**PREVALENCE AND OUTCOME OF ACUTE KIDNEY INJURY IN THE
INTENSIVE CARE UNIT AT MUHIMBILI NATIONAL HOSPITAL,
DAR ES SALAAM, TANZANIA**

BY

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DECLARATION AND COPYRIGHT

I Gyaviira Makanga, declare that this dissertation is my own original work and has not

been presented to any other university for a similar or any other degree award.

Signed...

Date...

Postgraduate Studies, on behalf of both the author and the Muhimbili University of Health and Allied Sciences.

DEDICATION

This book is specially dedicated to my dear parents Dr and Mrs. Boniface Makanga who

basically sacrificed their all to make certain that I get this far.

I also dedicate this work to my wife Philippa and our dear sons William and Arthur for

all the support and encouragement.

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LIST OF ABBREVIATIONS.

AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
APACHE	Acute Physiological and Chronic Evaluation Score
ARF	Acute renal failure
ATN	Acute tubular necrosis
CKD	Chronic kidney disease
GFR	Glomerular filtration rate
HIV	Human immunodeficiency virus
ICU	Intensive care unit
MNH	Muhimbili national hospital
MUHAS	Muhimbili University of Health and Allied Sciences
NSAIDS	Non-steroidal Anti-inflammatory drugs
PI	Principal Investigator
RRT	Renal replacement therapy
SOAP	Sequential Organ Failure Assessment score
WHO	World health organization

STUDY OPERATIONAL DEFINITIONS

Acute Kidney Injury: An abrupt (within 48 hours) reduction in kidney function defined as an absolute increase in serum creatinine of ≥0.3mg/dl (26.4µmol/l) or a percentage increase in serum creatinine of ≥50% or a reduction in urine output (documented oliguria of <0.5mls/kg/hr for >6 hours). *(Ref: 17, 18)*

Outcome event: This was either a mortality event that occurred during the ICU admission period or discharge from ICU.

ABSTRACT

Acute kidney injury (AKI) is common among hospitalized patients worldwide and has a poor prognosis among intensive care unit (ICU) patients with mortality rates ranging from 10-90%. The reported incidence of AKI in the ICU ranges between 1-24%; this high incidence varies from region to region and is attributable to factors such as differences in definition of AKI, regional disparities and etiological regional differences.

To date, there is a paucity of data on the burden and spectrum of AKI in the ICU in Tanzania and at Muhimbili National hospital (MNH).

We therefore conducted this study to determine the prevalence and some outcome predictor variables of AKI in the ICU at MNH that could be easy distinguishable outcome factors of AKI to aid in future prompt intervention.

Objective: The main objective of this study was to determine the prevalence and outcome of acute kidney injury in the intensive care unit at Muhimbili National Hospital.

Methodology: This was a retrospective descriptive study of all patients admitted to the MNH-ICU from January 2009 through December 2012. Medical records of the patients admitted to the ICU during the study period were reviewed and those with AKI were identified. Standardized pre-tested data instrument tools were used to collect socio-demographic data, clinical and laboratory parameters which included; date of admission to the ICU, type of patient (surgical or medical patient), duration of ICU stay, modality of ICU treatment for AKI, need for mechanical ventilation and or inotropic support. For purposes of this study, serum creatinine and urine output based on the AKIN criteria was used to define AKI.

Data entry was done using Epi Data (version 3.1) and statistical analyses performed using STATA (StataCorp. STATA 12.0, College Station, Texas 77845 USA). Continuous variables were summarized as means and standard deviations, categorical variables as frequencies and percentages. Bivariate analysis was used to test for the

association between the outcome of AKI in ICU which was death or survival and each predictor variable. The study was approved by the MUHAS review Sub-committee of senate research and publication with clearance reference number MU/PGS/SAEC/Vol. IV/.

Results: A total of seven hundred and sixty eight (768) patients were admitted to the MNH-ICU during the study period 2009-2012. Of these, two hundred and thirty three (233) patient files met the inclusion criteria and were accessible for review and included in the final analysis. Of these, 61.2% were male and the overall mean age was 45.7 years (SD 17.8). Patients with a medical diagnosis were 54% and the common underlying co-morbidities were; hypertension (33%), diabetes mellitus (15.5%), CKD (12%) and HIV (9%). The length of stay in the ICU for those with AKI was 2 days (IQR 2-6) while that for those with no AKI was 3 days (IQR 2-8), P=0.094. The prevalence of AKI in this study was 57.9% (135/233) with the different AKIN stages contributing: I-(19.2%), II-(28.1%) and III-(52.6%). Mortality among patients with AKI was 94.1% (127/135) while overall mortality of all study patients during the four year study period was 47.6% (301/632). Factors found significantly associated with AKI were underlying chronic kidney disease, (p=0.011) and needing vasopressor support in ICU (p=0.018). Needing mechanical ventilation was significantly associated with increased mortality among those with AKI (p=0.046). Among patients with AKI, 67.4 % had sepsis while 15.5% were recorded as having septic shock.

Conclusion: The prevalence of AKI among ICU patients at MNH-ICU is high and is associated with a marked in-hospital mortality rate.

Recommendation: All patients admitted to the ICU should be promptly screened for AKI at admission and through their ICU stay.

CHAPTER ONE

1.0   INTRODUCTION

Acute kidney injury (AKI) is a complex disorder that occurs in a variety of settings with clinical manifestations ranging from a minimal elevation in serum creatinine to anuric renal failure. It is often under-recognized and is associated with severe consequences[1-3].

Acute kidney injury is common among hospitalized patients worldwide and has a poor prognosis with the mortality ranging from 10-90% dependent upon the patient population studied and AKI definition used. Epidemiological studies have demonstrated wide variation in aetiologies and risk factors of AKI in developed and developing nations [1,4].

To date there is a paucity of data on the true incidence of AKI whether community or hospital-acquired. The reported prevalence of AKI from US data ranges from 1% (community-acquired) up to 7.1% (hospital-acquired) of all hospital admissions [5,6]. The reported incidence of AKI in the intensive care unit (ICU) varies from 1.5% to 24% [4], where it is associated with mortality rates as high as 70-90% (in those who require dialysis), and as many as one third of survivors may remain on chronic dialysis [7,8].

There is no reliable data on how often AKI occurs in Sub-Saharan African nations like Tanzania, and the incidence no doubt varies by region with some reports showing incidences of >150 AKI cases per 1,000,000   population[9,10]. This lack of epidemiological data is likely due to late presentation to health facilities, lack of renal registries, and under-reporting.

There is however, a stark contrast between AKI in developing countries like Tanzania and AKI in developed countries. In contrast to trauma, industrial accidents, drugs, cardiogenic shock, and

renal transplant rejection being the commonest cause of AKI in developed countries, acute tubular necrosis (ATN) due to community-acquired infections remains the commonest cause in the developing countries. In addition, nephrotoxins like herbal remedies, post-surgical and obstetric complications add to the burden of AKI in developing countries[9-12].

Numerous studies have identified factors that influence the outcome of hospitalized patients with AKI including the ICU; like inherent patient characteristics as well as some modifiable factors (i.e. nephrotoxic drugs, fluid status, infections, hemodynamics), need for dialysis, mechanical ventilation, ICU admission duration and non-patient related aspects like size of ICU, type of hospital [1,4, 13,14]. Despite this progress, several areas in the field of AKI remain uncertain especially in Sub-Saharan countries like Tanzania where data on the burden and spectrum of AKI is scarce. In addition, high risk population groups like ICU patients with AKI have not been studied in Tanzania despite a high national kidney disease burden [15].

1.1 LITERATURE REVIEW

1.1.1 Definition of Acute Kidney Injury

Acute kidney injury has now replaced the term acute renal failure and a universal definition and staging system has been proposed to allow earlier detection and management of AKI.

To address the lack of prior universal definition for AKI, a collaborative network of international experts representing nephrology and intensive care societies established the Acute Dialysis Quality Initiative (ADQI) and devised the Risk, Injury, Failure, Loss, End-stage (RIFLE) definition and staging system for AKI[16,17]. This was later modified by the Acute Kidney Injury Network (AKIN) group to reflect the clinical significance of relatively small rises in serum creatinine[18,19].

The AKIN definition for AKI was modified to (see table 1 below): An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3mg/dl ($\geq$ 26.4 μmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours)[17,18].

Table 1
The RIFLE and Acute Kidney Injury Network classifications of acute kidney injury

	GFR Criteria	Urine Output Criteria
Risk	Increased SCreat ×1.5 or GFR decrease >25%	UO <0.5 mL/kg/h × 6 h
Injury	Increased SCreat ×2 or GFR decrease >50%	UO <0.5 mL/kg/h × 12 h
Failure	Increased SCreat ×3, GFR decrease >75% or SCreat >4 mg/dL (acute rise >0.5 mg/dL)	UO <0.3 mL/kg/h × 24 h or anuria × 12 h
Loss	Persistent AKI: complete loss of kidney function >4 weeks	
ESKD	End-stage kidney disease: complete loss of kidney function >3 months	
AKIN 1	Increased SCreat by 1.5–2× above baseline or by 0.3 mg/dL	UO <0.5 mL/kg/h × 6 h
AKIN 2	Increased Screat by 2–3× above baseline	UO <0.5 mL/kg/h × 12 h
AKIN 3	Increased SCreat by >3× above baseline or by ≥0.3 mg/dL in patients with baseline SCreat >4 mg/dL	UO <0.3 mL/kg/h × 24 h or anuria for 12 h

Abbreviations: AKI, acute renal failure; GFR, glomerular filtration rate; SCreat, serum creatinine; UO, urine output.

Source: Ref 18

1.1.2 Epidemiology of Acute kidney Injury

The incidence rate of AKI around the world is not well known because of a number of factors including; underreporting, regional disparities, and differences in definition[10,20,21]. The epidemiology of AKI is different whether it occurs in the general population, the hospitalized population, or in critically ill patients admitted to the intensive-care unit (ICU).

The incidence of hospital acquired AKI is about 5-10 times higher than that of community-acquired cases, despite the fact that all surveys of hospital-acquired AKI underestimates its true incidence[22]. Data from the hospitalized Medicare beneficiaries in the USA, 1992-2001[23] revealed an overall incidence rate of AKI of 23.8 cases per 1000 discharges, with rates increasing approximately 11% per year. Old age, male gender, and black race were strongly associated with AKI. The population incidence of AKI from UK data ranges from 172 per million population

(pmp) per year from early data[24] up to 486-630 pmp/year from more recent series[25, 26], whereas in South Africa and India the incidence is approximately 20 pmp/year and 6.4 per 1000 admissions respectively[27, 28].

1.1.3 Acute kidney injury in the tropics

The true epidemiological picture of AKI in the tropics is not well understood due to the late presentation of patients to tertiary centers, lack of renal registries and lack of resources to support patients with established AKI[9]. Additionally, there is a general scarcity of epidemiological data on the burden and spectrum of AKI from many African regions including Tanzania.

There is however, a stark contrast between AKI in the tropics and that in temperate zones; In contrast to trauma, industrial accidents, drugs, cardiogenic shock and renal transplantation rejection being the common causes of AKI in the developed world, acute tubular necrosis (ATN) due to community-acquired infections (e.g. HIV/AIDS and related opportunistic infections, malaria, diarrheal diseases, etc.) remains the commonest cause in the tropics[29]. Natural medicines, used by traditional healers and post-surgical and obstetric complications add to the burden of AKI in many tropical areas including Tanzania[30].

1.1.4 Acute kidney injury in the ICU
Acute kidney injury is a common clinical problem in ICU patients and independently predicts poor outcome[31-33].The incidence of AKI in the ICU varies from 1.5% to 36%, where it is associated with mortality rates as high as 70-90% [4, 7, 8]. Moreover, additional observational data indicate that the incidence of AKI in the ICU is rising worldwide [23, 34] and probably in SSA as well.

Recent multinational databases from Europe, America, Australia, and Asia have provided good detail on the incidence, spectrum and outcome of AKI in ICU patients. Uchino and colleagues[4]

reported on 1738 cases of severe AKI complicating 22,269 ICU admissions in patients aged 12 years and older. Factors found significantly associated with mortality in this cohort included; older age (OR 1.02 [per year]), delayed fulfillment of inclusion criteria (OR 1.02[per day between admission and inclusion in study]), Simplified Acute Physiological Score II (OR 1.02[per point]), mechanical ventilation (OR 2.11), use of vasopressors and/or inotropes (OR 1.95), a hematological medical diagnosis as cause of admission to the ICU (OR 2.7), sepsis (OR 1.36), cardiogenic shock (OR 1.41), and hepatorenal syndrome (OR 1.87) [4].

This large increasing burden of AKI has in part been attributed to shifts in patient demographics (older, more co-morbid illness), severity of illness (multiple organ dysfunction syndrome), and AKI associated with complex interventions (organ transplantation) [35,36] as occurs in developed countries. The scenario however, is likely to be different in developing nations like Tanzania despite a general scarcity of data on the subject and additionally, different etiological factors like infections being the most common likely culprits.

Despite the multi-factorial nature of AKI in critically ill patients, sepsis and sepsis complications have consistently been found to be a leading contributing factor to AKI in critically ill patients [4, 33, 37-39].

It is upon this background that this study sought to address some of the factors associated with AKI in the ICU of MNH in Dar es Salaam, Tanzania.

1.1.5   Pathophysiology of acute kidney injury

There are numerous potential causes of AKI; many relate to a mismatch between oxygen and nutrient delivery to the nephrons, and energy demand of the nephrons. The causes of AKI have been traditionally divided into prerenal, intrinsic renal, and postrenal. In prerenal azotemia, there is a decrease in GFR with changes in serum creatinine (SCr), but no tubular injury. Intrinsic renal causes can be associated with ischemia, toxins, or primary interstitial or glomerular disease. It is

important to recognize that relative oxygen deprivation often is not generalized, but because of the complexity of vascular and tubular relationships in the kidney, functional consequences of localized tubular injury may be amplified. Other causes relate to direct toxic effects of substances on the vasculature or epithelium. The kidney is particularly susceptible to toxic effects from many environmental or therapeutic substances, since many of these compounds are concentrated by the tubule as the filtrate moves down the nephron. Acute injury is often superimposed on chronic kidney disease (CKD); as a result, AKI is increasingly recognized as an important precipitant in the progression to end-stage renal disease (ESRD).

The pathogenesis of AKI is complex and, to some extent, varies based on the particular cause; However, many convergent processes lead to tissue injury and organ dysfunction. Causes associated with toxins also have a final common pathway contributing to local or generalized ischemia.

Figure 1 summarizes the complex interplay between vascular and tubular processes that ultimately lead to organ dysfunction. AKI is a state often characterized by enhanced intrarenal vasoconstriction; it is also associated with enhanced renal-nerve activity and increased tissue levels of vasoconstrictive agents, such as angiotensin II and endothelin. A decreased responsiveness in the resistance vessels to vasodilators, such as acetylcholine, bradykinin, and nitric oxide (NO), as well as lower production levels of some vasodilators can enhance the impact of these vasoconstrictive agents. These effects on the resistance vessels are complemented by endothelial damage, enhanced leukocyte-endothelial adhesion (particularly in the postcapillary venules), and activation of coagulation pathways; together, these processes result in small-vessel occlusion and further activation of the leukocytes causing increases in inflammation and providing a positive-feedback network. The inflammation produces increased

levels of mediators expanding the interactions between leukocytes and endothelial cells, and activating the coagulation pathways. The resultant effects on oxygen and nutrient delivery to the epithelial cells result in damage to those cells; furthermore, damaged tubular cells also generate proinflammatory mediators. Repair involves the replacement of lost cells in the tubule by mechanisms that are not completely understood [40].

Figure 1: The pathophysiology of acute kidney injury (AKI).
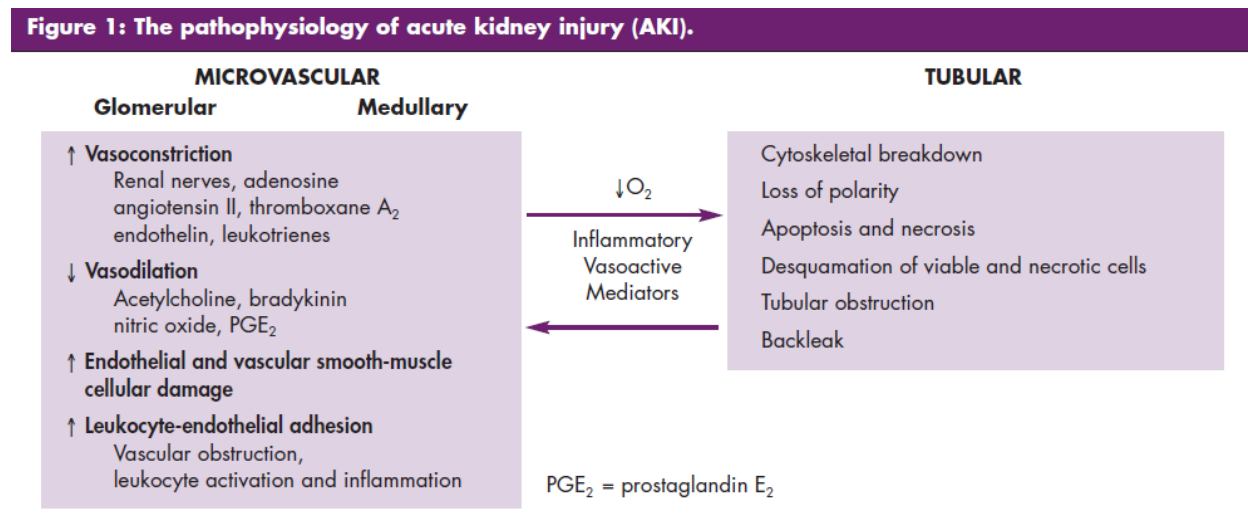
Source: ref: 41.

1.2 Diagnosis of acute kidney injury

The diagnosis of acute kidney injury at present, largely depends on the detection of changes in endogenous surrogate markers of kidney function, specifically, serum creatinine (SCr), urea, and urinary tests. Regrettably, these are not ideal, have limitations, and do not reflect genuine kidney injury or real-time changes in kidney function.

1.2.1 Serum creatinine as a marker of kidney injury

Serum creatinine (SCr) is an amino acid compound derived from the metabolism of creatine in skeletal muscle and from dietary meat intake. It has a molecular weight of 113 Da, is released into the plasma at a relatively constant rate, is freely filtered by the glomerulus, and is not reabsorbed or metabolized by the kidney. Accordingly, the clearance of SCr is the most widely

used means for estimating glomerular filtration rate (GFR). Serum Creatinine levels generally have an inverse relationship to GFR [42]. Thus, a rise in SCr is associated with a corresponding decrease in GFR and generally implies a reduction in kidney function and vice versa. There are limitations, however, with the use of SCr as a serum marker to estimate GFR. First, an estimated 10–40% of creatinine clearance occurs by tubular secretion of SCr into the urine [43]. This effect can potentially mask a significant initial decline in GFR. Moreover, SCr values may not show significant increases until approximately 50% of kidney function is lost. Second, several drugs can impair creatinine secretion and cause a transient and reversible increase in SCr (i.e. trimethoprim, cimetidine). Third, the production and release of creatinine into the serum can be highly variable and depends on; age, sex, dietary intake (i.e. vegetarian or creatine supplements) and muscle mass (i.e. neuromuscular disease, malnutrition, amputation) can result in significant variation in baseline SCr. Likewise, certain pathologic states may predispose to variable release of muscle creatinine e.g. in rhabdomyolysis, SCr levels may rise more rapidly due to release of preformed creatinine from damaged muscle or peripheral metabolism of creatine phosphate to creatinine in extracellular tissue. Fourth, there can be factors (i.e. ketoacidosis, cefoxitin, flucytosine) that reduce the accuracy of SCr assays and lead to artifactual increases in SCr levels. Finally, and perhaps most importantly, SCr does not depict real-time changes in GFR that occur with acute reductions in kidney function. Rather, SCr requires time to accumulate prior to being detected as abnormal, thus leading to a potential delay in the diagnosis of AKI [43].

1.2.2   Serum urea
Serum urea is a water-soluble, low molecular weight by-product of protein metabolism that is used as a serum marker of uremic solute retention and elimination. Similar to SCr, urea exhibits a nonlinear and inverse relationship with GFR. The use of urea to estimate GFR, however, is problematic due to the numerous extra-renal factors that influence its endogenous production and

renal clearance, independent of GFR. First, the rate of urea production is not constant. Urea can be grossly modified by a high protein intake, critical illness (i.e. sepsis, burns, and trauma), gastrointestinal hemorrhage, or drug therapy such as use of corticosteroids or tetracycline. Conversely, patients with chronic liver disease and low protein intake can have lower urea levels without noticeable changes in GFR. Second, the rate of renal clearance of urea is not constant. An estimated 40–50% of filtered urea is passively reabsorbed by proximal renal tubular cells. Moreover, in states of decreased effective circulating volume (i.e. volume depletion, low cardiac output), there is enhanced reabsorption of sodium and water in the proximal renal tubular cells along with a corresponding increase in urea reabsorption. Consequently, the serum urea concentration may increase out of proportion with changes in SCr and be under representative of GFR [44].

1.2.3 Urine as a marker in acute kidney injury

Urine output is routinely measured in critically ill patients. Trends in urine volume can be helpful in that continuous output can be used as a dynamic gauge of kidney function. Urine output however, generally lacks sensitivity and specificity for AKI. Even patients with severe AKI, characterized by markedly elevated SCr, can still maintain a normal or elevated urine output. Numerous biochemistry urinary tests (i.e. fractional excretion of sodium, fractional excretion of urea) have also been described and traditionally used to aid clinicians in the detection and classification of early AKI, in particular into so-called prerenal azotemia (PRA) and acute tubular necrosis (ATN) [45,46]. Regrettably, these tests too, lack sensitivity and specificity for the early characterization of AKI [47]. Moreover, these tests remain unproven and questionable in critically ill patients who often receive massive fluid resuscitation, diuretics, vasopressor infusions, radiocontrast media, and nephrotoxic drugs.

1.2.4 Significance of proteinuria in critically ill patients

Urinary excretion of protein has been described in numerous studies of AKI[48-52] and is frequently detected in urine of critically ill patients [53]. In a cohort of 104 critically ill patients, most with AKI or acute on CKD admitted to a medical ICU, 69% had evidence of microalbuminuria (<300 mg/g creatinine) or proteinuria (≥300 mg/g creatinine) on spot urine testing at the time of admission[53]. Urinary protein detection was more common in elderly patients, those with diabetes, CKD and shock. Moreover, a high albumin-to-creatinine ratio (≥100 mg/g) was associated with a significant increased adjusted odds of death (odds ratio 2.7; 95% confidence interval 1.1–7.2; P=0.04). This finding has similarly been shown in larger cohorts of mixed medical/surgical ICU patients [54,55].

1.2.5 Novel biomarkers for acute kidney injury

A variety of new protein-based biomarkers of kidney injury have been identified and may augment the traditional evaluation of kidney function, which has primarily relied on measurement of small molecules such as creatinine and urea. The novel biomarkers are described as below;

Serum and urinary cystatin c

Cystatin C is an endogenous cysteine proteinase inhibitor of low molecular weight. It holds many ideal features for use as a surrogate marker of kidney function and estimate of GFR and has been shown superior to serum creatinine [56,57]. It is synthesized at a relatively constant rate and released into plasma by all nucleated cells in the body. It is reportedly not significantly affected by patient age, sex, muscle mass or changes in diet. In a large cross-sectional study of 8058 patients, however, several factors were found to be associated with an elevated cystatin C, including older age, male sex, greater height, greater weight, current smoking status, and elevated C-reactive protein levels [58]. Urinary cystatin c in a small prospective study of critically

ill patients with AKI was shown to be highly predictive of subsequent need for acute renal replacement therapy (RRT) and outperformed several other urinary biomarkers [52].

Kidney injury molecule-1(KIM-1)

KIM-1 is a type 1 transmembrane glycoprotein that is normally minimally expressed in kidney tissue. It shows, however, marked upregulation in proximal renal tubular cells in response to ischemic or nephrotoxic AKI [59,60]. It is shed from proximal tubular cells and detected in the urine by immunoassay[61]. Kidney biopsies from patients with AKI also show increased and significantly greater KIM-1 tissue expression compared with other acute and chronic kidney diseases (i.e. urinary tract infection, contrast nephropathy, postrenal disease) [61]. In addition, urinary levels of KIM-1 were significantly higher in established AKI compared with other causes of AKI (i.e. pre-renal azotemia, contrast-induced nephropathy) or CKD. Thus, KIM-1 may represent an early, noninvasive biomarker for proximal tubular AKI.

Neutrophil gelatinase-associated lipocalin (NGAL)

NGAL belongs to the lipocalin superfamily of over 20 structurally related secreted proteins and is thought to participate in ligand transport with a b-barreled calyx [62]. The role of NGAL as a biomarker of human AKI has been established through a variety of studies in the settings of critical illness and postcardiopulmonary bypass (CPB), with the earliest reports coming from the pediatric literature. In 2005, a study of 71 children undergoing CPB was reported. In the 20 patients who developed AKI by creatinine criteria, both serum and urine NGAL levels rose significantly within 2 hours of surgery (mean urine NGAL rose from 1.6 ug/L to 147 ug/L while serum NGAL rose from 3.2 ug/L to 61 ug/L) [63].

Urinary cytokines

Numerous cytokines have now been detected in the urine of critically ill patients with AKI including IL-1, IL-6, IL-8, IL-18, tumor necrosis factor-a, and platelet activating factor (PAF) [61].

Inflammatory states characterized by increased production of these cytokines may be both a consequence of and predispose to AKI. These biomarkers however, though promising are early in their clinical application and not yet widely available.

1.2.6 Predictors of outcome in acute kidney injury

A number of variables that predict outcome among patients admitted to the ICU with AKI have been extensively studied in high-income countries [13, 14, 20, 25, 31]. In contrast, in resource-limited settings like Tanzania majority of critically ill patients are managed on the general medical wards and not in highly resourced intensive care units due scarcity of such resources. Outcome predictor variables in these low income settings remain largely unknown. Notably however, Friedericksen et al [14] in 2009 found an ICU mortality of AKI patients to be 47.8% in a medical ICU in South Africa. Factors found significantly associated with mortality were; high APACHE II scores ($p < 0.05$), need for dialysis ($p < 0.007$), multi-organ failure ($p < 0.01$), and oliguria ($p < 0.02$). Whereas predictors of survival were shorter duration of stay in ICU, low APACHE II scores, and avoidance of mechanical ventilation. These findings are similar to Uchino et al, 2005[4] whose findings in a multi-center study among AKI patients in ICU found the following factors as significantly associated with ICU mortality; use of vasopressors (OR 1.95; CI 1.50-2.55), need for mechanical ventilation (OR 2.11; CI 1.58-2.82), septic shock (OR1.4;1 CI 1.03-1.79), cardiogenic shock (OR 1.41; CI 1.05-1.90), and hepatorenal syndrome (OR 1.87; CI 1.02-3.28). More recently, Clec'h et al 2011, in their multiple center evaluation of mortality associated with acute kidney injury in critically ill patients also found similar findings [64].

CHAPTER THREE

2.1   PROBLEM STATEMENT

Acute kidney injury is a global problem among hospitalized patients with mortality rates of 50% and up to 90% in general admitted patients and ICU patients respectively.

To date, there is a paucity of data on the burden and spectrum of acute kidney injury among hospitalized ICU patients in Sub-Saharan African countries including Tanzania despite some reports showing infections, nephrotoxins and obstetric complications as leading etiological factors in the tropics.

Clinical characteristics and etiological factors of acute kidney injury among a selected high risk population of ICU patients at Muhimbili National Hospital in Tanzania have not been studied.

2.2   RATIONALE OF THE STUDY

There is a paucity of data on acute kidney Injury in hospitalized ICU patients in Tanzania despite high worldwide morbidity and mortality rates, with WHO reports indicating a high kidney disease burden in Tanzania of over 4,000 deaths/year (23.8 deaths per 100,000 population)

By documenting the burden and some of the etiological factors of AKI in the ICU in this resource limited setting, we hope that better management protocols for high risk patients will be developed with the aim of reducing the AKI mortality in the ICU. We also hope that by identifying some preventable risk factors, future early detection strategies will be sought to prevent the prohibitively high treatment costs that most Tanzanians cannot afford nor have access too. Additionally, we also hope to compare these findings to the international experience.

2.3   OBJECTIVES

2.3.1   Broad objective

To determine the prevalence and outcome of patients with Acute Kidney Injury admitted at the

Muhimbili National Hospital-Intensive Care Unit (MNH-ICU).

2.3.2   Specific objectives

- To determine the prevalence of Acute Kidney Injury among patients admitted at MNH-

  ICU

- To describe the clinical characteristics of patients with Acute Kidney Injury admitted to

  MNH-ICU

- To determine the outcome of patients with Acute Kidney Injury admitted to MNH-ICU

CHAPTER FOUR

3.0   METHODOLOGY

3.1   Study design

This was a retrospective descriptive study of patients admitted to the Intensive Care Unit at Muhimbili National Hospital from 2009 to 2012.

3.2   Study Area

The study was conducted at the Intensive care unit and medical records department at Muhimbili National hospital (MNH). We used data from both the computerized data base at the Medical records department and from the medical records book at the ICU. The computerized database was set up in July 2005 and captures data on all in and out-patients at MNH which includes; biodata, dates of admission and discharge or date of death, ward/unit, diagnosis, e.t.c. MNH is a tertiary referral and teaching hospital, situated in Dar es Salaam city. The hospital serves patients referred from other regional hospitals in the country. It has a bed capacity of approximately 1,500 and serves about 1,500 outpatients per day. The Muhimbili National hospital- ICU receives both medical and surgical patients. It was set up in the early 1970s and currently has 8 beds with 5 fully functional mechanical ventilators, and 6 bedside monitors. The staffs include 34 registered nurses who run 2-3 shifts a day with 4 in-house doctors, all of whom are qualified anesthesiologists. About 2-25 patients are admitted to the ICU monthly, these include surgical patients including obstetric and gynaecological cases, medical and pediatric patients.

3.3   Study population

All medical records of patients admitted to the MNH-ICU from the year 2009 to 2012 were reviewed, and using the AKIN criteria for defining AKI, those with AKI were identified and further studied.

3.3.1   Inclusion criteria
- We included all surgical and medical patients' charts showing admission to the MNH-ICU from 2009-2012 with completely filled clinical and laboratory data.

- Age ≥18 years

3.4   Sample size
We reviewed and analyzed all patients' charts meeting the inclusion criteria

3.5   Sampling procedure
The Principal Investigator (PI) recruited and trained a research assistant on use of a pre-tested instrument tool for data collection. Patient chart admission numbers from 1st January 2009 through 31st December 2012 were identified at the Muhimbili National hospital-ICU with the help of the ICU in-charge. These charts were then traced at the medical records department with the help of the in-charge medical records. Upon retrieval of the patient charts, a chart review was conducted.

Any missing data from the patient's charts was tracked from the ICU record books/database. Data collected included; demographic data like age, sex, and address. We also recorded duration of illness, ICU admission and discharge dates, admission and final diagnoses, ICU outcome (death/survival at discharge), any co-morbidities, mode of treatment including mechanical ventilation and Renal replacement therapy like hemodialysis. Admission vital signs like blood pressure, respiratory rate, temperature, oxygen saturation were also be recorded. Blood chemistries like serum creatinine, urea, and electrolytes, urine output, complete blood counts and liver function tests were recorded from the charts. The PI assigned a diagnosis of AKI after reviewing the blood chemistry and urine output data based on the AKIN operating definition for AKI. The diagnosis of AKI was based on two serum creatinine values separated by a time

duration of at least 48 hours with an increase in serum creatinine of ≥ 0.3mg/dl (26.4µmol/l) and or a urine output of <0.5mls/kg/hr.

3.6   Quality Control

The principal investigator (PI) and or trained research assistants used a pre-tested data collection instrument tool on all the patient's charts that fulfilled the inclusion criteria. The data forms were pre-tested in a pilot study for clarity and standardization to ensure internal validity.

All data from the patients' study charts was captured on the pre-tested instrument tool and double entered into Epidata. Check programs were used to minimize loss of the data.

3.7   Data Management

3.7.1   Data entry and analysis

All filled survey forms were coded and double entered into epi data version 3.1 and exported to STATA (StataCorp. STATA 12.0, College Station, Texas 77845 USA) for analysis.

Descriptive statistics were used to summarize the characteristics of the patients. Continuous variables were summarized into means, medians and ranges. Categorical data were summarized as frequencies and percentages. Comparisons of AKI patients according to the AKIN classification were based on chi-square test or Fisher's exact test for categorical data. We set a significant level at $p<0.05$.

To address study objective 1; the prevalence of AKI among patients admitted to MNH-ICU: this was reported as a percentage, where the numerator being the total number of study subjects who met the criteria for AKI and the denominator, the total number of all study subjects admitted to the ICU during the study period (2009-2012).

To address objective 2; to determine the outcome (death/survival) of patients with AKI admitted to the MNH-ICU: this was summarized as percentages where the numerator was patients with

AKI who died or survived and discharged from ICU within the study period and the denominator as the total number admitted with AKI. Probabilities of survival using Kaplan-Meier method were estimated with Log-rank tests.

To address study objective 3: To describe the clinical characteristics of patients admitted to the MNH-ICU; socio-demographic, clinical and some laboratory parameters were explored in relation to the outcome of interest.

3.8 Ethical Consideration

Ethical clearance and permission to conduct this study was sought from MUHAS ethical committee and MNH administration respectively with a clearance reference number; MU/PGS/SAEC/Vol. IV/. In addition, we sought for a waiver of consent since this was a retrospective chart review. Permission to use the medical records was also sought from the medical records administration through the MNH head of medicine department and the director of clinical services. All patient information was kept confidential and privately secured. We coded all the survey forms that were used in the study.

CHAPTER FIVE

4.0　Results

During the period January 2009 through December 2012, seven hundred and sixty eight (768) patients were admitted to the MNH-ICU. Of these, 233 (30%) met the inclusion criteria and were included in the final analysis. Five hundred and thirty five (535) patients were excluded. The main reasons for exclusion were: age <18 years (136), missing files from the medical records department (207), and incompletely filled files (192). (*Figure 1*). The excluded adult patients were similar in terms of some demographic characteristics like age and nature of patient (medical or surgical).

Figure 1.   Patient study profile

768 patients admitted to the ICU during the study period

Excluded:

136; age <18 years

632 medical records reviewed

Excluded from final analysis; 207 files physically missing from medical records. (84 of these recorded as died in ICU)

192 files with incomplete clinical and laboratory data

233 files met eligibility criteria

AKI 135

NO AKI 98

Died in ICU 127

Discharged from ICU 8

Died in ICU 90

Discharged from ICU 8

4.1   Baseline characteristics of study patients

The patients' socio-demographic characteristics at admission by AKI status are shown in table1.

Overall, males were 60.9% (142/233). The mean age of all study patients was 45.7 (SD 17.8).

There were no statistically significant differences between patients with AKI and no AKI in terms of sex (p=0.996), education level (p=0.924), and nature of patient, medical or surgical (p=0.076).

We however observed that the length of stay in the ICU for patients with AKI was shorter [2 days (IQR 2-6)] compared to 3 days (IQR 2-8) for those with no AKI,(p =0.094).

Patients with a medical diagnosis were 54.5% while those with a surgical diagnosis were 45.5%. Chronic kidney disease was present in 18 (18.4%) of the patients with AKI compared to 10 (7.4%) of patients with no AKI (p=0.011).   We also observed that more patients with AKI needed vasopressor support 35 (25.9%) compared to 13 (13.3%) without AKI,(p=0.018).

Table 1.   Characteristics of study patients

	AKI (n=135)	No AKI n=98	Total (n=233)	P-value
Age (yrs): mean(SD)	46.4(18.2)	44.8(17.3)	45.7(17.8)	0.495
Sex: n (%)				
Male	82(60.7)	60(61.2)	142(60.9)	0.996
Female	53(39.3)	38(38.8)	91(39.1)	
Education level: n (%)				
None	62(45.9)	46(46.9)	108(46.4)	
Primary	60(44.4)	44(44.9)	104(44.6)	
Secondary	9(6.7)	4(4.1)	13(5.6)	0.924
University	3(2.2)	3(3.1)	6(2.6)	
Unknown	1(0.7)	1(1.0)	2(0.9)	
Nature of patient: n (%)				
Medical	67(49.6)	60(61.2)	127(54.5)	0.079
Surgical ±	68(50.4)	38(38.8)	106(45.5)	
Co morbidities: n (%)				
Hypertension	44(32.6)	33(33.7)	77(33.0)	0.863
Diabetes	23(17.0)	13(13.3)	36(15.5)	0.432
Chronic kidney disease	18(18.4)	10(7.4)	28(12.0)	**0.011***
HIV	14(10.4)	7(7.1)	21(9.0)	0.396
Mode of referral: n (%)				
Self-referral	3(2.2)	5(5.1)	8(3.43)	
Hospital referral	71(52.6)	46(46.9)	117(50.2)	0.401
Undocumented	61(45.2)	47(47.9)	108(46.4)	
Duration of stay in ICU(days) median(IQR)	2(2-6)	3(2-8)	2(2-7)	0.094
Mode of treatment in ICU:				
- Mechanical ventilation±	90(66.7)	59(60.2)	149(63.9)	0.310
- Renal replacement therapy	4(2.9)	2(2.0)	6(2.6)	0.661
- Vasopressor support	35(25.9)	13(13.3)	48(20.6)	**0.018***

*p<0.05

4.2 Prevalence of acute kidney injury

The prevalence of AKI was 57.9% (135/233) with AKIN stages I, II, and III constituting 19.2%, 28.1% and 52.6% respectively.

The characteristics of AKI patients by AKIN stage are shown in table 2. Compared to patients with stage I AKI, duration of stay showed a decreasing trend as the AKI stage increased although this did not reach statistical significance, p=0.071. We noted that the proportion of patients with hypertension increased with increasing stage while that of hypotension decreased with increasing AKI stage, p=0.036. The mean hemoglobin level also decreased with increasing AKI stage, p=0.011.

For patients with AKI, 67.4% were recorded as having sepsis while 15.5% had septic shock. Other clinical diagnoses recorded by the clinicians were obstructive uropathy, hypovolemia, glomerulonephritis and others contributing 2.2%, 2.2%, 0.74% and 12% respectively.

Table 2.   Characteristics of patients by AKI staging (n=135)

Characteristics of AKI patients					
	All	Stage1 (n=26)	Stage 2 (n=38)	Stage 3 (n=71)	P-value
Age: mean (SD)	46(17.8)	46(16.7)	43(15.5)	50(18.9)	0.642
Sex: n (%) Male Female	86(63.7) 49(36.3)	18(69.2) 8(30.8)	21(55.2) 17(44.7)	47(66.2) 24(33.8)	0.426
Duration of stay in ICU in days: mean (SD)	4.9(6.0)	5.4(8.2)	4.8(7.0)	4.8(6.0)	0.071
Nature of patient; n (%) Medical Surgical	80(59.3) 55(40.7)	16(61.5) 10(38.5)	24(63.2) 14(36.8)	39(54.9) 32(45.1)	0.674
Mode of referral: n (%) Self Hospital Unknown	4(2.9) 68(50.4) 63(46.7)	1(3.8) 12(46.2) 13(50.0)	1(2.6) 21(55.3) 16(42.1)	2(2.8) 35(49.3) 34(47.9)	0.939
Co morbidities: n (%) Hypertension Diabetes CKD HIV	51(37.5) 20(14.7) 14(10.3) 14(10.3	8(30.8) 5(19.2) 1(3.8) 6(23.1)	16(42.1) 3(7.9) 6(15.8) 2(5.3)	27(38.0) 12(16.9) 7(9.9) 6(8.5)	0.587 0.370 0.283 0.065
Mode of ICU treatment: n (%) Mechanical ventilation RRT Vasopressor support	87(63.1) 3(2.2) 30(22.1)	13(48.2) 0(0.0) 6(22.2)	25(65.8) 2(5.3) 5(13.2)	49(69.0) 1(1.4) 19(26.8)	0.152 0.292 0.264
Blood pressure status: n (%) Normal Hypertension Hypotension	39(28.9) 45(33.3) 51(37.8)	8(30.8) 4(15.4) 14(53.8)	6(15.8) 14(36.8) 18(47.4)	25(35.2) 27(38.0) 19(26.8)	**0.036***
Respiratory rate; mean (SD)	27(10.6)	27.3(10.6)	27.3(10.3)	27.1(10.2)	0.992
Pulse rate: mean (SD)	108(23.8)	105(27.7)	106(21.8)	110(23.5)	0.684
Baseline serum creatinine: mean (SD)	237(324)	242(260)	315(478)	194(231)	0.168
Baseline urea: mean (SD)	16.5(18.7)	13.8(12)	24.1(27.8)	13.6(13.5)	0.127
Baseline WCC: mean (SD)	2.16(0.94)	2.04(0.99)	2.26(0.92)	2.15(0.95)	0.752
Baseline Hb: mean (SD)	10.9(3.2)	12.4(3.4)	10.0(3.6)	10.9(2.9)	**0.011***

4.3   Outcome of study patients in ICU

Mortality among patients with AKI was higher than in those without AKI, 94.1% (127/135) compared to 91.8% (90/98), p=0.0037(figure 3). We observed that mortality occurred earlier during admission to ICU with approximately 90% dying within 10 days (figure 3). The overall all-cause mortality among the study patients during the study period was 47.6% (301/632).

Bivariate analysis of the factors associated with mortality in ICU by AKI status is shown in table 3. Needing mechanical ventilation was the only factor found to be significantly associated with mortality among AKI patients (p=0.046 CI 1.049-2.262), table 3.

As shown in figure 3, AKI patients had a worse survival compared to those with no AKI during the first 2 weeks; however, mortality among the non-AKI group approximates that of the AKI group by the fifth week (p=0.0037).

Table 3. Bivariate analysis of predictors of mortality among AKI patients (n=135)

Variable	Discharged from ICU (%)	Died in ICU (%)	HR (95% CI)	P-value
Age: mean (SD)	66.6(6.4)	45.3(18.1)	0.998 (0.988-1.008)	0.747
Sex: n (%) Male Female	4(50) 4(50)	75(59.1) 52(40.9)	0.942 (0.655-1.353)	0.718
Nature of patient: n (%) Medical Surgical	3(37.5) 5(62.5)	60(47.2) 67(52.8)	0.958 (0.670-1.369)	0.723
Co morbidities: Hypertension Diabetes CKD HIV	1(12.5) 2(25.0) 2(25.0) 0(0)	38(29.9) 22(17.3) 10(7.8) 14(11.0)	1.307 (0.891-1.918) 1.100 (0.692-1.749) 1.217 (0.629-2.351) 1.276 (0.725-2.245)	0.551 0.514 0.677 0.616
Resp. rate: mean (SD)	22(10.2)	29(10.3)	1.013 (0.996-1.030)	0.140
Pulse rate: (SD)	95(7.1)	112(24.7)	1.003 (0.996-1.010)	0.419
Baseline Cr: (SD)	369.1(183.9)	302(364.3)	1.000 (0.999-1.000)	0.639
Baseline Urea: (SD)	21.3(1.1)	19.2(18.1)	1.002 (0.991-1.013)	0.750
Baseline Hb: (SD)	11.5(3.1)	10.6(3.2)	1.048 (0.990-1.109)	0.105
WCC: (SD)	2.41(0.9)	2.42(0.87)	0.979 (0.797-1.202)	0.840
Mode of treatment: n (%) Mechanical ventilation. Vasopressor support	0(0) 0(0)	84(67.2) 34(27.2)	1.540 (1.049-2.262) 1.108 (0.745-1.646)	**0.046*** 0.389

4.6   Kaplan-Meier survival curves

Fig. 2: Mortality curve for all study patients admitted to ICU during the study period

Kaplan-Meier survival estimate

N=233
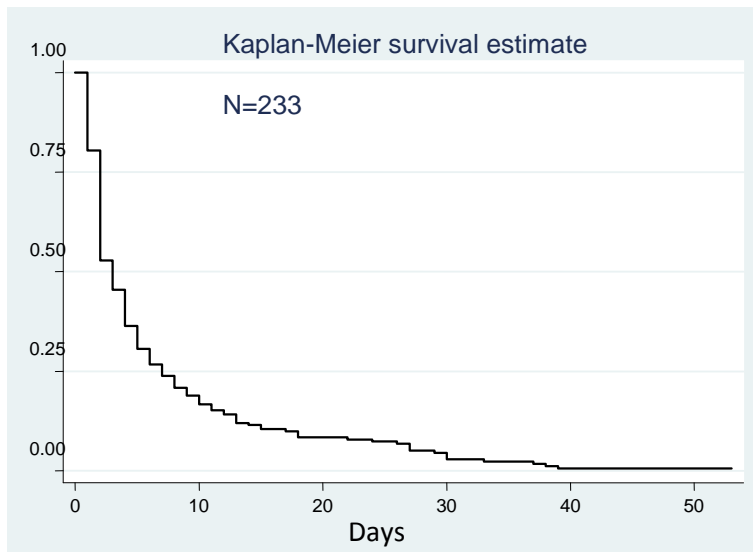
As shown in the mortality curve above, approximately 90% of all study patients had died by day 10 after admission to the ICU during the study period.

Fig 3: Mortality curve of study patients by AKI status

N=233

P=0.0037

No AKI   AKI
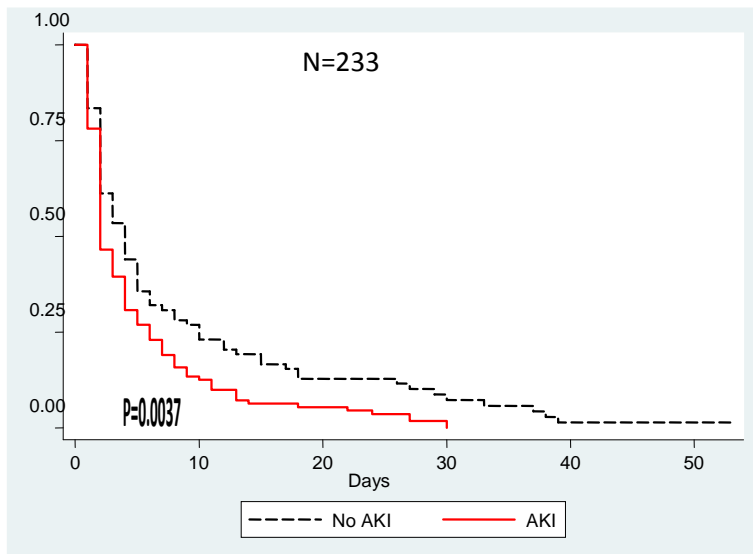
CHAPTER SIX

5.0   DISCUSSION

This was a retrospective descriptive study that aimed at determining the prevalence and outcome of patients with AKI admitted to MNH-ICU from January 2009 to December 2012. We identified 768 patient records from the ICU records and of these 233 files were available for the final analysis. This accounted for 30.3% (233/768) of all patients admitted to the ICU during the study period.

The prevalence of AKI in our study was 57.9% (135/233). Similar findings were observed by Ya-Wen et al[65] in Taiwan who found a prevalence of 59% among AKI patients in a medical ICU. In their study however, a highly selected population with underlying myocarditis was studied. Our prevalence of 57.9% is approximately thrice that observed in many centers in Europe, Canada and the United States of America whose prevalence rates of AKI in ICU ranges between 1.5-24%[3-6,66]. These marked differences may be explained by; differences in population and risk factors for AKI as well as different underlying co-morbid illnesses, the non-uniform criteria for defining AKI in the different studies, different sample sizes and possibly the different study designs. Additionally, in our study we excluded >50% of our study participants due to missing or incomplete data and this could have affected our final results.

Prevalence studies of AKI in Sub-Saharan Africa are generally lacking, however, recent studies done in a rural Ethiopian hospital[67] and in a medical ICU in S.Africa[14] showed prevalence rates of 20% and 23.2% respectively. These were however, selective non-ICU population in the Ethiopian study and medical ICU in the South African study. Our study population was taken from an ICU that admits both medical and surgical cases and occasionally pediatric patients.

In our study, neither demographic characteristics such as age, sex, education level nor co-morbidities like diabetes and hypertension were associated with AKI. This is in contrast to the data from other studies[4,7,31]. This could be explained by differences in the population baseline characteristics, our patients were relatively young with a mean age of 45 years compared to ICU patients in many high income countries whose mean age is 60 years or older and with different underlying co-morbid conditions[1,3,4,7,18].

We observed a male patient dominance of 61%, additionally, male proportions were higher among the three AKIN stages with 66% in stage 3 compared to 34% among the female patients. Similar findings were found in the study by Uchino et al[4]. Majority of our study patients had only attained primary level education (45%) while those with no formal education were 46%. Among those with AKI, 46% had no formal education compared to 2% with tertiary education. The lack of formal education could explain the high AKI rate among this group due to possible ignorance of their disease severity and possibly using traditional remedies as first line therapies. However, the differences in education levels were statistically not significant.

The duration of stay in the ICU was shorter among those with AKI, 2 days compared to 3 days among those without AKI, however, this difference was not statistically significant. Additionally, the duration of stay in ICU decreased as the AKI stage increased, this however did not reach statistical significance possibly due to our small sample size.

We noted among our study population an increasing proportion of patients with hypertension as the AKI stage increased. This could be explained by the fluid retention complication among AKI patients as one of the pathophysiological mechanisms. Similarly, the hemoglobin concentration

decreased with increasing AKIN stage and this could be explained by the hemodilution contributed to by fluid retention and the worsening underlying disease process.

We noted that between 2009-2012, only six (6) patients admitted to the MNH-ICU received renal replacement therapy (RRT) in the form of hemodialysis, 60% (4) of whom were in the AKI group. The low RRT among our study population was due to lack of an in-house (ICU) hemodialysis machine(s) during the entire study period.

We also noted in our study that underlying chronic kidney disease and needing vasopressor support in ICU were likely risk factors for AKI. Underlying chronic kidney disease could have predisposed our study patients to AKI through a number of mechanisms including; exposure to nephrotoxins in the ICU like some antibiotics, NSAIDs, or contrast media, and complications of the underlying disease process like sepsis.

Needing vasopressor support was also found to be a risk factor for AKI in our study and similarly, has been associated with increased morbidity and mortality in other studies[4,7,66]. Vasopressor support indicates poor peripheral perfusion with kidney hypoperfusion leading to a pre-renal failure state. Current evidence supports the fact that use of inotropic support in critically ill patients with associated AKI is associated with increased mortality[4,14,17].

5.1   Outcome of patients in the ICU
In our study, the overall all cause mortality rate among the study patients was 47.6% (301/632). This mortality rate is comparable to Friedericksen et al[14] who found an overall mortality of 50% among medical patients admitted to the ICU in South Africa.

Mortality among the AKI group was however markedly high at 94.1% whereas that in the non-AKI group was 91.8%. The 94.1% ICU mortality rate of AKI patients in our study is far higher

than that quoted in the literature.[4,7,23, 34,66].   Similar findings however, have been reported by Sural et al[8] in India where mortality in their study was 90%. Their study population however was younger with a mean age of 28 years compared to ours with a mean age of 45 years. Additionally, their study used a smaller sample size compared to our study. Our high mortality rate could also have been skewed by the many excluded patients who had missing data or incomplete data.

From the mortality curve comparing the two groups *(fig.3)*, it was observed that though mortality was significantly high in both groups, AKI patients died faster within the first 2-3 weeks with a significant log-rank test P=0.0037. This could probably be explained by the fatal acute complications of AKI like fluid overload, electrolyte abnormalities like hyperkalemia, metabolic acidosis that require prompt diagnosis and quick management with use of renal replacement therapies like hemodialysis which was lacking in the ICU during the study period, and management of established AKI therefore relied on conservative methods and additionally, late presentation of patients and or delayed referral of patients to the ICU.

Additionally, mortality in our study as shown in the mortality curve indicates that about 80% of study patients died within one week of admission. A number of factors could be attributed to this; delayed presentation and or late referral of patients from other health centers since majority >50% of the study patients were referrals from other health centers *(table 1)*, patients presenting with possible multiple organ dysfunction, delayed institution of appropriate treatment such as antibiotics coupled with possible antibiotic resistance to the commonly available antibiotic regimens and inadequate fluid therapy, lack of ICU admission screening tools like the APACHE II and SOAP scoring tools used in other studies[4,7,8,14], lack of advanced technologies like renal replacement therapies like hemodialysis hence using the non-effective conservative mode of

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treatment for AKI. Better and adequately equipped ICU settings could also explain the lower ICU mortality reported from other studies in Europe, the United States and South Africa[4,7,14, 23].

Need for mechanical ventilation was associated with mortality in our study on bivariate analysis. This finding is in agreement with many other similar studies conducted in ICU settings both in high income and low income countries [4,7,8,14,23,34]. This finding could be explained by the fact that patients who need mechanical ventilation are usually critically ill, often with multiple organ failure and hence poor outcome.

Sepsis was the most commonly recorded diagnosis and possibly underlying cause of the AKI followed by septic shock. These findings are very similar to the international experience where sepsis among ICU critically ill patients remains a major cause of mortality and is significantly associated with AKI[4,7,8,14,23,34,66]. Additionally, more patients in the AKI group in our study needed Vasopressor support 26% compared to 13% without AKI, (P=0.018). This probably was due to septic shock or other causes of shock necessitating vasopressor support. We were however unable to demonstrate sepsis as a predictor of mortality in our study or correlate the association between sepsis, Vasopressor support and outcome.

5.2   Study Limitations

Our study had several limitations:

- Over 50% of files were excluded from our study due to either missing from the records or had incomplete clinical data and this could have had a major impact on our final results.
- The study relied on recorded data from the patients' files, this could have introduced an information bias that could have affected our results.

- Due to the small sample size of measured variables, the study was not powered to provide statistically significant results with respect to subset analyses and the primary outcome.

Conclusions

This study found that the prevalence of AKI at the MNH-ICU was 58% (135/233). Mortality among those with AKI was 94.1% (127/135) while the overall cause mortality of the study patients during the four year study period was 47.6%. Need for mechanical ventilation was found to be significantly associated with increased risk of mortality among our study patients. Among patients with AKI, sepsis and septic shock, 67.4% and 15.5% respectively, were the most common underlying diagnoses recorded by the ICU clinicians.

Recommendations

- Active screening of all ICU patients for renal function with intensive monitoring during the patient's stay in ICU.

- A larger and prospective study is recommended to evaluate AKI in the ICU with a follow up plan of the patients.

- Further prospective studies needed to evaluate the relationship between mechanical ventilation and AKI in a low income setting like Tanzania.

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Building Note (HBN) 27. 1970

Appendices

APPENDIX 1: SURVEY FORM

STUDY TITLE: PREVALENCE AND OUTCOME OF ACUTE KIDNEY INJURY IN THE

INTENSIVE CARE UNIT AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM,

TANZANIA

Study Number: ……………   Hospital Number: …………………………….
Hospital admission date: ……../………./……….
Date of Admission to ICU:……/………/………
Date of discharge/death: ……/…………./……….
Time from hospital admission to ICU admission: ………… days
Duration of stay in ICU…………………days
Nature of patient (tick): (i). Medical:…….   (ii). Surgical:……..
Outcome in ICU (tick): (i). Discharge: (ii). Death: ……………..
If Death, possible cause(s) of death at ICU
………………………….
………………………….
SOCIO-DEMOGRAPHIC DATA
Age (complete years): ……………

Sex: 1. Male (   )   2. Female (   )

Address: …………….   Phone contact(s) ………………. ……………………

Marital status (choose one);
1. Married (   )   2. Widowed (   )   3. Divorced (   )   4. Single (   )

Educational level. 1. None (   )   2. Primary (   )   3. Secondary (   )   4. University (   )

CLINICAL BACKGROUND
Admission to ICU complaint(s);
…………………………………

……………………………………..
Duration of complaint(s)…………………….. (days)
Co-morbidities

Co-morbidity	Yes	No
Hypertension		
Diabetes mellitus		
Dyslipideamia		
Chronic kidney disease		
Malignancy		
HIV infection		
Liver disease		
Chronic obstructive pulmonary disease (COPD)		
Others		

Admission to ICU vital signs
Blood pressure…………..mmHg,   Respiratory rate………….breaths/minute
Pulse rate   ……………..beats/minute,   Oxygen saturation ………….
LABORATORY DATA

Parameter	Baseline	48hours post admission	1 week post admission
SCr (mg/dl)			
Urea (mg/dl)			
Na^+ (mmol/l)			
K^+ (mmol/l)			
Cl^- (mmol/l)			
Hb (g/dl)			
Plt			
WCC			
PCO_2			
HCO_3^-			

Urine output
At admission: ………………..mls   6 hours: ………………………mls
12 hours: ……………………...mls 2   4 hours: ……………………….mls

Probable cause (s) of AKI: ………………, …………………,
…………………………..
AKIN stage: 1………... 2…………. 3 ………………
LIFE SUPPORT PROCEDURE(S)

PROCEDURE	Yes	No	Duration in days
Mechanical ventivation			
Renal replacement therapy (hemodialysis)			
Vasopressor support			

AKI diagnosis: Yes (   )   No (   )

Final diagnosis at ICU:
…………………………

APPENDIX 2: WAIVER OF CONSENT

Request for Waiver of informed consent

Study title: Prevalence and outcome of acute kidney injury in the intensive care unit at Muhimbili National Hospital, Dar es Salaam.

My name is Gyaviira Makanga, a post graduate student in the department of Internal medicine at Muhimbili University of Health and Allied Sciences.

As part of the training, am required to conduct a research which will be a retrospective chart review of patients admitted to the intensive care unit at Muhimbili National hospital from January 2009 through December 2012.

My research will involve no more than minimal risk to the study subject and the request for the waiver of informed consent will not affect the rights of the subjects as we will have no contact with the patients but rather their medical charts.

All records of the study subjects as obtained from their respective medical charts will be kept confidential and for only the use of this research.

I therefore request for a waiver of informed consent to carry out this study to fulfill the partial requirement of my Masters degree.

My contact during the study period will be via;

Telephone: +255 784135234

Email: gmakanga2000@gmail.com

Gyaviira Makanga