knowledge on AKI-D both locally and internationally in line with the 0 by 25 initiative.

Furthermore, over the last few years, there have been patients who have been crash-landing into the dialysis unit at KNH and from the history, they had been managed for AKI previously and most probably lost to follow up after recovery of AKI. The cost of care for managing such patients when they develop ESKD requiring lifelong KRT is high for both the patient and the health system.

The renal department in KNH has put deliberate efforts to follow up patients with AKI and in

2021, the department has established a register for patients with AKI in the hospital. The status of the patients is also presented during weekly major ward rounds in the department. This study aims to establish the clinical presentation and 90-day outcomes of the AKI patients who require haemodialysis. This will help improve our knowledge on the various factors associated with AKI-D in our setting, hence give us a chance for modification of these factors in order to reduce AKI-D cases and improve on their outcomes.

2.8 Objectives

2.8.1 Research question

What are the short-term outcomes of haemodialysis-treated AKI patients?

2.8.2 Broad objective

To determine the 90-day outcomes of haemodialysis-treated AKI patients

2.8.3 Specific objectives

2.8.3.2 Primary Objective

1) To describe the clinical presentation of haemodialysis-treated AKI patients at KNH
2) To determine the 90-day outcomes (dialysis independence, dialysis dependence and death) of haemodialysis-treated patients with AKI at KNH

2.8.3.2 Secondary objectives

1) To describe the association between the patients' characteristics and the 90-day outcome of hemodialysis-treated patients with AKI at KNH

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study design

Retrospective cohort study.

3.2 Study setting

The study was carried out at Kenyatta National Hospital (KNH) which is a tertiary referral hospital located in the capital city of Kenya, Nairobi. It serves as the teaching hospital for the University of Nairobi, Faculty of Health Sciences, both for the Undergraduate and the Postgraduate programs. KNH offers both outpatient and inpatient haemodialysis (HD) services. The HD services are offered at the renal unit and the medical intensive care unit (ICU). The renal unit has approximately 20 dialysis machines with a capability of dialyzing 40 to 50 patients in a day whereas the medical ICU has one dialyzing machine with a capability of dialyzing 2 to 3 patients in a day. KNH uses both a manual and digital record system for recording both admission and discharge information. Data for those who have a diagnosis of AKI including those who have undergone dialysis is captured at the KNH statistics department using the International Classification of Diseases revision 10. It is generated using the discharge and death summary and captures all the diagnosis listed. This data is stored for reference and is also available for research purposes. A list of diagnosis of interest and period of cover can be made available upon request and due process.

3.3 Study population

The Study population consisted of records of haemodialysis-treated AKI patients (AKI-D) admitted at Kenyatta National Hospital between January 2020 to December 2021.

3.4 Case definition

1. Haemodialysis treated AKI patients where Acute Kidney Injury was defined according to KDIGO as (11)
    - Increase in serum creatinine (Scr) by ≥ 26.5 µmol/L within 48 hours
    - Increase in Scr by ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days.

2. The baseline creatinine was as recorded in the file for patients whose baseline creatinine had been established and for the rest of the patients whose baseline is unknown it was estimated using the simplified modification of diet in renal disease (MDRD) formula, assuming a GFR

of 75ml/min per 1.73m2. This is as recommended by KDIGO

$$epCr = \left(\frac{GFR}{Sex \times Race \times 186 \times Age^{-0.203}} \right)^{-\frac{1}{1.154}} (\text{mg/dl})$$

Where *GFR* was the assumed GFR (ml/min); *Sex* = 1 if male and 0.742 if female; *Race* = 1.21 if black, otherwise *Race* = 1; and *Age* was in years. To convert from mg/dl to µmol/L we will multiply by 88.5

3. Aetiology categorization and definition were as follows:
   - The aetiologies were clinically categorized into 3 categories namely: pre-renal, renal and post renal/obstructive based on the diagnosis and history recorded in the file. This was as per Makris *et al.* classification shown in table 2 (16). Though, patients were categorized into 3 distinct categories, some of the patient had two or more risk factors from the same category or from the other two categories.
4. CKD was defined according to the KDIGO guidelines as kidney damage or decreased glomerular filtration (GFR) of less than 60 mL/min/1.73 m2 for at least 3 months (11).
5. Indications for dialysis were categorized into hyperkalaemia, severe metabolic acidosis, volume overload and clinical complications of uremia. This was as recorded in the file.
6. An acceptable recorded case was defined as a file that has the following data:
   - Demographics
   - Comorbidities
   - Indication for dialysis
   - Capacity to clearly know the 90-day outcome
7. The outcomes were defined as follows:

   - **Kidney recovery (Dialysis independence)** was defined according to the Acute Disease Quality Initiative (ADQI) consensus report as sustained (> 14 days) independence from KRT (17). The recovery can be complete or partial as defined below:

     a) Complete recovery was defined as a return to their baseline Risk, Injury, Failure, Loss and End-stage kidney disease (RIFLE) classification or within 50% of baseline creatinine

b) partial renal recovery was defined as a persistent change in RIFLE classification (R, I or F), or failure to recover within 50% of baseline creatinine, but not a persistent need for haemodialysis

- **End stage kidney disease (Dialysis dependence)** was defined as the persistent need for haemodialysis at 90-days after AKI

- **Death** was defined as any patient certified by a medical officer as being dead in the file.

3.5 Sample size estimation

All consecutive files of adult patients with a diagnosis of AKI requiring haemodialysis from January 2020 to December 2021 meeting the inclusion criteria were used for data collection. Therefore, a sample size calculation was not necessary.

3.6 Inclusion criteria

- Records of patients with a diagnosis of AKI as per the KDIGO criteria who underwent haemodialysis during the study period.

3.7 Exclusion criteria

- Records of patient who are known to have stage 5 of CKD (end-stage) at the initiation of HD.
- Records of patient below 18 years of age.
- Incomplete or missing medical records.

3.8 Screening and recruitment

The principal investigator obtained a list with all the inpatient numbers of adult patients with a diagnosis of AKI who were admitted at KNH from January 2020 to December 2021 from the KNH Statistics Department. Their files were then retrieved with the help of the records staff. The principal investigator (P.I) with the help of two trained research assistant then went through all the files and selected those who had undergone dialysis. The files were then evaluated using the inclusion/exclusion criteria above. The files which met the inclusion criteria were then attributed an individual number and enrolled into the study.

3.8 Data management

3.8.1 Data collection

Data for all those who were enrolled into the study was collected using a hard copy data abstraction form. The following data was recorded:

- Clinical characteristics- age, sex, comorbidities, indication for dialysis, time to haemodialysis, length of hospital stay, ward versus Intensive Care Unit admission, baseline estimated kidney function prior to initiation of haemodialysis
- Ninety-day outcomes- dialysis independence with partial or complete kidney recovery, dialysis dependence (ESKD) and death

3.8.2 Data analysis and presentation

The data abstraction forms were checked for completeness by the P.I who ensured every parameter was entered in correctly and appropriately. The data was then entered into excel database, cleaned and transferred to SPSS (Statistical Package for Social Sciences) for analysis. Age was described using median, interquartile range and age groups. Time to haemodialysis and length of hospital stay were presented using mean, standard deviation and range.

Categorical data such as sex, ward versus ICU admission, baseline eGFR, risk factors, and outcomes were presented using frequency tables, percentages and proportions. Comorbidities and indications for haemodialysis were presented using charts. Univariate and multivariate analysis was carried out using logistic regression to determine the association between some of the patients' characteristics and the 90-day outcome of haemodialysis-treated AKI. A P-value <0.05 (at 5% level of significance) was considered significant at all analysis.

3.8.3 Data Dissemination Plan

The study findings shall be presented as a dissertation in partial fulfillment of the requirements for the award of the Master of Medicine in Internal Medicine at the University of Nairobi and thus will be available in the university repository and a hard copy in the library. The findings will also bepresented to members of staff working in Renal Unit, Kenyatta National Hospital and the relevant authorities at KNH in order to inform decisions and policies that will lead to improvement and management of adult patients with AKI requiring haemodialysis.

3.9 Ethical Consideration

This study was undertaken after approval from the Department of Clinical Medicine and Therapeutics, University of Nairobi (UON) and the KNH/UON Scientific and Ethical Review Committee. Authority to use the medical records at KNH was sought from the Head of Department, Health Management Information System (Appendix 2).

This was a review of records therefore they were no direct contact with the participants. Utmost confidentiality of the information contained in the patients' records was upheld throughout allthe stages of research. All data gathered has been stored securely and will only revealed upon a need-to-know basis. Electronic data is password protected and only accessible to study personnel.

4.0 CHAPTER FOUR: RESULTS

Subject Enrollment

A total of 1298 files of adult patients (18 years and above) with AKI were screened for eligibility, out of which 168 had undergone haemodialysis. We excluded a further 24 patients who did not meet the study criteria.

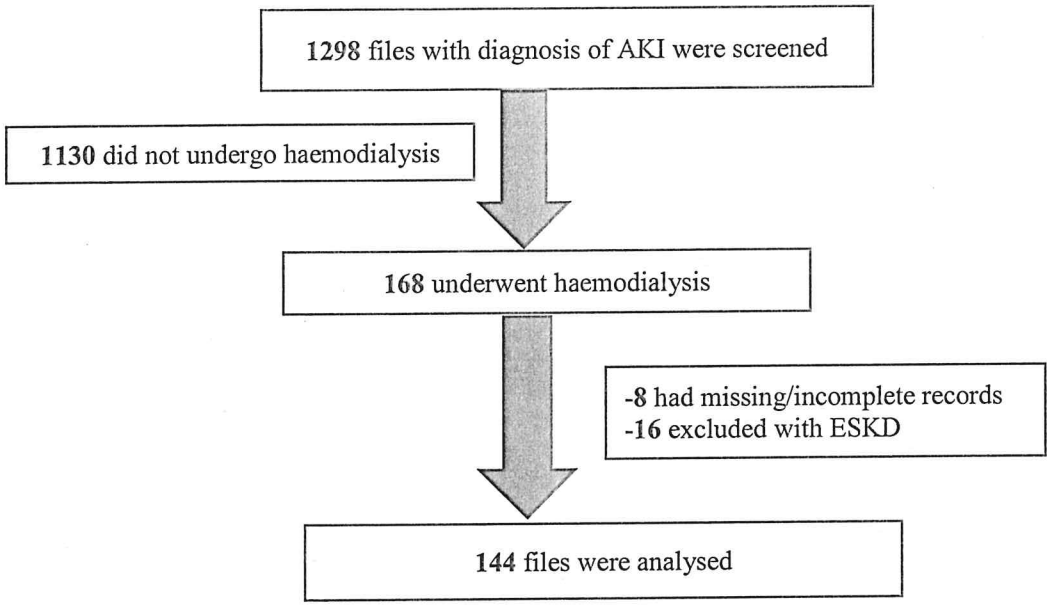

Figure 1: Study Flow Chart

4.1 Baseline Characteristics

Of the 144 enrolled patients, female accounted for 68.1%. The median age was 33.0 (IQR 27.0 – 47.0) years. Majority of the patients were in the 18 to 35 age group (59.7%). Seventy-six patients were admitted into the various ICU units representing 52.8% of the patients. Most of the patients (64%) had a baseline eGFR of ≤ 15mL/min/1.73 m2 before initiation of haemodialysis.

Table 4: Baseline Characteristic Of AKI-D patients at KNH

	Frequency, *n=144*	**Percent**
Sex		
Male	46	31.9
Female	98	68.1
Age		
18 - 35	86	59.7
36 – 45	20	13.9
46 - 64	27	18.8
65+	11	7.6
Site of care		
Ward Admission	68	47.2
ICU Admission	76	52.8
Baseline eGFR		
≤ 15mL/min/1.73 m2	92	64.0
≥ 15mL/min/1.73 m2	52	36.0

4.2 Comorbidities

Obstetric complications were the most common comorbidity (figure 1) among patients with AKI-D in KNH at 46.5% (n=144). This included HELLP syndrome at 34.3% (n=67), Pre-eclampsia Spectrum 32.8% (n=67), postpartum hemorrhage 10.4% (n=67), antepartum hemorrhage (9%) (n=67), puerperal sepsis (9%) (n=67), and septic abortions (4.5%) (n=67).

Medical comorbidities present in the study population included infectious diseases at 36.1% (n=144) and Non-communicable diseases such as cardiovascular disease at 11.1% (n=144), CKD 9.7% (n=144), hypertension 9.0% (n=144) and diabetes 7.0% (n=144). Infectious disease observed included Sepsis at 40.3% (n=52), HIV at 17.3% (n=52), Malaria at 15.4% (n=52), Covid 19 at 9.6% (n=52), Gastroenteritis at 7.7% (n=52), meningoencephalitis at 5.8% (n=52) and TB peritonitis at 3.8% (n=52). Other comorbidities present include malignancy (5.6%) with half of them being cervical cancer, ruptured aortic aneurysm (2.8%), nephritic syndrome (2.1%), trauma (2.1%) amongst others.

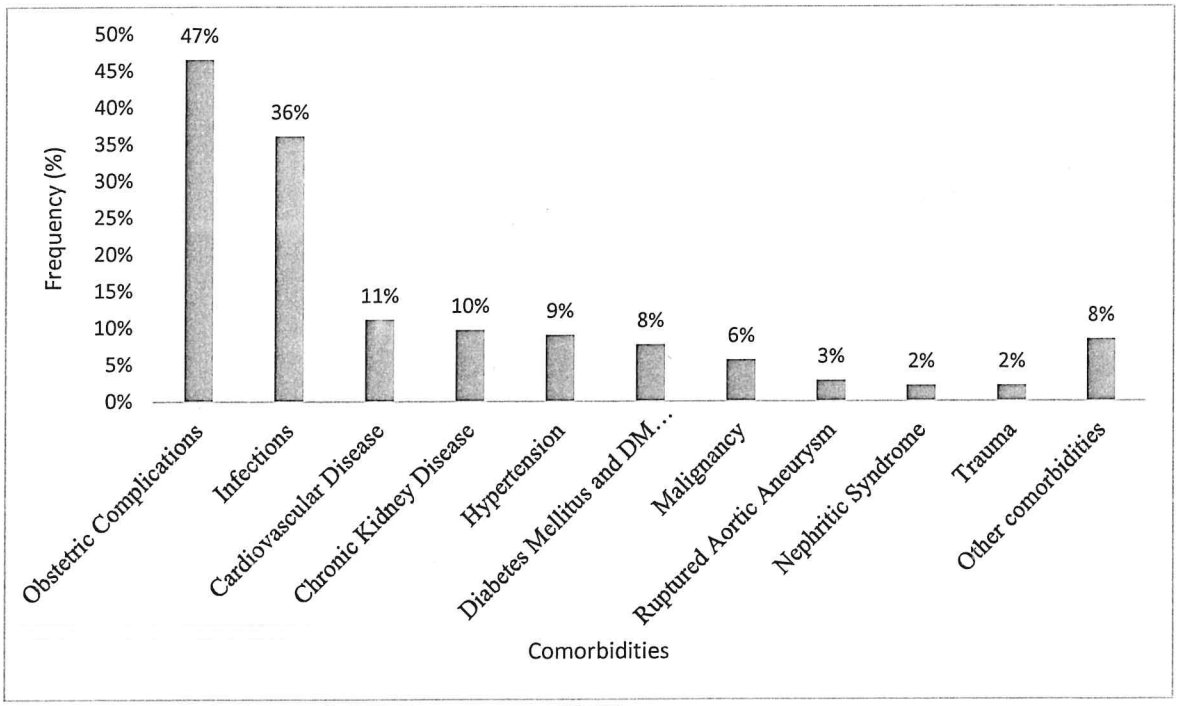

Figure 2: Comorbidities of AKI-D patients at KNH

4.3 Aetiologies of AKI-D

The aetiologies were categorized into Pre-renal, Renal and Post-renal. Thirty-eight percent (n=144) of the patients had more than one precipitant for the AKI-D hence falling into the various categories. Sixty percent of the patients had AKI-D attributable to renal causes (86 out of 144), while 35% (50 out of 144) had pre-renal causes and 6% (8 out of 144) had post renal causes. The specific causes in each category have been listed in table 5 below.

Table 5: Aetiologies of AKI-D at KNH

Pre-renal	**50**
Haemorrhage	22
Congestive heart failure	12
Vomiting	6
Vomiting and diarrhea	4
Pancreatitis	2
TB peritonitis	2
Renal fluid loss	2
Renal	**86**
HELLP syndrome	23
Preeclampsia Spectrum	22
Sepsis	21
Malaria	8
Covid 19	5
Drugs	5
Multiple myeloma	1
Post-renal	**8**
Cervical cancer	4
Prostate hypertrophy	2
Nephrolithiasis	1
Prostate cancer	1

4.4 Timing and Indications for Haemodialysis (n=144)

The mean time to haemodialysis is 1 day (SD+/-0) with a range of 6 days. Sixty-three percent of the patients had more than one indication for urgent dialysis. The most common indications for dialysis were refractory hyperkalaemia at 84 (58%), followed by clinical complications of uremia at 59 (41%), severe metabolic acidosis at 52 (36%) and volume overload at 22 (15%).

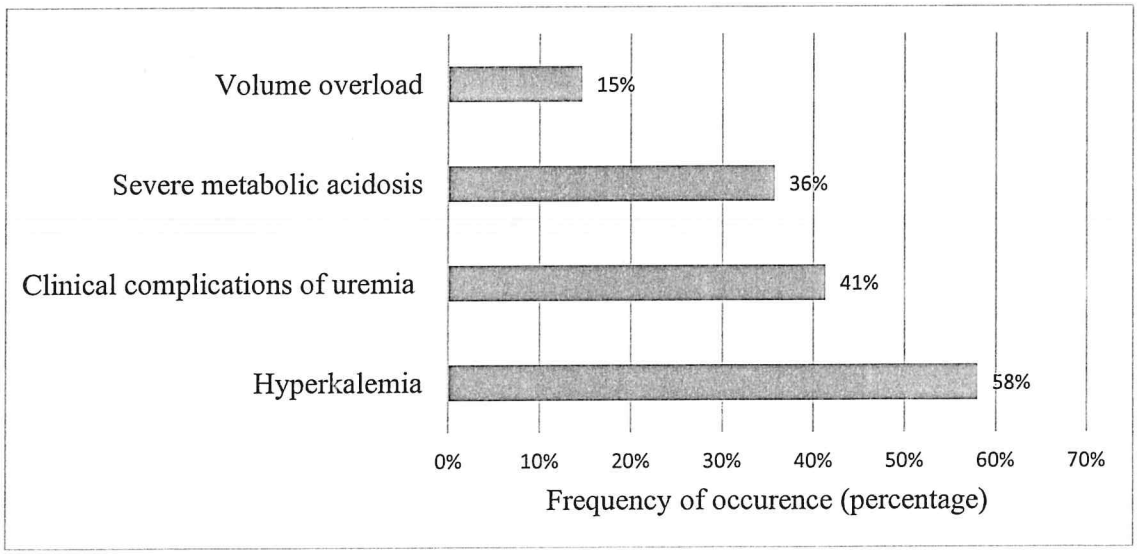

Figure 3: Indications for HD for AKI-D patients at KNH

4.5 Clinical outcome at 90-days

Half of the patients became dialysis independent (recovered) within the 90-day study period. Amongst these, 36.1 % had a full recovery whereas 13.9% had a partial recovery. It is noted that majority recovered before being discharged from the hospital. Around fifteen percent were still required to continue with haemodialysis at the end of the study period hence becoming end stage kidney disease patients. The mortality rate of AKI-D patients at KNH is 34.7% with all deaths occurring within the hospital. Eighty-five percent of the patients were admitted for more than 1 week, with the mean length of hospital stay being 21.7 days (SD+/-16).

Table 6: 90-days clinical outcomes AKI-D patients at KNH

Clinical Outcome	Frequency, *n=144*	Percent
Death	**50**	**34.7**
Dialysis Dependence (ESKD)	**22**	**15.3**
Dialysis Independence	**72**	**50.0**
Full Recovery	52	36.1
Partial Recovery	20	13.9

4.7 Association of factors with Outcomes

Results on the analysis of the factors associated with mortality show that the male patients were 1.7 times more at odds of death when compared to females, but there was no statistical association between sex of the patient and the outcome. Patients above 35 years were 2.4 times the odds of death when compared to those 35 years and below, and the association between age and mortality was statistically significant.

Patients who had positive indications for dialysis with hyperkalemia, severe metabolic acidosis, and volume overload were 1.2, 2.3 and 2.5 times more at odds of death compared to those without these indication, and only the association between severe metabolic acidosis and volume overload were statistically associated with death, while hyperkalemia was not. For clinical complication of uremia, patients with positive results were less at odds of death when compared to those without, though there was no statistical association.

Those patients whose time to hemodialysis was a day or less were 2.5 times at odds of death when compared to those with more than a day. Patients with obstetric complication were found to be less at odds of death when compared to those without, and the association was statistically significant. Those patients with infections were 1.8 times more at odds of death when compared to those without, but there was no statistical association between infections and mortality. The results are as shown on Table 7.

Table 7: Univariate analysis of factors associated with mortality

	Death	Alive	OR (95% CI)	P-value
Sex, *n (%)*				
Male	20 (40.0)	26 (27.7)	1.7 (0.8 – 3.6)	0.131
Female	30 (60.0)	68 (72.3)	Reference	
Age, *n (%)*				
≤ 35	23 (46.0)	63 (67.0)	Reference	**0.014**
> 35	27 (54.0)	31 (33.0)	2.4 (1.2 – 4.8)	
Indications for dialysis, *n (%)*				
Hyperkalaemia				
Yes	30 (60.0)	53 (56.4)	1.2 (0.6 – 2.3)	0.676
No	20 (40.0)	41 (43.6)	Reference	
Severe metabolic acidosis				
Yes	24 (48.0)	27 (28.7)	2.3 (1.1 – 4.7)	**0.021**
No	26 (52.0)	67 (71.3)	Reference	
Volume overload				
Yes	17 (34.0)	16 (17.0)	2.5 (1.1 – 5.6)	**0.021**
No	33 (66.0)	78 (83.0)	Reference	
Clinical complication of uraemia				
Yes	18 (36.0)	41 (43.6)	0.7 (0.4 – 1.5)	0.376
No	32 (64.0)	53 (56.4)	Reference	
Time to Haemodialysis, *n (%)*				
≤ 1 day	47 (94.0)	81 (86.2)	2.5 (0.7 – 9.3)	0.155
More than 1 day	3 (6.0)	13 (13.8)	Reference	
Comorbidities, *n (%)*				
Obstetric complications				
Yes	12 (24.0)	52 (55.3)	0.3 (0.1 – 0.5)	**<0.001**
No	38 (76.0)	42 (44.7)	Reference	
Infections				
Yes	19 (38.0)	24 (25.5)	1.8 (0.9 – 3.7)	0.120
No	31 (62.0)	70 (74.5)	Reference	

Significant factors from the univariate analysis i.e. age, severe metabolic acidosis, volume overload and obstetric complications were subjected to a multivariate analysis, and the results are as shown on Table 8. The results indicate that age was no longer statistically significantly association with mortality, and that the odds of mortality had reduced to 1.4 for the above 35 years. On severe metabolic acidosis the odds had a negligible increase but remained statistically significantly associated with mortality, and this was the case for volume overload where there was statistical association with mortality and a slight increase to the odds of mortality. There was no change to the obstetric complications which still maintained the odds as well as its association with mortality.

Table 8: Multivariate analysis of factors associated with mortality

	Death	Alive	cOR (95% CI)	P-value	aOR (95% CI)	P-value
Age, *n (%)*						
≤ 35	23 (46.0)	63 (67.0)	Reference		Reference	
> 35	27 (54.0)	31 (33.0)	2.4 (1.2 – 4.8)	**0.014**	1.4 (0.6 – 3.6)	0.441
Indications for dialysis, *n (%)*						
Severe metabolic acidosis						
Yes	24 (48.0)	27 (28.7)	2.3 (1.1 – 4.7)	**0.021**	2.4 (1.1 – 5.2)	**0.026**
No	26 (52.0)	67 (71.3)	Reference		Reference	
Volume overload						
Yes	17 (34.0)	16 (17.0)	2.5 (1.1 – 5.6)	**0.021**	3.0 (1.2 – 7.1)	**0.015**
No	33 (66.0)	78 (83.0)	Reference		Reference	
Comorbidities, *n (%)*						
Obstetric complications						
Yes	12 (24.0)	52 (55.3)	0.3 (0.1 – 0.5)	**<0.001**	0.3 (0.1 – 0.8)	**0.012**
No	38 (76.0)	42 (44.7)	Reference		Reference	

5.0 CHAPTER FIVE: DISCUSSION

Little is known about AKI requiring dialysis in resource limited settings including Kenya where kidney replacement therapy (KRT) is limited. Our study sought to determine the clinical presentation and the outcomes of patients with AKI requiring haemodialysis (AKI-D) admitted at KNH between January 2020 to December 2021.

Our research found that AKI-D primarily affects young adults (median age was 33) which is keeping with other studies done in sub-Saharan Africa. Igiraneza *et al.* in a study done in Rwanda found a median age of 38 and Kwizera *et al.* in a study done in Uganda found a median age of 38.5 (33,34). Locally, a study done at KNH by Tayabeli *et al.* in 2016 on prevalence and outcome of community acquired AKI found that 67% of the patients were less than 50 years of which majority ranging between 30-39 ages (35). This shows that the same age group of patients getting AKI at KNH are the same who are at risk of getting AKI-D. Studies done on AKI-D in the developed world on AKI-D patients report a higher median age for example a study done by Lorien *et al.* in the United States reported that the mean age of the cohort was 63 (27).

The young age of AKI-D patients in this study may be reflective of the underlying causes of AKI, particularly infections and pregnancy-related conditions which impact younger individuals. The finding that young and middle aged people constitute the majority of cases of AKI-D is concerning as it has downstream socioeconomic costs including decreased productivity and increased economic burden to their households and society. They are also at future risk of getting CKD and Hypertension which are chronic conditions requiring high health cost to manage

Our study found that pregnancy related conditions are the leading cause of AKI-D in our setting (46.5%). This explains why majority of our study patients were women at 68.1%. This is similar with a review done by Prakash and others that found pregnancy-related AKI, especially the severe form, is associated with significant morbidity and mortality in young and healthy women more so in the developing world (54). The most common obstetric complication in our study were hypertensive related conditions at 67.1% with HELLP syndrome contributing 34.3% and Pre-Eclampsia spectrum 32.8%. Kivai *et al.* in a study done at KNH found similar findings with hypertension disorders of pregnancy (80.3%) being the predominant condition associated with the development of pregnancy related AKI (56).

Other Obstetric conditions observed in our study included post- and antepartum hemorrhage, puerperal sepsis and septic abortion. Research done in other sub-Saharan Africa have reported similar results. In the study done in Rwanda, pregnancy-related conditions were the second most common comorbidities in AKI-D patients after infections, accounting for 26.9% (34). This included eclampsia, postpartum hemorrhage and post-caesarian section peritonitis. Kenyatta

National Hospital, being a referral hospital, receives a high number of obstetric complications which sometime come in late referrals and this could explain the high number of AKI requiring haemodialysis among the pregnant women. These complications are preventable which indicates the need for increasing access to appropriate and good quality prenatal and emergency obstetric care services in peripheral facilities.

Infectious diseases were also a common comorbidity among AKI-D patients in our study. This included Sepsis (40.3%), HIV (17.3%), Malaria (15.4%), Covid 19 at (9.6%), Gastroenteritis (7.7%), meningoencephalitis (5.8%) and TB peritonitis (3. 8%). The study done by Tayabeli *et al.* at KNH reported similar findings among AKI patients with sepsis contributing to 51.2% of pre-renal causes of AKI (35). This is also consistent with other research findings from Africa for example Emem-Chioma *et al.* in their study found that medical aetio-pathologies were a leading cause of AKI with sepsis (22.7%) being the most common (9). The reason patients with sepsis may end up with AKI requiring dialysis may be due to late onset of presentation with infection, late referral, poor adherence to treatment protocols, adverse effects of treatments offered and limited critical care capacity in our setting.

HIV was also a common comorbidity and this could be due to the high prevalence of HIV in our setup. Kidney disease among HIV patients could be because of the HIV virus itself, the opportunistic infections arising from the immune-deficient state and the drugs that these patients take. Malaria is still a public health concern in our setup and our study found that it is among the infections causing AKI-D. Patients with AKI-D have a low immunity and which also puts them at risk of getting Malaria. Though AKI in malaria is multifactorial, there are measures present to prevent progression to AKI requiring haemodialysis. From observation, early dialysis reduces morbidity and mortality associated with Malaria (72). Covid 19 pandemic was at its peak during our study period and this explains the number of cases seen. This number could have been higher but some of the Covid 19 patients were missed due to referral to Mbagathi for isolation and further care including dialysis.

Non-communicable diseases such as cardiovascular disease (11.1%), CKD (9.7%), hypertension (9.0%) and diabetes (7%) were also present in AKI-D patients at KNH though at a lower rate compared with the developed world. They are important risk factors for AKI recurrence and progression to end stage kidney disease and therefore such patients require long term follow up (5,24,53). Patients with Acute on Chronic Kidney Disease were few in our study but it is possible we may have missed others given we did not have documented baseline creatinine and data on Kidney Ureter Bladder (KUB) ultrasound. Chronic kidney disease and AKI are inter-related and

long term follow up of AKI-D patients is needed to ensure measures to retard progression to CKD are in place.

The most common indication for haemodialysis was hyperkalaemia followed by metabolic acidosis. This is similar to a study done in a critical care center in Morocco which also found the most common indications to be refractory hyperkalaemia, followed by metabolic acidosis (70). Other AKI-D studies done in sub-Saharan found varying indications for haemodialysis. This could be due to varying lab capabilities to accurately detect metabolic acidosis and electrolyte abnormalities.

Majority of patients with AKI-D were admitted for more than a week (85%) with a mean stay of 21 days. This is similar to what Igiraneza and colleagues found (mean of 23 days) in Rwanda (34). In the study done by Tayabeli *et al.* at KNH, the mean length of hospital stay for all AKI patients was shorter at around 9 to 11 days (35). This shows severe AKI requiring haemodialysis is associated with prolonged hospital stay at KNH.

Our study found that half of the patients became dialysis independent within the 90-days study period; with majority recovering before being discharged from the hospital. Amongst these, 36.1 % had full recovery whereas 13.9% had partial recovery. Fifteen percent were still dialysis dependent (ESKD) at the end of the study period. Locally a study done by Ngami *et al.* at a referral center looking at the 90-days outcome of AKI patients found that 52.7% had complete recovery of renal functions at 3 months, while 14.5% had partial recovery, and 32.7% progressed to ESKD (71). The total number of those recovered in their study is higher probably because they involved patients with milder form of AKI not requiring dialysis

Tayabeli in a similar study done at KNH looking at AKI outcomes in 2 weeks found a complete recovery rate of 18.6%, while 28.3% had partial recovery, and 53.1% failed to recover (35). Despite including patients with mild form of AKI not requiring dialysis, their rate of recovery was low, probably because it was looking at the outcomes over a very short period (2 weeks). The studies we came across on haemodialysis treated AKI done in Africa only looked at mortality as an outcome with none reporting on the degree of recovery (9,33,34). A study done on AKI-D patients in India by Jaryal *et al.* reported that 39% had full recovery at 3 months, 14.1% had partial recovery and 2.3% had reached end-stage renal disease (31). Their level of recovery is slightly higher compared to our AKI-D patients and fewer of them became dialysis dependent at 90-days. This could be probably because they offer better dialysis services in terms of exposure but this needs to be explored further. Studies done in the developed world show a lower rate of recovery (21%-42%) and higher rate of transition to ESKD (37%-49%) (3,27,28,29). This could be because their patients are much older with more comorbidities.

Our study found a mortality rate of 34.7% among AKI-D patients at KNH. This rate is high and could be because it is a referral center handling very sick patients who sometime come in as late referral with multi organ failure requiring admission into the critical care unit. This is however much lower compared to the data from a worldwide meta-analysis done by Susantitaphong *et al.* which found that the pooled associated mortality rate for dialysis requiring AKI to be 49.4% (1). Igiraneza in the study done in Rwanda observed an almost similar mortality rate to our study at 34.1 % (34). Kwizera *et al.* in the study done in Uganda observed a higher mortality rate (52.5%) and this could be because it involved only critically ill patients admitted in ICU (33). Emem-Chioma in the study done in Nigeria also found a high mortality rate of 43.9% which they attributed to poor dialysis exposure of their patients in terms of dialysis frequency and total number of sessions received (9). Our study did not look at dialysis exposure hence unable to do a comparison.

The study by Jaryal and colleagues in India also found an almost similar mortality rate to our study at 36.7% (31). Another done in Taiwan by Wu *et al.* found a mortality rate of 41.3% at 90-days (32). Studies done in the developed world show a much lower mortality rate. Lorien *et al.* in a study involving a large cohort of over 9000 patients found a mortality rate of 10% (27). Pajewski and Gautam in different studies involving smaller cohorts (100-300), found a mortality rate of around 9% (3,29). The lower mortality rate in the developed world could be because of adequate dialysis exposure and better laboratory service to allow frequent monitoring of electrolytes especially hyperkalaemia. Though our study did not asses' causality of mortality, it is important to note that majority of the patients who required dialysis had hyperkalaemia which can lead to arrhythmia and death without proper monitoring.

On multivariate analysis, our study found that severe metabolic acidosis (aOR = 2.4, 95% CI 1.1-5.2, $P = 0.026$) and volume overload (aOR = 3.0, 95% CI 1.2–7.1, $P = 0.015$) were significantly associated with mortality. Obstetric complications were significantly associated with survival (aOR = 0.3, 95% CI 0.1–0.8, $P = 0.012$). Igiraneza *et al.* in the study done in Rwanda found that receipt of <5 sessions of HD and hyperkalaemia were associated with a higher mortality (34). Studies done in the developed world show varying results in terms of the risk factors association with haemodialysis requiring AKI. Hickson *et al.* found that higher baseline eGFR, acute tubular necrosis from sepsis or surgery and heart failure were independent predictors of recovery of AKI-D within 6 months, whereas first RRT in the intensive care unit and catheter dialysis access were not (28). Our study lacked strong statistical power for co-relation analysis and therefore there is need to do further research to explore the risk factors associated with AKI-D in our set up.

6.0 CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

AKI requiring haemodialysis mainly affects the young adults at KNH with pregnancy-related conditions and infections being the most common comorbidities. AKI-D has a high mortality rate at KNH. Even though half of the patients recovered their kidney functions, a significant number had partial recovery of renal functions with some being dialysis dependent at 90 days.

6.2 Study limitations

1. The study was retrospective study and therefore the study variables obtained from the files were only limited to the data available and recorded in the files. This was counteracted by excluding the files with incomplete data from the study as outlined in the exclusion criteria
2. Our baseline serum creatinine was based on estimations because of lack of previous known baselines, therefore, we may have diagnosed AKI in place of missed CKD in some of the patients
3. KNH is a referral facility where more severe cases are referred and therefore may not be representative of those at lower level health facilities within Kenya.

6.3 Recommendations

1. We recommend a long term follow up plan for AKI-D patients who recovered to prevent and slow down progression to end stage kidney disease.
2. Future studies may benefit by looking in depth the risk factors to prevent the development of AKI-D and also the long term outcome of AKI requiring dialysis.

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Appendix 1: Data Abstraction Form

CLINICAL PROFILES AND SHORT-TERM OUTCOMES OF HAEMODIALYSIS-TREATED ACUTE KIDNEY INJURY (AKI) ADULT PATIENTS AT THE KENYATTA NATIONAL HOSPITAL

Date.....

IP number..... .....

Study number.....

Eligibility

Does the patient meet the inclusion criteria? Yes [ ] No [ ]

Does the patient meet any of the exclusion criteria? Yes [ ] No [ ]

- If yes, specify the met exclusion criteria

1. Stage 5 CKD [ ] 2. Below 18 years [ ] 3. Incomplete or missing records [ ]

PART 1

Patients Demographics

1. Age (Years).....
2. Sex Male [ ] Female [ ]

PART 2

Clinical Characteristics

1. **Etiologies**

Etiology category	**State if any**
Pre-renal	
Renal	
Post-renal	

2. **Indication for dialysis**

Indications of RRT	**Tick if any**
Hyperkalaemia	
Severe metabolic acidosis	
Volume overload	

Pronounced Azotemia	
Clinical complications of uraemia	

3. **Comorbidities**

Comorbidities	Tick if any
Prior AKI	
Chronic Kidney Disease	
Covid-19	
Diabetes Mellitus	
Obstetrics Complications (specify)	
Cardiovascular disease (specify)	
Other Comorbidities (specify)	

4. **Length of hospital stay**

Date of admission	
Date of discharge	

5. **Time to haemodialysis**

Date of diagnosis of AKI-D	
Date of initiation of haemodialysis	

6. **Ward versus Intensive Care Unit admission**

Ward admission (specify)	
ICU admission (specify)	

7. **Baseline eGFR prior to initiation of haemodialysis** .....
8. **Aetiology of AKI-D** .....

PART 3

OUTCOME IN 90-DAYS (Tick where applicable)

1. Dialysis Independence (Kidney recovery)

   eGFR at 90-days .....

   Full Recovery ☐

   Partial Recovery ☐

2. Dialysis Dependence (ESKD) ☐

3. Death ☐

   Date of death .....

Appendix 2: Ethical Approval

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23rd May, 2022

KENYATTA NATIONAL HOSPITAL APPROVED 23 MAY 2022 KNH/UoN-ERC P. O. Box 20723 - 00202 NAIROBI

Dr. Roy Katisya Musya
Reg. No. H58/33254/2019
Dept. of Clinical Medical and Therapeutics
Faculty of Health Sciences
University of Nairobi

Dear Dr. Musya,

RESEARCH PROPOSAL: SHORT-TERM OUTCOMES OF HAEMODIALYSIS TREATED ACUTE KIDNEY INJURY ADULT PATIENTS AT THE KENYATTA NATIONAL HOSPITAL (P151/02/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P151/02/2022.** The approval period is 23rd May 2022– 22nd May 2023.

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

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