THE CLINICAL PROFILE, MANAGEMENT, AND OUTCOME OF PATIENTS PRESENTING WITH EMERGENCY COMPLICATIONS OF RENAL FAILURE AT EMERGENCY DEPARTMENT OF MUHIMBILI NATIONAL HOSPITAL

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By

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Dissertation Submitted in (partial) Fulfillment of the Requirement for the Degree of Master of Medicine (Emergency Medicine) of

Muhimbili University of Health and Allied Sciences
June 2018

CERTIFICATION

The undersigned certify that they have read and hereby recommend for examination of dissertation entitled **"*Clinical profiles, management and outcomes of patients presenting with emergency complication of renal failure at Emergency Department of Muhimbili National Hospital*"** in fulfillment of the requirements for the degree of Master of Medicine (Emergency Medicine) of the Muhimbili University of Health and Allied Sciences.



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DECLARATION

AND

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I, **Erasto Sylvanus**, hereby declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature_____ Date_____

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DEDICATION

My darling wife, Joyce and my daughter Xylisa-Michelle have provided me with tremendous support and encouragement every day since I left for school. They have remained strong even during testing times of my absence and kept me close to their hearts and in prayers every moment of the passing day. They are a constant reminder of the dream I must realize and the goals I have set to achieve. With love and appreciation of who they are to me, I dedicate this work to them.

ABSTRACT

Background: Renal failure carries high mortality rates even in high-resourced countries, however, early recognition of acute presentations and appropriate interventions including dialysis, is known to reduce mortality and long-term morbidity. In Tanzania, the overall prevalence of renal failure is around 7%. However, little is known about the clinical profile and outcomes of patients with acute complications of renal failure that present to Emergency Medicine Department (ED) in need of dialysis.

Aim: The aim of the study was to describe the profile, management strategies and outcome of patients presenting with emergency complications of renal failure at ED of Muhimbili National Hospital (MNH) in need of dialysis.

Material and Methods: This was a prospective cohort study of adult patients with renal failure presenting to ED-MNH between September 2017 and February 2018. A structured data collection sheet was used to gather demographic information, clinical presentation, management strategies, and outcomes. Data summarized with descriptive statistics including mean, median, and frequencies were reported. Logistic and linear regressions were done to determine factors associated with mortality and access to dialysis respectively.

Results: Total of 775 (5.3%) out of 14,487 patients who presented to ED during the study period had renal disease. We enrolled 146/775 (18.8%) patients with acute symptoms of renal failure requiring emergent dialysis. The median age was 49 years (interquartile range 32 to 66 years), and 110 (75.3%) were male. Shortness of breath 67(45.9%) and reduced urine output 58 (39.7%) were the top presenting complications. Majority of patients 85(58%) were managed conservatively while 61(42%) were dialyzed. The overall mortality was 57 (39%). The mortality in non-dialysed patients vs. dialysed patients was 53% (45/85) vs. 20% (12/61) ($p<0.0005$) respectively. Predictors of mortality were vomiting (OR=6.23), oliguria (OR=3.4), pulmonary edema (OR=4.6), or creatinine levels >1200umol/L (OR=5.02), and not receiving dialysis (OR=8.02). Female sex had lower odds of dying (OR=0.13). The independent predictor of dialysis was having health insurance. 54% of patients with health insurance were dialyzed, compared to 39% who paid out of pocket (OR= 0.3).

Conclusion: In a cohort of patients with renal disease presenting to ED, acute complications of renal failure necessitate a significant need for emergent dialysis. The overall in-hospital mortality was 39%, and patients who received conservative care had a significantly higher mortality compared to dialyzed patients.

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LIST OF ABBREVIATIONS

AIDS	-	Acquired Immune Deficiency Syndrome
AKF	-	Acute kidney failure
AKI	-	Acute Kidney Injury
AMS	-	Altered mental status
BUN	-	Blood urea nitrogen
CKD	-	Chronic Kidney Disease
CPAP	-	Continuous positive pressure ventilation
DM	-	Diabetes Mellitus
ECG	-	Electrocardiogram
ED	-	Emergency Medicine Department
EMD	-	Emergency Medicine Department
GFR	-	Glomerular Filtration Rate
HIC	-	High-income Countries
HIV	-	Human Immune Deficiency Virus
HTN	-	Hypertension
ICU	-	Intensive Care Unit
INR	-	International Normalized Ratio
IRB	-	Institutional Review Board
IV	-	Intravenous
IVF	-	Intravenous fluids
LIC	-	Low-income Countries
MNH	-	Muhimbili National Hospital
MUHAS	-	Muhimbili University of Health and Allied Sciences
MUHASIRB	-	Muhimbili University of Health and Allied Sciences Institutional Review Board
POC	-	Point-of-care
SBP	-	Systolic blood pressure
SOB	-	Shortness of breath
SPSS	-	Statistical Package for Social Sciences
UPT	-	Urine for pregnancy test

DEFINITION OF KEY TERMS

i. **Tachypnea** is a term used to describe any abnormally high respiratory rate, above the upper limit of a normal range for adults (>20breaths/minute)(1).

ii. **Sepsis** is a life-threatening organ dysfunction caused by a dysregulated host response to infection (2).

iii. **Hypotension** is blood pressure lower than the lowest normal ranges (SBP<90mmHg)(1).

iv. **Hypertension** is blood pressure higher than the highest normal range (SBP>140mmHg).

v. **Hypertensive Emergency** is an acute elevation of blood pressure of 180/120 or above, which is associated with end-organ damage(1).

vi. **Emergency Department** is a hospital-based medical department that provides medical services to acute, undifferentiated and unscheduled patients with any kind of medical condition, critical and non-critical, of all ages and at all times involving the initial evaluation, resuscitation and stabilization, diagnosis and treatment before discharge home or disposition to other departments for definitive care(3,4).

vii. **RIFLE criteria** is acronym of Risk, Injury, Failure, Loss and End-stage kidney disease criteria, which was developed by kidney physicians to allow acute kidney injury to be defined objectively and uniformly(5).

viii. **Acute renal failure or Acute kidney injury (AKI)** is the deterioration of renal function over hours or days resulting in the accumulation of toxic wastes and the loss of fluid and electrolyte balance(1,6). It may or may not be reversible.

ix. **Chronic renal failure** is the irreversible loss of renal function, resulting in the accumulation of toxins and fluid(1).

x. **Dialysis** is the process of removing waste and excess water from the blood as an artificial replacement for lost kidney function in people with kidney failure(7).

xi. **Hyperkalemia** is serum potassium level higher than the highest normal range (>5.5mmol/L).(1).

xii. **Renal replacement therapy (RRT)** is the therapy involving artificial filtering of wastes from blood in kidneys failure. It includes dialysis (hemodialysis or peritoneal dialysis), hemofiltration and hemodiafiltration (8).

xiii. **Uremia** is elevated higher than the highest normal range (>7.1mmol/L). It may present with signs of encephalopathy or pericarditis (2).

CHAPTER ONE

1.0 INTRODUCTION

1 .1 Background

Definition and Risk Factors

Renal failure is one of the leading causes of hospital mortality in the world(9).

Clinically it is defined as a condition of impaired kidney function in which the kidneys fail to adequately filter metabolic wastes from the blood. This results in fluid, electrolyte and homeostasis dysregulation (1). Renal failure is classified as acute and chronic kidney failure. Acute kidney failure is a potentially reversible dysfunction of kidney function to remove wastes and maintain fluid and electrolyte balance which occurs over hours to days(6). Chronic kidney failure develops over a longer period where there are permanent damage and loss of nephrons and their functions(10). When the kidney fails, life-threatening accumulation of nitrogenous wastes, fluid retention, and electrolyte imbalance develops(11). These patients may present to ED acutely with severe and progressive hyperkalemia, refractory metabolic acidosis, pulmonary edema and uremic syndrome. These symptoms have poor prognosis if not emergently attended at emergency departments and finally in respective renal units(11).

Generally, elderly and patients with comorbidities such as liver diseases, diabetes mellitus, heart diseases, preexisting chronic kidney disease and peripheral vascular disease are at a relatively higher risk of developing acute kidney injury whenever they succumb to an acute illness(11).

The burden of renal failure

The incidence of kidney disease resulting in renal failure is a growing problem. Studies show significant burden of kidney failure with over 200 million cases worldwide(12).

Chronic kidney disease (CKD) affects up to 16% of the world population(13). About 2 million of them receive dialysis and other renal replacement therapy, but this is just 10% of the people who need this treatment for their survival(13). It is estimated that 70% of end-stage renal disease patients will be in low-income countries(5), and less than 5% of them have access to dialysis and renal replacement services(1).

In high-income countries such as the United States, the prevalence of CKD ranges from 11-16.8% of adults population (14), while in Europe, chronic kidney disease carries an average prevalence of 10% with wide variation from 3% to17% across European countries(15).

Prevalence of CKD in Sub-Saharan Africa is 13·9%, while that of acute kidney injury is up to 7% (6). More than 500,000 individuals develop end-stage renal disease annually and are likely to die of it(12). There is a slight difference in etiology in developing Sub-Saharan African countries. As in high-income countries, non-communicable diseases such as hypertension, diabetes, lipid disorders contribute but communicable diseases such as kidney infections, schistosomiasis, leishmaniasis and HIV infections are major risk factors for the development of renal injury and subsequently renal failure when not managed successfully (2).

In Tanzania there are limited data, however, data published in 2015 showed a prevalence of CKD of 7%(16). There was no difference by gender, age or education but higher risk was significantly associated with urbanicity in which non-communicable co-morbid conditions such as diabetes, hypertension, HIV, obesity, or history of heart disease, were directly implicated(16).

Prevalence of acute kidney injury (AKI) in high-income countries ranges 5-20% of hospital admission(17). In the United States, for example, 6% of hospitalized adult patients have acute kidney failure while in Europe it is 20%(18). In such settings, AKI is commonly hospital-acquired and is attributed to multiple co-morbidities affecting multiple organs and exposure to polypharmacy and invasive procedures(19). There are limited data in low-income countries although one study which was done seventeen years ago in Congo-Brazzaville suggested almost similar prevalence (15%) among children(20,21). However, the magnitude of AKI in ED settings is less studied and under-documented(11).

Management of renal failure

Management of the complications of renal failure at the ED rests on early recognition, early resuscitation, and treatment of the underlying causes to prevent further renal damage(11). General treatment options include fluid therapy, vasoactive and antihypertensive drugs, antibiotics and diuretics, depending on the clinical presentation. Some patients may present with life-threatening electrolyte imbalance commonly hyperkalemia, severe metabolic acidosis and uremic complications such as pulmonary edema, uremic pericarditis, and encephalopathy. Non-invasive ventilation such as continuous positive airway pressure or intubation is used in the management of pulmonary edema and in patients with respiratory failure. Availability of ventilators may not be a problem in high-income countries but poses a

serious challenge in low-income countries(11). The mainstay management of acute complications of renal failure is dialysis because medical treatment usually is unable to completely resolve the complications. This management, however, is challenging in low-income countries due to limited dialysis services(21). In these settings, patients with acute complications of renal failure depend on the medical intervention in many acute-intake settings.

Outcome of renal failure

The outcome of renal failure depends on the clinical presentation, early diagnosis, and management(17). However, renal failure itself is associated with high mortality rates even in developed countries with advanced medical care (60-70%) (22,23). Not only is mortality in renal failure associated with underlying clinical conditions but the presence of renal failure itself causes other severe forms of non-renal complications that contribute to mortality, including sepsis, bleeding, delirium, and respiratory failure(24).

In high-income countries, studies show in-hospital death rate is around 33% in discharges with AKI that required renal dialysis and 27.5% in those with AKI that do not require dialysis(22).

In developing countries, late presentation and financial inability to access advanced care such as dialysis and renal transplantation contribute to higher mortality rates (47.6%) (9). There are limited data on the outcome of renal failure patients who require dialysis and those who do not.

In Tanzania, the outcome of renal failure is less studied but one study done in 2014, showed that 88.2% of patients admitted in ICU due to kidney failure died(25). This is relatively higher rate compared to the overall renal failure mortality rate in low-resource settings.

Role of emergency care

Emergency departments in high-income countries play a vital role in the provision of the initial stabilization of patients and early recognition of the need for emergent dialysis and immediate consultation to renal units for dialysis(26). Those who are unstable, example intubated patients or on vasopressors can even be dialyzed even at ED using portable dialysis machines(27). In contrast, in low-income countries, specialized renal services including dialysis are limited by lack of resources, lack of available equipment and insufficient funding to support such therapy(28). Additionally, most episodes of acute renal injury in low-income countries occur pre-hospital and are due to hypovolemia, severe hypertension and pulmonary

edema, sepsis and drugs toxicity. Many of these are treatable with medical therapy So the role of ED can be focused in volume depletion, reduction of blood pressure, decongestion of lungs and early antibiotic while avoiding nephrotoxic medications and managing acute uremic complications(19). However, in most cases, medical therapy is no definitive. Dialysis is mostly unavailable immediately even at the national hospital and patients stay at ED for longer hours depending entirely on the temporizing medical stabilization at ED.

1 .2 Literature Review

Burden comparison

The burden of renal failure is variable in different regions globally (14). It affects over 200 million people worldwide(12). Generally, elderly and patients with comorbidities such as liver diseases, diabetes mellitus, heart diseases, preexisting chronic kidney disease and peripheral vascular disease are at a relatively higher risk of developing acute kidney injury whenever they succumb to an acute illness(11). There is some difference in etiology in developing countries, however, where non-communicable diseases such as hypertension, diabetes, lipid disorders, are coupled with communicable diseases such as kidney infections, schistosomiasis, leishmaniasis and HIV infections. These communicable diseases are major risk factors for the development of renal failure when not managed successfully(12). The overall prevalence of CKD in Sub-Saharan Africa alone is 13·9%, while that of AKI ranges from 5-7%(29). Of those with CKD, more than 500,000 individuals develop end-stage renal disease annually and are likely to die of it(12).

Studies by Nash *et al.* and Hou *et al.*, demonstrated that in most high-income countries, the incidence of hospital-acquired AKI ranges from 5-7% and is mostly attributed to sepsis, critical illness, decreased renal perfusion, major surgeries, and exposure to radiocontrast materials (30,31). The incidence of community-acquired AKI is twice or three times that of hospital-acquired AKI (27,32), and is largely associated with pre-existing systemic diseases including chronic kidney disease (33). Nephrotoxic medications both pre-admission and during-hospitalization increase risk of both community and hospital-acquired AKI.

In Tanzania, Stanifer *et al.* studied the epidemiology of CKD in 2014 among 481 adults and found overall prevalence of 7% with no difference by gender, age or education but higher risks were associated with urbanicity in which non-communicable co-morbid conditions

such as diabetes, hypertension, HIV, obesity, or history of heart disease, were directly implicated (16). Unfortunately, we could not find other studies done in this regard.

Clinical Presentation

Clinical presentation of renal failure is variable causing several systemic complications such as cardio-respiratory failure, encephalopathy, coagulopathy, life-threatening electrolyte imbalances, and metabolic acidosis. Patients will present with symptoms depicting failure of one or combination of above systems. In a retrospective study done by Sacchetti *et al.* in New Jersey, United States, to determine the pattern of utilization of emergency department by renal dialysis patients, it was found that patients with renal failure who required dialysis presented at emergency department mostly with shortness of breath, chest pain and weakness(26). In this study, 61% of patients with shortness of breath required emergency dialysis(26). These patients were commonly diagnosed to have fluid overload and congestive heart failure, electrolyte imbalance and anemia(26).

Furthermore, in 2012, Joslin and Ostermann from King's College London in the United Kingdom published a review article on critically ill patients with AKI in the ED. They pointed out that the main emergency complications are a consequence of uremia and these include fluid overload/ pulmonary edema, severe hyperkalemia with cardiac arrhythmias, acute metabolic acidosis, uremic pericarditis and encephalopathy(11).

Treatment of renal failure in HIC and LIC

Management of acute complications of renal failure is challenging and it involves multiple interventions targeting the offending cause. In hypovolemia and hypovolemic shock, management of such patients should involve fluid replacement therapy and use of inotropes and vasopressors if needed. Several studies as shown in the meta-analysis of randomized controlled trials by Wiederman *et al.* have proposed the use of balanced hyperoncotic colloids such as albumin, to avoid and treat hypovolemia. This meta-analysis also provided evidence of albumin safety to dispute the preexisting hypothesis that it might contribute to acute kidney injury (34). In a multi-center, two-by-two factorial trial conducted in Germany by Brunkhorst FM *et al.*, it is advocated to avoid molecular weight starches because they are harmful to kidneys with increasing toxicity with subsequent doses (35).

During fluid therapy, it is important to use ultrasound's caval index to guide fluid responsiveness. This is shown by the study done by Weekes *et al.* in Las Vegas, United States where they recommend evaluation of the fluid status of the patient and their response to therapy by using the caval index as opposed to left ventricular systolic function (36).

In septic shock, studies including the one done by Albanèse J *et al.* in France, favor the use noradrenaline to improve kidney perfusion, restore urine output and improve the creatinine clearance(37). However, Holmes and Walley from Canada, in their critical care review, concluded that low dose dopamine as deemed helpful by previous studies has been shown not to be helpful in critically-ill patients with oliguric states(38,39).

Diuretics have been used in patients with progressive fluid accumulation to minimize overload and to aid other ongoing conservative management. However, in a single-center randomized, double-blind, placebo-controlled study done in Netherlands by Van der Voort *et al.* among 36 furosemide-treated adult patients in a mixed ICU, it was shown that furosemide can only increase urine volume and sodium excretion but it cannot reduce duration of renal failure and has no role in improving renal recovery (11,40).

Fluid overload/ pulmonary edema, severe hyperkalemia >6.5mmol/L and metabolic acidosis are other emergency complications that need immediate attention (6). It is challenging to manage an anuric patient with pulmonary edema. These patients usually have respiratory distress and oxygen therapy should be instituted together with non-invasive positive pressure ventilation and if necessary intubation should be done. And while temporizing measures such as oxygen, diuretics, morphine, and nitrates may be used to reduce respiratory efforts and improve breathing, often the only life-saving treatment is dialysis (26).

In the study by Pani *et al.* in the US, the incidence of hyperkalemia >5.5mmol/L in CKD increases from 2%- 42% as glomerular filtration rate (GFR) decreases from 60- 20ml/minute respectively(41). Hyperkalemia, when severe, can be associated with life-threatening cardiac arrhythmias which need to be managed first by stabilizing cardiac membranes using calcium gluconate, then two other medical modalities to reduce serum potassium are employed (11,42). One, by agents that shift potassium from the serum into the cells (insulin with glucose, sodium bicarbonate, Beta 2-adrenergic agonist) and two, by removing it from the body through resins and renal replacement therapy (hemodialysis, peritoneal dialysis, hemofiltration, or renal transplant) (6,43). Dialysis is indicated in severe hyperkalemia with

ECG changes which don't respond to medical treatment. In the same study, Pani *et al.* showed that 4.5-6.3% of pre-dialysis patients had hyperkalemia of >6mmol/L (41).

Emergent dialysis is commonly indicated for patients presenting at ED with acute complications of kidney failure. In one study done in New Jersey, USA by Sacchetti *et al.* to determine the pattern of ED utilization by renal dialysis patients, it was found that 30% of renal disease patients needed emergent dialysis(26). They were started on temporizing measures at ED and would be taken to renal dialysis units within 15minutes (26). Unstable patients including those who were intubated or on nitrates were dialyzed at ED using a portable dialysis unit(26).

Stanifer *et al.* studied the epidemiology of chronic kidney disease in sub-Saharan Africa and it was estimated that 70% of end-stage renal disease patients will be in the low-income countries. This shows the magnitude of need for dialysis in this region(44), but less than 5% of them have access to dialysis and renal replacement services(1). Lack of routine dialysis contributes to larger numbers of patients coming to the emergency department with complications of their renal failure.

The outcome of renal failure

The outcome of renal failure involves survival to hospital discharge or death. Renal failure is associated with high mortality even in high-income countries with advanced medical care(9) However, in low-income countries, renal failure is associated with a high mortality rate of more than 47%(9). This is thought to be due to late presentation and financial inability to access advanced care such as dialysis and renal transplant. In Tanzania, sub-Saharan Africa, Sawe *et al.* conducted a retrospective study between 2009-2011 on the disease patterns and clinical outcomes of patients admitted in intensive care units of tertiary referral hospitals. In this study, it was found that mortality rate due to renal failure was 88.2% (25). This is higher than the average mortality rate recorded in developing countries, such as India (47.6%)(9).

Renal failure also has a significant impact on length of stay and cost (11). There are many factors that predict such outcomes. A study on predictors of mortality among patients with acute renal failure was done in India by Kohli *et al.* where it pointed out that age, causes of ARF, complications of ARF, pre-existing diseases and their severity are potential predictors of mortality(9). In the same study it showed sepsis caused 63.26% of mortality in adult patients with acute renal failure and elderly patients with >60yrs seemed to have higher

mortality(9). This was attributed to pre-existing diseases such as cardiovascular, respiratory and cerebral diseases, HTN, DM and malignancy (9). However, a study by Bagasha *et al.* in Uganda, on short-term outcomes of patients with AKI with sepsis, found that mortality in adult patients with sepsis was 21%, which is lower than that of India(28).

In the presence of renal dysfunction, quantitative changes in serum creatinine and urine output are used to determine severity(45). Even minor changes in serum creatinine suggest increased severity and are associated with poor prognosis regardless of underlying cause(29). In the study done in the United States by Chertow *et al.*, the odds of mortality in patients with ≥0.5mg/dl increase of serum creatinine, increased more than 6 times; 3.5 more days for length of hospital stay and excess of about USD7,500 hospital costs(29).

Role of acute care in HIC and LIC

In high-income countries, emergency departments play a vital role in the provision of initial stabilization of patients and early recognition of the need for emergent dialysis and immediate consultation to renal units for dialysis (26). Unstable patients including those intubated patients or on vasopressors can be dialyzed even at ED using portable dialysis machines.

In contrast, low-income countries, specialized renal services including dialysis are limited by lack of resources, lack of available equipment and lack of funding to support such therapy(28). Dialysis is mostly unavailable immediately even at the national hospital and patients stay at ED for long hours depending solely on the temporizing medical stabilization measures administered at ED.

1.3 Problem Statement

More than 200 million people globally are suffering from chronic kidney disease; in addition, kidney failure may present acutely in the emergency departments with life-threatening symptoms(12). Mortality rates in acute kidney failure have remained as high as 27% to 47% (9). Acute complications of chronic renal failure carry mortality of 34% and are mostly managed in ED, although, in most developing countries, ED's are not available or not well established (29). This fact is believed to add to the existing high mortality rates.

In high-income countries, emergency departments have a great role in early recognition of acute renal injury or failure, recognition of the offending disease process, provide early

management of presenting emergent condition and to prevent long-term morbidity and mortality(14). Patients with chronic kidney disease also present at ED with complications of acute exacerbation of renal failure. Some of them are chronically receiving renal replacement therapy (RRT) but may have missed dialysis sessions, so they come with life-threatening fluid overload and electrolyte imbalance which are managed and stabilized at ED and immediately disposed for emergent dialysis(14).

In Tanzania, development of infrastructure for emergency care is still on-going in different regions while currently, Muhimbili national hospital is among few public hospitals in the country with full capacity emergency department which can adequately provide emergency care including early recognition, stabilization, and treatment of patients with acute complication of renal failure. However, the proportion of patients presenting at ED with renal failure is not known. Furthermore, clinical profile and their management options are not well characterized, and outcome of ED stabilization has not been studied before. Dialysis services are currently very expensive and the proportion of patients who meet the criteria for emergent dialysis and are dialyzed is unknown.

1.4 Rationale of the study

Many patients may present to ED with emergency complications of renal failure due to either an acute renal insult or acute exacerbation of chronic kidney disease. But in resource-limited countries such as Tanzania, there are limited nephrology services and most facilities are unable to recognize, diagnose and manage kidney failure early (21). An emergency department is very crucial for these patients since they may not get nephrology services including dialysis on time and so will depend on the temporizing and resuscitative measures provided at ED for many hours.

This study will describe the clinical presentations, management and associated outcome after stabilization at ED and after disposition to renal units or ICU. Also, the study will determine how many patients who need emergency dialysis are ultimately dialyzed and what the impact is on mortality.

It is important to be able to characterize the emergency complications of renal failure that present to ED for emergency physicians to be prepared to treat these patients appropriately and have on hand the appropriate resources (medications, personnel, equipment) to manage

them. Understanding the prognosis of these patients can help direct resources to where we can make a difference. Additionally, understanding the association between patient's clinical presentation and in-hospital treatment will allow us to develop management protocols and begin to develop better policies that will provide guidance to which patients should receive dialysis or renal replacement therapy in Tanzania.

1.6 Research Question

What are the demographic and clinical characteristics, management strategies, and outcome of adult patients presenting at ED-MNH with emergency complications of renal failure in need of emergent dialysis?

1.7. Objectives

1.7.1 Broad objective

To describe the clinical profile, management strategies and outcome of patients presenting in need of emergent dialysis at ED-MNH

1.7.2 Specific Objectives

1. To determine the prevalence of patients presenting at ED in need of emergent dialysis
2. To describe the management provided at Emergency Department to patients with acute complications of renal failure
3. To describe the outcome of patients after ED stabilization
4. To determine the proportion of patients admitted from the ED who received dialysis
5. To determine factors associated with treatment outcome (hospital mortality and access to dialysis) among patients presenting requiring emergent dialysis

CHAPTER TWO

2. 0 STUDY METHODOLOGY

2.1 Study design

This was a prospective cohort study of patients aged 15years and above presenting to ED with acute symptoms of renal failure requiring emergent dialysis between September 2017 – February 2018

2.2 Study area

The study was conducted at the emergency medicine department and nephrology unit of Muhimbili National Hospital (MNH). MNH is a tertiary hospital located in Dar es Salaam, Tanzania, with around 1500 hospital bed capacity. The hospital, serving patients referred from all over the country, admits up to 1200 patients every week through ED-MNH (38). ED-MNH was established as a full capacity department in 2010 and it is staffed with interns, registrars, residents, emergency physicians and nurses who attend patients 24 hours every day (46).

Most of the referrals and other cases of complications of renal failure are first received at the emergency medicine department, where they are evaluated, resuscitated, stabilized and treated before being admitted for definitive care or discharged home (38).

2.3 Target Population

All patients aged 15years and above with acute symptoms of renal failure presenting in acute-intake units within Tanzania requiring emergent dialysis. For this study, adult patients were considered from 15 years and older.

2.3.1 Accessible Population

All patients aged 15years and above presenting at ED-MNH with emergency indications for dialysis.

2.3.2 Study population

A consecutive sample of patients aged 15years and above presenting at ED- MNH in need of emergent dialysis who met pre-defined criteria within the period of study.

2.4 Sampling Design

A consecutively enrolled sample of all patients aged 15years and above presenting at the ED at all times during study period, who met modified RIFLE criteria of renal failure and presented with emergent indications for dialysis, which included severe metabolic acidosis, electrolyte imbalance, uremic syndrome, fluid overload, and acute ingestion of toxins/poisoning were enrolled.

RIFLE criteria is the classification of renal failure, which defines and stratifies the severity of renal failure (5). It uses two criteria namely, serum creatinine and urine output. The RIFLE criteria use urine output measured at 12hours or 24 hours intervals. This is not feasible in the emergency setting where a patient may spend less time. Therefore, for this study, *modified RIFLE* criteria were developed which included *reported or observed* oliguria or anuria for 12 hours and above.

2.5 Subjects

2.5.1 Inclusion Criteria

All patients aged 15years and above with reported or observed reduced urine output (i.e. despite proper urinary catheter placement) or anuria for 12hours or more and elevated creatinine level $\geq$ 3 times normal (i.e. 253umol/L and above) and any of the following indications for emergent dialysis:

- Fluid overload: e.g. pulmonary edema, SOB
- Acute ingestions of poison or drugs
- Acidosis: PH <7.2
- Electrolyte abnormality: Hyperkalemia (K >5.5mmol/L) with or without ECG changes.
- Altered Mental status: GCS <15/15 with other uremic symptoms such as chest pain, epigastric pain and bleeding

2.5.2 Exclusion criteria

1. Acute trauma patients with renal failure
2. Pregnant women
3. All patients who did not consent or whose proxy did not consent.
4. Obstructive oliguria

2.5.3 Variables in the Study

The main objective of this study was to determine the clinical presentation, management strategies and outcome of patients presenting with complications of renal failure. The variables were as follows;

2.5.4 Independent (Predictor) variables

Demographics

i. Age, gender, level of education, payment method and type of referral.

Clinical Presentation

i. Symptoms associated with acute renal failure such as dyspnoea/SOB, AMS, chest pain, reduced urine output, edema.
ii. Vital signs such as blood pressure, respiratory rate, heart rate, oxygen saturation and temperature
iii. Co-morbidities (DM, HTN, HIV, sepsis, hepatitis, kidney diseases)
iv. Physical findings such as CHF/fluid overload with pulmonary edema, respiratory distress/ failure, anemia, edema, bleeding.

Management Options

i. Diagnostic workup: X-ray, Ultrasound, CT Scan, POC and laboratory investigations such as urine dipstick, UPT, FBP, blood gases, electrolytes, BUN and serum creatinine
ii. Conservative treatment such as insulin therapy, CPAP, mechanical ventilation, inotropes /vasopressors, diuretics, antihypertensives, pericardiocentesis, sodium bicarbonate, calcium gluconate and IVF)
iii. Dialysis: hemodialysis or peritoneal dialysis

2.5.5 Dependent (Outcome) variable

i. Primary outcomes: 30-days hospital mortality and the proportion receiving dialysis
ii. Secondary outcome such as the effectiveness of ED stabilization and factors influencing access to dialysis.

2.6 Sample size estimation

The sample size was estimated from the mortality rate of 34%(29)**.**
Therefore, the calculation was made from this proportion formula;

$$N=\frac{4Z^2p(1-p)}{\varepsilon^2}$$

Where:
N = estimated sample size,
Z = standard normal deviate, which is 1.96 at 95%,
p = expected proportion, which is 0.34 (34%),
ε = the margin of error, which is p/2.

The sample size was therefore **119 patients** who presented at ED-MNH with the indication for emergency dialysis.

2.7 Sampling Procedure

2.7.1 Sample recruitment and Data Collection

i) Patients presenting with the clinical criteria suggestive of renal failure and a need for emergent dialysis as outlined above: SOB, AMS, hyperkalemia, oliguria/ anuria, were tested for urea and creatinine. Additionally, all patients with a known or suspected previous diagnosis of renal failure, or for whom the ED physician suspected renal failure were tested for urea and creatinine.

- POC /laboratory renal function tests and blood gases testing were done for all patients with suspected symptoms and all non-trauma, non-obstructive oliguria, and non-pregnant patients attended at resuscitation rooms. This ensured minimal or no patients with kidney failure were missed at ED.
- Research assistant(s) entered all patients who were suspected to have renal failure and creatinine levels were tested. The attending doctor would be asked about any patients suspected to have renal failure and who were tested for creatinine levels to aid in the follow-up. Laboratory results were followed up through *Jeeva* system to get the data for creatinine levels in case the results

were not recorded in the *Wellsoft* electronic medical record or in the patient file.

- A search work was run from the *Wellsoft* for patients diagnosed as renal failure before admission.
- A research assistant passed through resuscitation rooms and asked about patients diagnosed with renal failure.

ii) Research assistant(s) opened the patient charts and entered data into an electronic structured data collection tool (Redcap) for each patient diagnosed with renal failure (acute or chronic) listing the presenting symptoms, vital signs, point-of-care results, and laboratory results. Then the researcher would screen the data sheets for any missing or insufficient information and queries were made to try to resolve the issues.

iii) The patients were followed on the ward to collect data on their treatment options and progress. The outcomes were recorded after discharge to record survival at 30 days or non-survival rates and whether they got dialysis or not. All the data collected were duly filled in the electronic structured questionnaires as prepared by the investigator in the redcap software.

2.8 Data Management and Analysis

Data obtained in the questionnaires were then automatically exported into excel sheet, and then transferred to the Statistical Package for Social Sciences (SPSS), version 20 for analysis. The data were stored in password-protected software (Redcap) in the computers with access limited to only study personnel and confidentiality was strictly observed.

Analysis

We summarized continuous variables into their measures of central tendencies with their respective measures of dispersion while we summarized categorical variables into frequencies and percent. Logistic regression was done to determine factors associated with mortality among participants. Linear regression was done to determine factors associated with access to dialysis. A probability value of less than 5% was considered statistically significant. We determined final logistic and linear regression models by likelihood ratio test. Then data were presented in tables and figures.

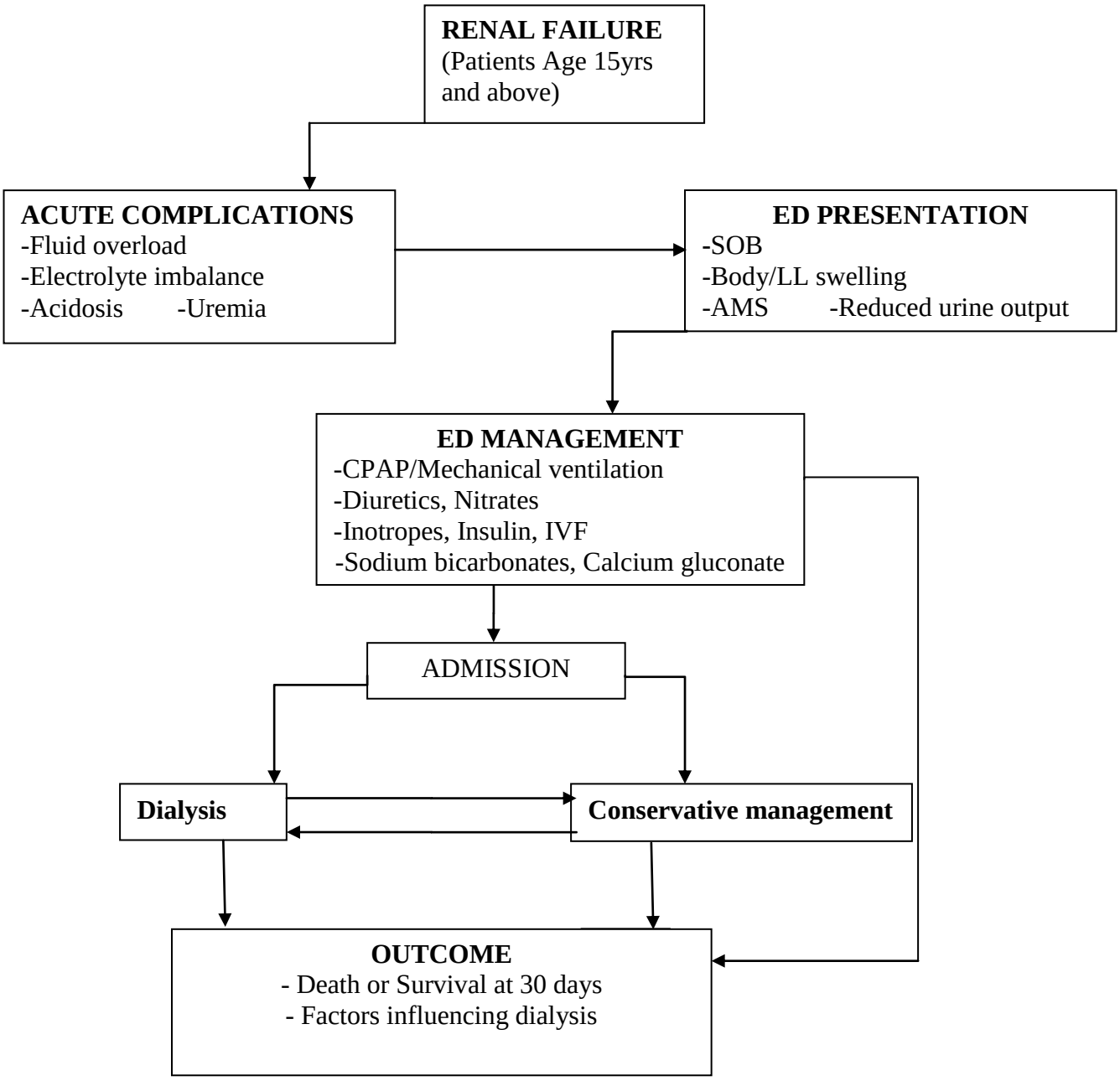
2.9 Ethical Clearance

Permission to do the study was requested and granted from Muhimbili national hospital after ethical clearance had been sought and approved from MUHASIRB.

A written consent for participation in the study was requested from patients/their proxy who opted to sign. The hospital registration numbers were used for participants and were assigned serial numbers to conceal their identity. Those patients with < 18yrs had their consent forms signed on their behalf by guardians.

Those who refused to consent were excluded from the study.

2.10. Conceptual Framework



The study included all patients aged 15years and above presenting to ED with acute complications of renal failure who met criteria for emergent dialysis. Their demographics (age, sex, level of education, referring hospitals, mode of payment and their co-morbidities) and clinical characteristics (presenting symptoms and clinical findings) were recorded. Management at ED to stabilize them was done according to the current standard of practice and patients were admitted for dialysis. Information on management modalities (dialysis or conservative management) and their outcome (discharged alive or dead and factors associated with mortality and access to dialysis) were obtained.

CHAPTER THREE

3. 0. RESULTS

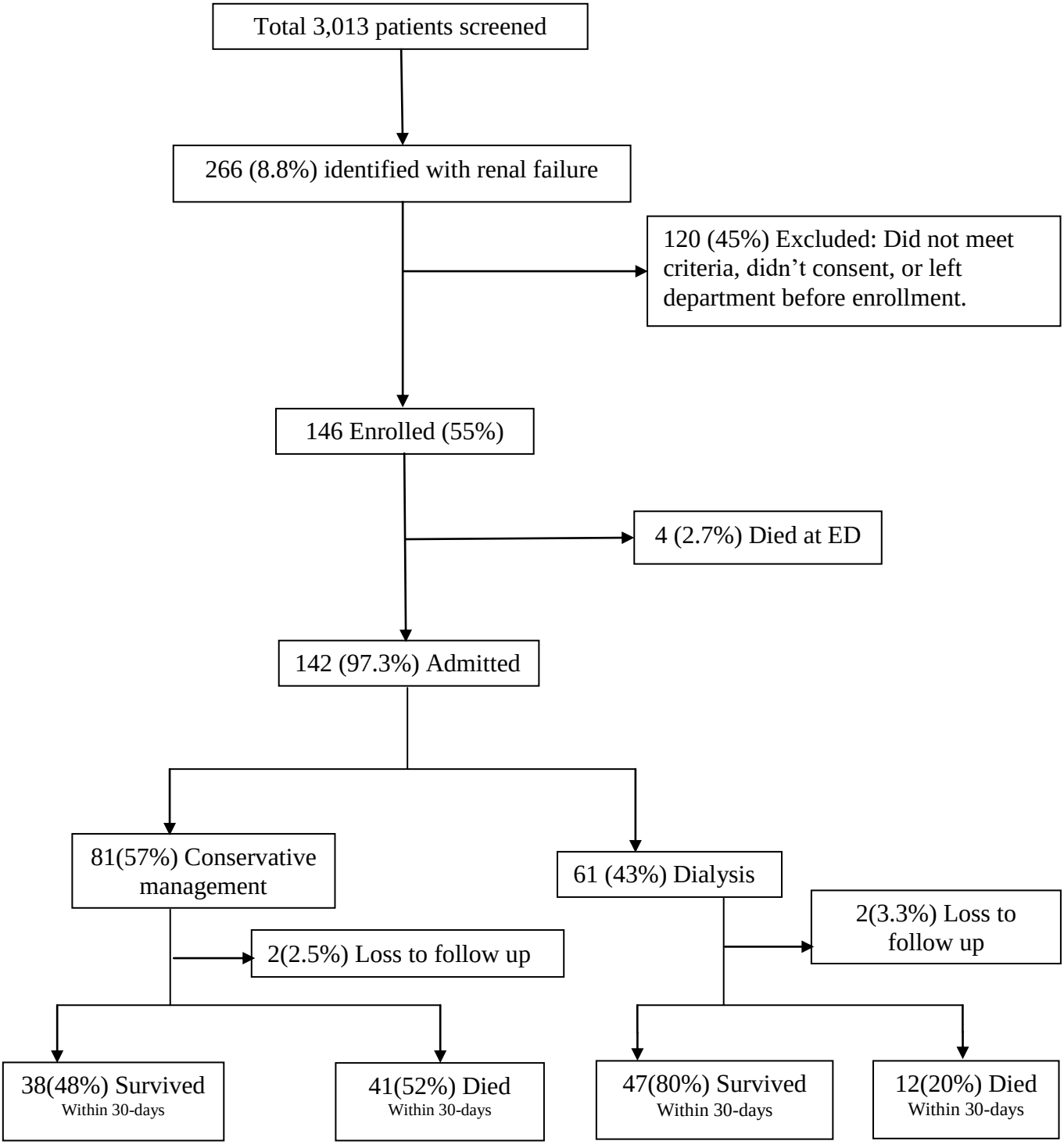


Figure 1: Prospective cohort flow chart of patients presenting at ED with emergency complication of renal failure

3.1. Demographics and Clinical Characteristics of study participants

Of the 3,013 adult patients admitted to resuscitation rooms during the study period, 266 (8.8%) had a diagnosis of renal failure (71 AKI versus 195 CKD). Among these, we enrolled 146 (55%) patients who had indications for dialysis. Majority of participants were male 110 (75.3%) and aged above 55 years 55(37.7%) while median age was 49 years (IQR 32 to 66 years). The majority 88 (62%), had not gone beyond primary school education. More than half (52%) were referred from government health facilities; 74% (108) were uninsured and paying out of pocket. (Table 1)

Table 1: Demographic characteristics of participants

Demographic characteristics	**Number (N=146)**	**%**
Age		
15-34	36	24.60
35-54	55	37.70
55+	55	37.70
Sex		
Male	110	75.30
Female	36	24.70
Education *		
Higher education	17	12.00
Secondary	27	19.00
Primary	88	62.00
Informal Education	10	7.00
Payment		
Insurance	38	26.00
Pay from pocket	108	74.00
Referred from **		
Private	23	15.90
Government	76	52.40
Self-referral	46	31.70
Co-morbidities		
No Known comorbidities	28	22
Diabetes Mellitus	25	19.7
Hypertension	66	52
HIV infection	12	9.4
Malignancy	4	3.1

* 4 Missing ** 1 Missing

Education levels were not recorded for 4 participants, referral type not recorded for 1 participant.

The most common complaints of participants were shortness of breath 67(45.9%), reduced urine output 58 (39.7%) and generalized swelling 51(34.9%). (Table 2)

Table 2: Clinical characteristics of participants

Presenting Symptoms	N=146	%
Shortness of breath	67	45.90
Reduced urine output	58	39.70
Generalized/LL swelling	51	34.90
Vomiting	35	24.00
Altered mental status	22	15.10
General body malaise	21	14.40
Diarrhea	9	6.20

Participants could have more than one clinical characteristic. Therefore, adding the frequencies will give a larger number than N=146

The main presenting complications diagnosed among study participants were hyperkalemia 77(53%), uremic encephalopathy 66 (45%) and pulmonary edema 54 (37%). (Table 3)

Table 3: Presenting Complications of participants

Presenting Complications	N=146	%
Hyperkalemia (K^+ >5.5)	77	53.0
Uremic encephalopathy	66	45.0
Pulmonary edema	54	37.0
Metabolic acidosis (PH≤7.2)	28	19.0

Participants could have more than one complication. Therefore, adding the frequencies will give a larger number than N=146

3.2. Management given at ED

Most of ED management was directed for treatment of hyperkalemia and pulmonary fluids overload (Figure 3). The ED administered non-invasive ventilation (NIV) (33%), Calcium gluconate (33%), insulin with dextrose (32%), diuretics (30%), and nebulization with salbutamol (24%), antibiotics (20%), nitrates (19%) and sodium bicarbonates (16%). Few patients received antihypertensives (4%) and 1% of the participants received invasive ventilation and inotropes. See figure 2 below;

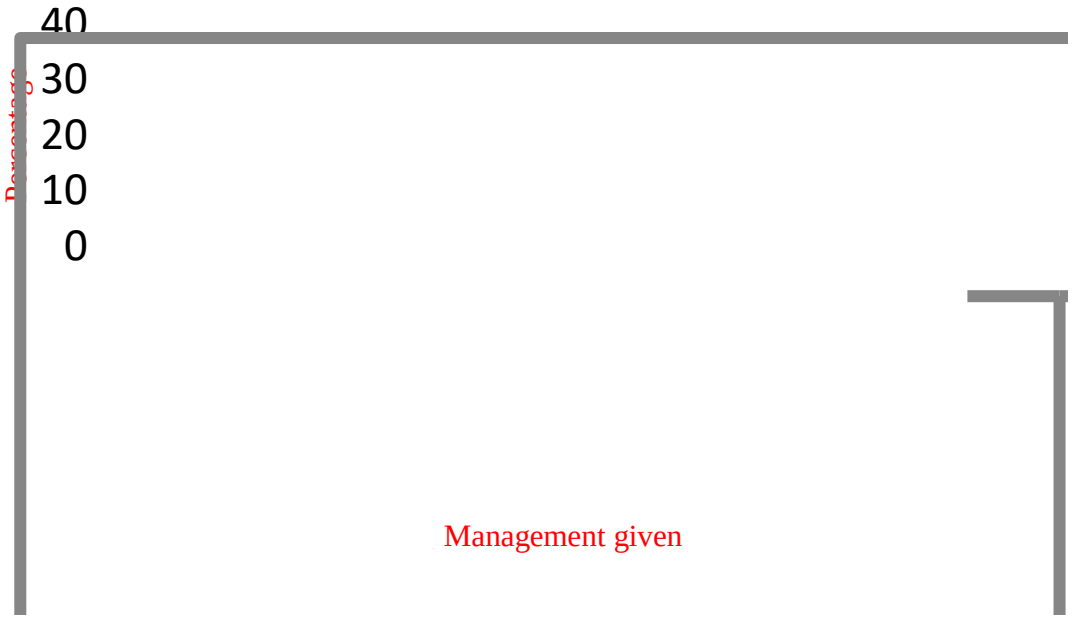


Figure 2: Management at ED

3.3. The outcome of patients after ED stabilization

2.7% (4/146) patients died at ED, while 97.3% (142/146) were admitted alive. Most of the patients with SOB reported relief after temporizing measures at ED before admission to renal units. 10% of patients with hyperkalemia had their potassium levels reduced, and 5% completely normalized after ED hyperkalemia management. However, ED temporizing management didn't show improvement in sodium, creatinine and BUN levels.

3.4. The proportion of patients who received dialysis and outcome.

Out of 142 patients who were admitted, with emergency complications of renal failure in need of dialysis, 61 (42.8%) received dialysis while 81 (57.2%) were managed conservatively. The 4 patients who died at ED also didn't get dialysis. The overall mortality was 39% (57/146). The total mortality in non-dialysed patients vs. dialysed patients was 53% (45/85) vs. 20% (12/61) ($p<0.0005$) respectively. See table 4 below

3.5. Factors associated with Mortality

In multivariate analysis, sex, vomiting, oliguria, body swelling, altered mental status; pulmonary edema, creatinine level and hospital management (dialysis versus conservative management) were independent predictors of mortality. Females had 87% [OR: 0.13; 95%CI:

0.03-0.53] less odds of dying compared to their male counterparts. Patients who presented with vomiting had more than six times higher odds of dying compared to those not (OR: 6.23[1.75 -22.2], while those with altered mental status had more than seven times higher odds of dying 7.48[1.90 - 29.41]. Participants with body swelling [OR: 3.40; 95%CI: 1.17 - 9.88] and those with reduced urine output [OR: 3.40; 95%CI: 1.22 - 9.48]] had more than three times higher odds of dying than those not. Participants with pulmonary edema had more than four times higher odds [OR: 4.60; 95%CI: 1.6 - 13.3] of dying than those not while those with creatinine level above 1200ummol/L had more than five times higher odds [OR: 5.02; 95%CI: 1.4 - 18.2] of dying than those below 700umol/L. In addition, non-dialyzed participants had more than eight times higher odds [OR: 8.02; 95%CI: 2.7-23.5] of dying than the dialyzed participants.

Table 4: Factors associated with mortality (Logistic regression analysis)

	Total	Alive	Died	Logistic Regression			
				Univariate		Adjusted	
	N=142	n (%)	n (%)	OR[95%CI]	P-Value	OR[95%CI]	P-Value
Age							
<30	26	10[38.5]	10[38.5]	1		1	
30-54	64	24[37.5]	24[37.5]	1.6[0.38 - 6.94]	0.932	2.81[0.44 -17.89]	0.825
55+	52	23[44.2]	23[44.2]	0.7[0.17 - 3.24]	0.627	1.13[0.17 - 7.37]	0.782
Sex							
Female	34	28[32.9]	6[10.5]	0.2[0.09 0.63]	0.003	0.13[0.03-0.53]	0.004
Payment							
Insurance	37	22[25.9]	15[26.3]	1			
Pay from pocket	105	63[74.1]	42[73.7]	0.9[0.46 - 2.10]	0.954		
Hospital Management (n=138 *)							
Dialyzed	59	47[55.3]	12[22.6]	1		1	
Not dialyzed	79	38[44.7]	41[77.4]	4.2[1.9 -9.1]	0	8.02[2.7-23.5]	0
Potassium in mmol/L (n=119*)							
<7mmol/L	98	65[66.3]	33[33.7]	1			
7+mmol/L	21	12[82.4]	9[42.9]	1.5[0.56 - 3.86]	0.426		
Reduced urine output (n=138*)							
Yes	57	32[37.6]	25[43.9]	1.3[0.65 -2.56]	0.459	3.40[1.22 - 9.48]	0.005
Altered mental status (n=138*)							
Yes	66	37[43.5]	29[50.9]	3.6 [1.36-9.67]	0.01	7.48[1.90 - 29.41]	0.004
Shortness of breath (n=138*)							
Yes	33	20[23.5]	13[22.8]	1.3[0.69 - 2.63]	0.39		
Vomiting (n=138*)							
Yes	43	29[34.1]	14[24.6]	1.6[0.71 - 3.42]	0.266	6.23[1.75 -22.2]	0.005

Physical and Lab findings							
Pulmonary edema (n=138*)							
Yes	54	27[31.8]	27[47.4]	1.9[0.97 - 3.86]	0.062	4.60[1.6 - 13.3]	0.005
Creatinine in umol/L (n=133*)							
<700	31	21[67.7]	10[32.3]	1		1	
700-1200	32	20[62.5]	12[37.5]	1.3[0.45-3.56]	0.663	1.52[0.40 - 5.75]	0.539
1201+	70	38[54.3]	32[45.7]	1.8[0.73-4.30]	0.208	5.02[1.4 - 18.2]	0.014
BUN Level in mmol/L (n=134*)							
<20	18	12[11]	4[25.0]				
20+	116	66[28.8]	48[42.1]	2.2[0.66 - 7.18]	0.199		

** N's vary as all patients did not have all tests in the ED. 4 participants who were lost to follow-up and 4 other patients who died at ED were not included in the analysis.*

3.7. Factors influencing dialysis

In multivariate logistic regression (LR), not being insured (paying out of pocket) and age of 55yrs and above reduced the odds of dialysis by 70% (OR: 0.30; 95%CI: 0.1-0.9) and by 80% (OR: 0.2; 95%CI: 0.1-0.9) respectively.

See table 5 below

Table 5: Factors influencing access to dialysis (n=142)

	Total	**Dialyzed**	**Not Dialyzed**	**Multivariate LR**
Age categories				
<30	25	15[60]	10[40]	
30-54	63	28[44.4]	35[55.6]	0.70[0.2 - 2.3]
55+	54	18[33.3]	36[66.7]	0.20*[0.1 - 0.9]
Total	142	61[43]	81[57]	
Mode of payment				
Insured	37	20[54.1]	17[45.9]	
Out of pocket	105	41[39]	64[61]	0.30*[0.1 - 0.9]
Total	142	61[43]	81[57]	
Creatinine (umol/L)				
<700	32	11[34.4]	21[65.6]	
700-1200	33	13[39.4]	20[60.6]	1.3[0.3 - 5.4]
1201+	68	32[47.1]	36[52.9]	2.0[0.6 - 6.8]
Total	133	56[42.1]	77[57.9]	
BUN (mmol/L)				
<20	18	9[50]	9[50]	
20+	112	47[42]	65[58]	0.50[0.1 - 1.9]
Total	130	56[43.1]	74[56.9]	
Potassium(mmol/L)				
<7	102	46[45.1]	56[54.9]	
7+	20	8[40]	12[60]	1.10[0.3 - 3.5]
Total	122	54[44.3]	68[55.7]	

* P<0.005

CHAPTER FOUR

4. 0. DISCUSSION

Renal failure is one of the most prevalent medical conditions in both high-income and low-income countries, carrying high rates of mortality. Many previous studies provide information about overall prevalence and mortality of AKI and CKD in developed and developing countries, and fewer determined the prevalence of CKD and AKI at ED (15,16,29,30,44,47). Yet little is known about the proportion of patients presenting at ED with emergency complication of renal failure, particularly in limited income countries. Likewise, those studies didn't describe the clinical profile, the outcome of ED stabilization, treatment options and their respective outcomes. This study is the first to focus on these factors for Tanzania and can serve as a foundation for similar studies in future.

Our study found that the proportion of patients presenting at ED with emergency complications of renal failure in need of emergent dialysis is almost eleven percent less than the proportion found in one single centered prospective study done in the US (i.e. 30% of them needed dialysis) (26). We could not find other previous studies that were done to determine the proportion of patients presenting at ED with emergency complications of renal failure to make a comparison. However, the proportion found in our study looks low and it can be explained by the fact that there are limited renal screening services across the regions in the country. So, some patients who receive a new diagnosis of kidney failure in the ED already have acute complications of renal failure.

Most patients (75.3%) in our study were males, similar to previous studies by Kazancioglu *et al.* in Turkey and by Hecking *et al.* across European countries, in which the proportion of males was higher than females in all age groups (48,49). The reasons why are not clear but could be attributed to a tendency of male patients to seek healthcare late when renal disease has already advanced compared to females, or to an increased vulnerability of male gender to renal failure risks.

The study also showed an interesting picture relating to age groups and education levels in relation to renal failure, where middle-aged people and those with low education levels and no health insurance are more likely to come to a public ED with emergency complications. People with higher education and health insurance are more likely to opt for other centers when seeking medical care. Or because they get healthcare more regularly, are less likely to present to any ED with complications of renal failure.

We noted as well, that more than fifty percent of our patients come as referrals from other government (public) hospitals, followed by one-third who are self-referrals and very few as private. This finding may be consistent with the fact that there is good adherence to the formal referral system in place and it is a way to avoid relatively higher hospital charges which will be encountered by those who come as self-referrals or private. These referral differences were not described in prior studies from high-income countries. This could be because of the difference in health systems and mode of healthcare delivery.

Main presenting symptoms at ED included shortness of breath, reduced urine output, chest pain, palpitations from arrhythmias and generalized /lower limb swelling. In this study, we found that the majority of participants (45.9%) presented to the ED with shortness of breath due to pulmonary edema, consistent with the previously published study in the US, although the proportion of patients with pulmonary edema was even higher (61%) (26). Shortness of breath appears to be the most frequent complication of renal failure, in most settings, regardless of geographical difference or whether they are from high-income or lower income countries.

The second most common presenting symptom in this study was decreased urine output (oliguria), followed by generalized or lower limb swelling. This study had a relatively higher proportion of patients with uremic encephalopathy (45%) and vomiting (24%) compared to 6.6% and 8.2% respectively in previous HIC literature (26,48). While in previous HIC studies, the prevalence of hyperkalemia in patients presenting to ED with renal failure requiring dialysis was less than ten percent (41), our study showed that more than fifty percent of the participants had hyperkalemia of >5.5mmol/L. This could be because the patients do not get routine renal check-up or dialysis even if they have known renal failure and could be because they seek care for renal failure late (don’t know they have it earlier)

About one third required hyperkalemia management as per protocol before being admitted to the ward or renal units for dialysis. As in emergency departments in HIC, management as per standard of care was observed in our ED by use of calcium gluconate to stabilize membranes, insulin, sodium bicarbonates and salbutamol nebulization to shift potassium intracellularly in hyperkalemia; and non-invasive positive pressure ventilation, nitroglycerine, and furosemide were used for fluid overload/pulmonary edema in one-third of the study participants.

Post-treatment levels for point-of-care electrolytes, urea and serum creatinine levels, or subjective relief of shortness of breath in pulmonary edema, were not recorded in most

patients. Example, potassium levels, sodium, serum creatinine and urea after ED treatment were not recorded for more than 63% of the participants, so it is hard to objectively measure the effectiveness of the ED management in renal failure. Main reasons could be forgetting to record the values in the electronic file system. A clinician made a judgment on when to stop management using the results gotten immediately after point-of-care tests in form of a small piece of paper, which most of the time was also not attached with the main printed file. Nevertheless, with the temporizing management given at ED, less than three percent of patients died at ED while others were admitted alive suggesting that treatment was effective.

Our study found that, the overall mortality of patients who needed dialysis was 39% and of those who died 77.4% were those who were not dialyzed. This is somewhat higher than the previous studies in developed countries, in which the hospital mortality rate was 33% and lower than in developing countries whose mortality rate was 47.6% (9,22). Higher mortality rates found in our study compared to developed countries can be attributed to late presentation to the hospital; financial constraints to meet dialysis costs and limited access to dialysis centers across the country, whereby only a few patients among those who need emergency dialysis get dialyzed. In this study, for example, only 42% of patients who needed dialysis got dialyzed compared to a study in the US where 81.8% of those admitted to renal and dialysis unit were dialyzed (26). The difference may be explained by the affordability of dialysis costs and relatively bigger capacity to dialyze patients in high-income countries, as in this study majority of patients were not insured hence had to pay out of pocket.

Our study like some of the previous studies showed that sex, increased level of serum creatinine, having pulmonary edema and dialysis are predictors of mortality. However, other studies conducted in developing countries like India showed age (>60yrs OR 5.6) was also a predictor of mortality, which is different from our study findings where age was not associated with mortality (9). Old age is associated with comorbidities, but this would be true in both populations in India and Tanzania. So, this difference may be due to the fact that Tanzania's life expectancy is relatively higher than India's (66 years versus 61) and there could also be a difference in the prevalence and types of comorbidities in these two groups (9,50).

Creatinine levels were also associated with mortality in this study. Studies in HIC have shown varying results. For example, while some studies reported that oliguria and increased creatinine levels of >265umol/L increased the risk of dying (29,31), others demonstrated that

higher serum creatinine levels were associated with greater survival; in a study by Park et al, patients with serum creatinine <442umol/L had higher risks of death while those with serum creatinine levels of >800- 1237umol/L had a lower risk of death (51). Our study, however, showed a different picture whereby patients with creatinine levels of higher than 1200umol/L had more than five times odds of dying than those with 700-1200umol/L. And creatinine less than 700umol/L didn't predict mortality. It is yet clear as to the reasons for these variations in the association of creatinine levels and mortality. Future and bigger studies can be done to solve this puzzle.

Another major finding in our study was that, whether or not the patient receives dialysis is a strong predictor of mortality, such that, non-dialyzed patients had more than eight times higher odds of dying than those who received dialysis. This is consistent with previous study done in high-income settings in which less than ten percent of those who were dialyzed died (48).

Although our study wasn't designed to determine the length of hospital stay, previous literature found that patients with increased creatinine stayed 3.5 days longer in the hospital than those with lower creatinine levels. Our study did not capture that association but described the length of stay in relation to dialysis: mean hospital stay for those dialyzed were 10.5 (SD±8.8) while those who didn't get dialysis had 9.9 (SD ±6.9). These findings, however, were not statistically significant and one of the limitations was that this outcome was recorded for only 50 participants (35%), making it hard to generalize these findings. Additionally, these numbers do not consider that patients who died might have had shorter lengths of stay.

Less than fifty percent of all patients who needed dialysis were dialyzed. This study didn't look at how long it took for these patients before they got dialyzed. We found that mode of payment and age of 55+ years were some of the factors associated with the probability of being dialyzed or not, contrary to previous studies, which showed shortness of breath was the only factor with statistical significance in predicting dialysis (26). Patients were more likely to be dialyzed if they had health insurance; not having health insurance (i.e. paying out of pocket), reduced the odds of dialysis by 70%. In our system, patients who didn't have insurance would not be able to pay immediately for dialysis costs and they would most likely opt to go home to obtain the money before they come back when they are ready. **This clearly could affect their clinical care and outcome**. The other predictor of not receiving dialysis

was the age of more than 55years, which decreased the odds of dialysis by almost 30%. It is widely accepted, however, that more advanced age is associated with poor outcome; and in Tanzania, due to limited resources and relatively better outcome, the younger population is usually preferred. We were unable to find other studies for comparison on the mode of payment or age.

4.1 Study Limitations

i. There was some missing patient information at medical records and uncharted documentation of point-of-care and laboratory results, clinical variables such as age or weight and treatment given. However, cross-checking was done by the principal investigator using the questionnaires to detect missing information early. Medical personnel were encouraged to chart and keep proper records of all patients. This minimized missing data.

ii. This was a single-centre, prospective cohort study which may affect the generalizability of its results. However, ED-MNH serves patients referred from all parts of Tanzania and **it was the only public dialysis centre during study period.** So, we tried to get the appropriate sample size which we believe would increase its representativeness to the general population.

iii. There were times when research assistants were not present at ED to be able to approach all patients and therefore this could affect getting all possible patients for enrolment. And this could underestimate the prevalence of the problem.

CHAPTER FIVE

5.0. CONCLUSION AND RECOMMENDATION

5.1. Conclusion

In a cohort of patients with renal disease presenting to ED, acute complications of renal failure are complications necessitating a significant need for emergent dialysis. **Lack of insurance limited some patients to get emergency dialysis.** The overall in-hospital mortality was 39%, and patients who received conservative care had a significantly higher mortality compared to dialyzed patients.

5.2. Recommendation

i. Future larger studies are required to study the association between serum creatinine levels and mortality because our study added a new finding that was not seen in prior studies which we were able to find. Also, to study how soon those who need emergency dialysis get dialyzed will be more informative.
ii. Only 43% of patients who needed dialysis were dialyzed. This could be attributed to the limited capacity of dialysis machines and costs. More funds should be allocated to capacitate the renal units to be able to attend more patients in need of dialysis.
iii. Because dialysis saves lives if performed quickly, patients with emergency need of dialysis should be considered regardless of their inability to pay to supplement the management done by emergency physicians at ED. The payment could be followed up afterward because these procedures are undeniably expensive, and cost-sharing is necessary.

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6. APPENDICES

Appendix 1: Questionnaire

Record ID _____

INCLUSION CRITERIA
- ☐ Age 15yrs and above
- ☐ Emergency symptoms: Metabolic acidosis, Electrolyte imbalance, anuria /oliguria, Fluid overload, uremia, Intoxication
- ☐ Creatinine levels 253umol/L or more

NAME _____

AGE _____

MR NUMBER _____

GENDER
- ○ Male
- ○ Female

EDUCATION
- ○ Higher education
- ○ Secondary education
- ○ Primary education
- ○ Informal education

MARITAL STATUS
- ○ Single
- ○ Married/Cohabiting
- ○ Divorced
- ○ Widow

REFERRAL FROM
- ○ Private Hospital
- ○ Government hospital
- ○ Self-referral

DISTRICT/REGION _____

MODE OF PAYMENT
- ○ INSURED
- ○ NOT INSURED

PRESENTING SYMPTOMS
- ☐ Generalized/LL swelling
- ☐ Reduced urine output
- ☐ Altered mental status
- ☐ Shortness of breath
- ☐ General body malaise
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Other

body swelling duration _____

reduced urine duration _____

AMS duration _____

SOB duration _____

Vomiting duration _____

Diarrhea duration _____

Other _____

duration of other
- ○ < 48hrs
- ○ < 1week
- ○ >1week

VITALS SIGNS

SBP _____

DBP _____

Pulse rate _____

Respiratory rate _____

Temperature _____

Random Blood Sugar _____

GCS level _____

COMORBIDITIES
- ☐ No known comorbidity
- ☐ Diabetes Mellitus
- ☐ Hypertension
- ☐ HIV
- ☐ Liver disease
- ☐ Sepsis
- ☐ Malaria
- ☐ CKD
- ☐ Malignancy
- ☐ Other

On dialysis
- ○ Yes
- ○ No

PHYSICAL FINDINGS
- ☐ Anemia
- ☐ crackles/Crepitations
- ☐ cold extremities
- ☐ capillary refill > 2seconds
- ☐ Altered mental status
- ☐ Unilateral weakness
- ☐ lung dullness
- ☐ urine retention
- ☐ Body/Facial/LL edema
- ☐ Other

_____

POC RESULTS

Serum creatinine
- ○ Results
- ○ Not tested

Creatinine results _____

BUN
- ○ Results
- ○ Not done

BUN results
_____

Serum K+
- ○ Results
- ○ Not done

Potassium results
_____

Serum Na+
- ○ Results
- ○ Not done

Sodium results
_____

Serum Cl-
- ○ Results
- ○ Not done

Chloride results
_____

Serum Lactate
- ○ Results
- ○ Not done

lactate results
_____

UPT
- ○ Positive
- ○ Negative
- ○ N/A
- ○ Not tested

RDT
- ○ Positive
- ○ Negative
- ○ Not tested

HIV Results
- ○ Non-reactive
- ○ Reactive
- ○ Indeterminant
- ○ Not tested

HB
- ○ Results
- ○ Not tested

HB Results
_____

ECG findings
- ○ Abnormal
- ○ Normal
- ○ Not done

PH
- ○ PH Results
- ○ Not Tested

PH results
_____

EMD MANAGEMENT GIVEN

- ☐ Not given
- ☐ IVF
- ☐ Bicarbonates
- ☐ Antihypertensives
- ☐ Non-invasive ventilation (CPAP/BiPAP)
- ☐ Dialysis
- ☐ Inotropes/Vasopressors
- ☐ Antibiotics
- ☐ Diuretics
- ☐ Nitrates
- ☐ Invasive ventilation
- ☐ Antiseizures
- ☐ Nebulization with beta agonists
- ☐ Calcium gluconate
- ☐ Dextrose with Insulin
- ☐ Others

LABORATORY RESULTS

Creatinine level _____

BUN level _____

K+ level _____

Na+ level _____

Ca2+ level _____

CL- level _____

BS RESULTS

- ○ Parasites seen
- ○ No parasites seen
- ○ Not tested

WBC Results _____

PLT Results _____

Hb Results _____

ALT _____

AST _____

RADIOLOGIC/SONOGRAPHIC TESTS

- ○ Done
- ○ Not done

Radiology/USS findings

- ☐ CXR Pleural effusion
- ☐ CXR Pulmonary edema
- ☐ CXR cardiomegaly
- ☐ POC USS B-lines
- ☐ POC USS Pleural effusion
- ☐ POC USS Pericardial effusion
- ☐ Other

POC RESULTS DURING DISPOSITION

Potassium level
- slightly reduced
- Same
- increased
- completely normalized
- Not tested

Sodium level
- slightly Reduced
- Same
- increased
- completely normalized
- Not tested

creatinine level
- slightly Reduced
- Same
- increased
- completely normalized
- Not tested

BUN level
- slightly Reduced
- Same
- increased
- completely normalized
- Not tested

GCS level
- Improved
- Same
- Reduced
- Not assessed

OUTCOME AT ED
- Died
- Admitted
- Transferred
- Discharged home
- Absconded
- Other

Disposition
- ICU
- HDU
- Nephrology Ward
- Dialysis Unit

Transfer
- NO TRANSFER
- JKCI
- MOI
- Outside Muhimbili

Other_____

HOSPITAL MANAGEMENT
- Dialysis
- Conservative management

Reasons why not dialyzed
- Financial constraints
- Not met criteria
- Pt refusal
- IV Access failure
- Machines are full
- Other_____

dialysis frequency

- ○ 1x
- ○ 2x
- ○ 3x
- ○ >3x
- ○ Not indicated

HOSPITAL OUTCOME

- ○ Discharged home alive
- ○ Died
- ○ Loss to follow-up
- ○ Transfer

Hospital stay
_____

Days of stay before death
_____

FINAL HOSPITAL DIAGNOSIS

- ☐ AKI
- ☐ CKD
- ☐ SEPSIS
- ☐ SHOCK (SEPTIC, CARDIOGENIC HYPOVOLEMIC)
- ☐ HYPERTENSION
- ☐ RENAL INFECTION
- ☐ OBSTRUCTIVE UROPATHY
- ☐ DIABETIC NEPHROPATHY
- ☐ Other _____

Appendix 2: Consent form (English version)

ID NO…….
PERMISSION FOR YOU/YOUR RELATIVE TO TAKE PART IN RESEARCH

Study title: THE CLINICAL PROFILE, MANAGEMENT STRATEGIES AND OUTCOMES OF THE ADULT PATIENTS PRESENTING AT ED IN NEED OF EMERGENT DIALYSIS AT MNH

Introduction
Greetings, I am a third-year resident in the course of Emergency Medicine at Muhimbili University of Health and Allied Sciences (MUHAS).
I am conducting a study with a title above as part of my study program. I hereby request your participation and cooperation in my study once I or my research assistant approaches you. Your decision to participate or not will have no effect on the care and management to you/ your relative.
Please ask questions if there is anything about this study you do not understand.

Aim of the study
The aim of the study is to assess the profile, management strategies and outcome of patients presenting at emergency department at Muhimbili national hospital in Tanzania with acute complication of renal failure

Benefits and Risks
There will be an overall benefit of improving care for all patients after knowing the results and its implication to the hospital. There will be no payment for participation in the study.
There is no risk in participating in this study.

What does this study involve?
This study involves the research assistant or principal investigator asking structured questions to the informant or relatives and filling the responses in the prepared questionnaire. Also, information about the patient will be obtained from the patients' file.

Consent
Your consent to be involved in the study is completely voluntary and agreeable by signing the consent form. If you are not free you are allowed not to consent and this will not affect your (your relative's) care and management offered. You may choose to stop taking part in this study at any time for any reason.

Confidentiality
The information you provide is highly valued and will be kept strictly confidential. The study information will be stored in protected computer files and in paper records stored in a locked filing cabinet. Only study staff will have access to the information.

Access to information
By signing this form, you allow the research team to use the information and give it to others involved in the research. The research team includes the researcher, facilitators plus others working on this study at MUHAS and MNH.

For further information, questions or queries, you can contact:

1. The Principal Investigator,
   Dr. Erasto Sylvanus
   Department of Emergency Medicine,
   MUHAS,
   P. O. Box 65001,
   Dar es Salaam, Tanzania.
   Tel: +255 713962628
   Email: erasto_syl@yahoo.com

2. Dr. Hendry Sawe
   Head, Department of Emergency Medicine,
   MUHAS
   P. O. Box 65001,
   Dar es Salaam, Tanzania.
   Tel: +255 754 885658
   Email: hendry_sawe@yahoo.com

3. Dr. Bruno Sunguya,
   Director of Research and Publications,
   MUHAS,
   P.O. Box 65001,
   Dar es Salaam, Tanzania.
   Tel no; 2150302-6, 2152489.

Signature:
I, _____ have read/been told the contents of this form. My questions have been answered. I agree to participate in this study.
Signature of participant _____
Date of signed consent _____

Appendix 3: Consent form (Swahili version)

FOMU RIDHAA YA KUSHIRIKI KWENYE UTAFITI HUU

Utangulizi

Jina langu naitwa Dkt. Erasto Sylvanus, mwanafunzi wa udaktari bingwa wa magonjwa ya dharura (Emergency Medicine) katika Chuo Kikuu Cha Afya na Sayansi Shirikishi Muhimbili (MUHAS). Ninahitaji kufanya utafiti kwa wagonjwa wa figo. Ninaomba ushiriki wako/ kwa niaba ya mgonjwa wako katika utafiti huu endapo mimi ama msaidizi wangu atakapokufuata ili kukuuliza taarifa muhimu za mgonjwa wako.

Madhumuni ya utafiti:

Dhumuni la utafiti huu ni kuchunguza hali, matibabu yanayotolewa na matokeo ya wagonjwa wa figo wanaokuja kwa matibabu idara ya dharura ya Hospitali ya Taifa ya Muhimbili.

Ushiriki katika utafiti:

Wagonjwa wa figo ndio wanaombwa kushiriki. Na ushiriki katika huu utafiti ni wa hiari kabisa. Unaweza kujitoa muda wowote kwa sababu zozote bila kuathiri huduma kwa namna yoyote.

Faida na Athari:

Kwa kutoa ridhaa ya mgonjwa wako kushiriki katika utafiti huu, tutaweza kuboresha huduma za wagonjwa wa figo kwa ujumla. Kwa kushiriki kwenye utafiti huu, hautalipwa wala hautalipa gharama yeyote

Hatutarajii kuwepo na athari/hatari yeyote itokanayo na ushiriki katika utafiti huu.

Usiri:

Taarifa zote zitakazokusanywa katika utafiti huu zitakuwa siri, hivyo ushiriki wako hautajulikana na mtu. Taarifa hizi zitajulikana kwenye timu ya watafiti tu.

Utoaji na upatikanaji wa taarifa

Mtafiti mkuu (mimi), msimamizi wa utafiti na wasaidizi wa utafiti na wahusika wengine wa tafiti wa chuo kikuu cha sayansi na tiba cha Muhimbili wataweza kuona taarifa zako.

Ukiwa na swali au tatizo lolote, unaweza kuwasiliana na wafuatao:

1. Mkuu wa Utafiti

Dkt. Erasto Sylvanus,

Idara ya Magonjwa ya Dharura na Mahututi (Emergency Medicine),

MUHAS,

S.L.P 65001,

Dar es Salaam, Tanzania.

Simu: +255 713962628

Barua pepe: erasto_syl@yahoo.com

2. Dkt. Hendry R Sawe

Idara ya Magonjwa ya dharura na Mahututi,

MUHAS,

S.L.P 65001,

Dar es Salaam, Tanzania.

Tel: +255 754 885658

Barua pepe: hendry_sawe@yahoo.com

3. Dr. Bruno Sunguya

Mkurugenzi wa utafiti,
MUHAS,
S. L. P. 65001,
Dar es Salaam, Tanzania
Simu: 2150302-6, 2152489.

Kuweka sahihi ya makubaliano:

Mimi, _____, nimesoma/nimesomewa maelezo yote yaliyomo kwenye fomu hii na nimeelewa. Maswali yangu yamejibiwa vizuri na niko tayari kushiriki.

Sahihi ya mshiriki _____

Sahihi ya Mtafiti _____Tarehe _____