



St. Paul Hospital Millennium Medical College

Graduate Study Program

**Prevalence of Acute Kidney Injury and associated factors among
Patients Admitted to the Medical Ward of St. Paul's Hospital
Millennium Medical College, Ethiopia.**

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Abbreviation

ACEI/ARB: Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker

AKI: Acute Kidney Injury

AKIN: Acute Kidney Injury Network

APACHE: Acute Physiology And Chronic Health Evaluation

CKD: Chronic Kidney Disease

CNS: Central Nervous System

DVT: Deep Vein Thrombosis

EPO: Erythropoietin

GFR: Glomerular Filtration Rate

GI: Gastrointestinal

HIV: Human Immunodeficiency Virus

ICU: Intensive Care Unit

KDIGO: Kidney Disease: Improving Global Outcomes

PE: Pulmonary Embolism

PPI: Proton Pump Inhibitor

SAPS 3: Simplified Acute Physiologic Score 3

SOFA: Sequential Organ Failure Assessment

SPHMMC: St. Paul's Hospital Millennium Medical College

SPSS: Statistical Product and Service Solutions

TB: Tuberculosis

WBC: White Blood Cell

QSOFA: Quick Sequential Organ Failure Assessment

List of tables

Table 1: Sample size calculation using Epi Info

Table 2: Socio –demographic and Clinical Characteristics of study participants, Addis Ababa, Ethiopia, 2022

Table 3: Diagnosis of patients at admission and medications of the study population Addis Ababa, Ethiopia, 2022 (N=341)

Table 4: Factors associated with AKI among patients admitted to the medical ward, Addis Ababa, Ethiopia, 2022

List of figures

Figure 1: Conceptual framework of risk factors for developing AKI adopted from a UK study published in May, 2017

Figure 2: Prevalence of AKI among the study population Addis Ababa, Ethiopia, 2022 (N=341)

List of annexes

Annex 1: Consent form

Annex 2: Data abstraction tool

Table of Contents

Acknowledgments.....	II
Abbreviation	III
List of tables.....	IV
List of figures.....	IV
List of annexes	IV
Abstract	1
1. Introduction.....	3
1.1. Background.....	3
1.2. Statement of the problem.....	5
1.3. Rationale of the study	6
2. Literature review	7
2.1. Definition of acute kidney injury.....	7
2.2. Prevalence of AKI.....	8
2.3. Risk factors and outcome of AKI	10
3. Conceptual framework.....	12
4. Objectives	13
4.1. General objectives.....	13
4.2. Specific objectives	13
5. Methodology	14
5.1. Study area and period.....	14
5.2. Study design.....	14
5.3. Population	14
5.3.1. Source population	14
5.3.2. Study population	14
5.3.3. Inclusion and exclusion criteria	14
5.4. Sample size determination and sampling technique	15
5.4.1. Sample size determination	15
5.4.2. Sampling technique.....	15
5.5. Variables of the study	16
5.5.1. Dependent variable	16

5.5.2. Independent variables	16
5.6 . Operational definitions	17
5.7. Data collection procedures.....	17
5.8. Data quality assurance	17
5.9. Data Management and Data Analysis.....	18
5.10. Ethical Considerations	18
6 Result	19
6.1 Demographic and Clinical Characteristics of study participants.....	19
6.2 Prevalence of AKI and outcome	21
6.3 Factors associated with AKI.....	22
7. Discussion	24
7. Strength and Limitation of the study	26
7.1 Strengths	26
7.2 Limitations	27
8. Conclusion	27
9. Recommendation	27
10. Reference	28
Annex 1	33
Information Sheet.....	33
Annex 2.....	34
Data collection tool	34
Annex 3.....	36
Declaration.....	36

Abstract

Introduction: Acute kidney injury (AKI) is the acute decrease in kidney function usually within hours due to damage to the structure or functional capability. There is a clear lack of data in the prevalence of AKI in Sub Saharan African countries. This holds true in Ethiopia also. Most of the studies done are in intensive care unit (ICU) patients and there is especially data lacking in the prevalence of AKI in patients admitted to the medical ward and their outcome. Furthermore the importance of this study is amplified as it is conducted in a setting where the services for treatment of kidney disease is the most optimal in the country.

Objective: To assess the prevalence of AKI and associated factors among patients admitted to the medical ward of St. Paul's Millennium Medical College in Ethiopia from July 2019 to December 2021.

Methodology: A retrospective chart review study was conducted among a total of 341 systematically selected patients admitted to the medical ward from July 2019 to December 2021. Data was collected from patient's chart using a structured data collection tool the data was analyzed using SPSS software version 25. Descriptive statistics was computed and presented with frequency tables and measures of central tendency. Bivariable and multivariable logistic regression analysis was used to test the association between the independent variables and the outcome variable. Those variables with $P < 0.05$ at a 95% confidence interval were considered as statistically significant.

Result: The overall prevalence of AKI was 36.4%. Factors that affected the prevalence of AKI were hypertension (AOR=1.903, 95% CI 1.019, 3.554) sepsis (AOR=2.672 95% CI 1.207, 5.915) diuretics use (AOR= 4.755 95% CI 2.730, 8.284) hemoglobin (AOR=2.413 95% CI 1.346, 4.328) and potassium (AOR= 2.030 95% CI 1.117, 3.688).

Conclusion & Recommendation: Prevalence of AKI was high among patients admitted to the medical ward of St. Paul's Hospital Millennium Medical College as compared to other studies done in Ethiopia and elsewhere. The study showed that hypertension, sepsis, diuretics, hemoglobin and potassium value derangements were significantly associated with AKI. This study contributes to the better characterization of AKI and its risk factors in non-critical, medical ward admitted patients. Clinicians should be vigilant to identify patients with the above

significant factors as these patients are at higher odds of having AKI. With a prevalence of AKI this high, there is a need for additional research aimed at further characterization of risk factors for AKI to better predict the risk of AKI.

Key words: Acute Kidney Injury, St. Paul's Hospital Millennium Medical College, Ethiopia

1. Introduction

1.1. Background

Acute kidney injury (AKI) is the acute decrease in kidney function usually within hours due to damage to the structure or functional capability (1). AKI is not a specific disease entity but a manifestation of renal injury due to a mixture of etiologies, each etiology contributing to the impairment in renal function. As the causes of AKI can be multiple it is simpler to classify it anatomically as pre renal, intrinsic or renal, and post renal. As the name denotes pre renal and post renal are extra renal causes and intrinsic is renal causes that affect the functional capability of the kidney (1). This functional capability is usually measured by the Glomerular Filtration Rate (GFR). Although there are several other functions that are performed by the kidneys like production of Erythropoietin (EPO), activation of vitamin D, ion and solute transport; GFR is the most useful measurement of kidney function (2)(3). GFR is the volume of plasma ultra-filtrate presented to the nephrons per unit time in the process of urine formation. This makes GFR the best clinical test for estimating functional renal mass enabling the physician to detect renal injury early and examine the progress and grade it (2). It can also be used to appropriately dose medications that have renal clearance once the GFR has stabilized. GFR can be directly measured by the clearance of exogenous filtration markers such as inulin and iohexol or calculated indirectly by the clearance of endogenous filtration markers like serum creatinine and cystatin C (3). The most extensively used approach in clinical practice and epidemiologic research is estimated GFR (eGFR), which is computed using serum creatinine and/or cystatin C. Direct measurements of GFR are cumbersome and are difficult to apply to clinical practice but are accurate and precise while indirect measurements are easy to collect and interpret as they are estimates of GFR but lack the accuracy and precision (3). But the indirect measurements are the mainstay of estimating GFR in clinical practice as well as epidemiologic research.

Based on this estimate of GFR and urine output AKI has been defined by different organizations so that there can be a consensus in the practice of medicine. Acute Kidney Injury Network (AKIN) has defined AKI as an increase in serum creatinine of greater or equal to 0.3 mg/dl or a 50% or greater increase in serum creatinine within 48 hours. It is also defined by a urine output of less than 0.5 ml/kg/hour for more than 6 hours. Kidney Disease: Improving Global Outcomes (KDIGO) has defined AKI as an increase in serum creatinine of 0.3 mg/dl or higher within 48

hours or 50% or more increase in serum creatinine within seven days. It has also defined it based on urine output as less than or equal to 0.5 ml/kg/ hour for more than 6 hours. These organizations have also put out a grading system for AKI based on the serum creatinine and urine output (4).

These definitions of AKI have been the backbone of epidemiologic and outcome studies as they have defined a common understanding of what is meant by AKI. But despite this there are several challenges when using these definitions for research. The changes in definition through the years as more understanding is gained, the need for a previous measurement of creatinine for the evaluation of AKI and the variation in intensity of evaluations of these investigations are some of the challenges faced when studying AKI(5). But despite these limitations it is still used and is an important source of information aiding pushing the sciences forward.

A meta-analysis that tried to study the incidence of AKI throughout the world found that the incidence of AKI in adults was 21.6%. The study also calculated AKI associated mortality from the pooled data and found that it was 23.9% in adults. One of the major drawbacks of the study was that even though it tried to estimate the incidence of AKI in the world, majority of the data that was used was from developed countries especially North America, Northern Europe and East Asia(6). A US based study that evaluated the incidence of AKI using changes in creatinine between 1996 and 2003 found that the non-dialysis requiring AKI had increased from 322.7 to 522.4 whereas that of dialysis-requiring AKI increased from 19.5 to 29.5 per 100 000 person-years (7).

In Sub Saharan Africa it is postulated that the burden on AKI is high and is an important contributor to morbidity and mortality. But the data that is available is small and the available data is from small and single center studies (8). A meta-analysis of 41 studies done in sub Saharan Africa found that about 70% of the patients presented with severe AKI requiring dialysis which is very high as compared to the world estimate for severe AKI at presentation (9).

There is limitation in the number of studies in Ethiopia with regards to AKI, especially in patients admitted to medical wards but a hospital based study done in Gondar found that the community acquired AKI accounted for 69.5% of cases which was consistent with other studies done in Sub Saharan Africa (10).

1.2. Statement of the problem

AKI is a major global public health problem which can occur both in the community setting and in the hospital setting (11). Globally it is found that over 13 million people are affected by AKI every year and AKI is responsible for 1.7 million deaths annually (5). The outcome of patients with AKI in low to middle income countries is alarming due to mainly lack of early recognition, late presentation of patients and low resources for the care of these patients (12,13). AKI commonly occurs in hospitalized patients and can be recognized by relatively small increase in concentration of creatinine in serum. A study done in university of Alabama on the incidence of AKI in admitted patients and its relation with mortality found that among 19,249 hospitalizations the incidence of AKI was 22.7%. The most common primary admitting diagnosis was circulatory problems and infections. There was a fourfold increase in mortality in the patients who had AKI (14). A study done in a tertiary referral hospital Cameroon prospectively evaluated 2402 patients and found that the incidence of AKI was 22.3% with the main causes for this was sepsis and volume depletion (15). The mortality rate associated with AKI was 36.9%. A prospective study done in the University of Gondar to assess the incidence of AKI in admitted patients found that about 20% of medical ward patients had developed AKI. It also found that the patients that developed AKI were younger than those documented in western studies (10). These studies show that AKI in admitted patients is a common occurrence and that it is associated with an increased mortality rate. It is also associated with poor patient outcome with regards to increases in length of hospital stay, progression to chronic kidney disease and costs. It therefore is important that patients with AKI, or those at risk of developing it, are recognized at the earliest opportunity following hospital admission and that early management is directed at minimizing the development of complications (16).

There is also clear lack of data in the prevalence of AKI in Sub Saharan African countries (8)(6). As to the author's knowledge this holds true in Ethiopia also as there are very few published studies on this issue (10). Most of the studies done are in intensive care unit (ICU) patients and there is especially data lacking in the prevalence of AKI in patients admitted to the medical ward and their outcome.

Hence the aim of this study is to assess the prevalence of AKI and associated factors in the medical ward of St. Paul's Millennium Medical College in Addis Ababa, Ethiopia

1.3. Rationale of the study

There have been many advances in the definition and management of AKI over the past decades. But despite this the inpatient mortality and morbidity caused by AKI remains high (13). Most of the studies regarding AKI, its prevalence, risk factors and outcome originate from developed countries and there is a gap in data from developing countries (12).

Different studies have identified important risk factors for development of AKI in hospitalized patients. A meta-analysis done to study the risk factors associated with the development of AKI in critically ill patients reviewed 31 studies that was from different countries had a cohort of 504,535 critically ill individuals from a variety of ICUs and found that the major risk factors seen that significantly increased the rates of AKI were older age, diabetes, hypertension, higher baseline creatinine, heart failure, sepsis/systemic inflammatory response syndrome, use of nephrotoxic drugs, higher severity of disease scores, use of vasopressors/inotropes, high risk surgery, emergency surgery, use of intra-aortic balloon pump, and longer time in cardiopulmonary bypass pump (17). A study done in china to assess the incidence, risk factors and outcome of AKI in hospitalized patients with atrial fibrillation found that atrial fibrillation on admission was 2.6 times higher than that in a patient with sinus rhythm. Age diuretics therapy before admission and lower baseline hemoglobin were significant risk factors for in hospital AKI (18). Another study in china tried to evaluate the epidemiology and risk factors for AKI in hospitalized patients across nine hospitals and found that the prevalence of hospital acquired AKI was 9.1% and community acquired was 2.5%. They also found that CKD was a major risk factor for both. Drug related AKI accounted for 40% of the AKI which was the major risk factor identified (19). These studies highlight that there are different risk factors for AKI in hospitalized patients and that the risk factors are somewhat different in different regions and in different hospitals. This underscores the importance of recognizing risk factors that play a major role in causing AKI and this will play a crucial role in identifying these risk factors in clinical settings and intervening early to bring about a better outcome for patients. This study will shed light on the risk factors and outcome of patients admitted to St. Paul's Hospital Millennium Medical College medical ward.

2. Literature review

2.1. Definition of acute kidney injury

AKI as a disease has been present since the beginning, but our understanding and framing of the disease has developed especially over the past 50 years. The earliest descriptions of disease of the kidneys have been with regards to pain and change in urine output. Increased urine output which had been labeled diabetes but decrease in urine output was not put into a category of disease but was considered a factor that was associated with worse outcome. The first description and differential for decreased urine was proposed by Galen around the third century by describing the problem as bladder distended decreased urine or not. If bladder was not distended Galen's differential were kidney stones, blood urine, tissue fragments and kidney infection. Kidney infection at this time meant that the kidney was injured or diseased not infection in the current term. It was in the eighteenth century the next stride in kidney disease took place when Giovanni Batista Morgagni described decreased urine or suppressed urine (ischuria) based on anatomy into ischuria vesicalis, ischuria ureterica, ischuria urethralis, and ischuria renalis. In the nineteenth century William Heberden and John Abercombie described the condition on ischuria with the clinical picture of acute renal failure which they described it as a sudden decrease in urine output that is followed by complete suspension of urine after wards followed by patient talking incoherently followed by stupor and coma around the fifth day. By the nineteenth century Richard Bright had described this disease as acute and chronic and further developed and described by William Osler in his book Text Book of Medicine. After the two world wars, where traumatic shock and oliguria were common, laid a foundation to the understanding of the function of the kidney and value of decreased blood supply to the kidney and injury to the kidney caused oliguria. This was named acute renal failure and subsequent studies all used this term. With the advent of dialysis in the twentieth century it was termed a treatable condition. This century also saw the description of the term chronic kidney disease, insult to the kidney lasting more than 3 months. Acute renal failure was changed to AKI because epidemiologic data clearly elucidated that kidney injury was a public health problem that is potentially preventable and treatable at earlier stages of the disease (20).

AKI is defined as refers to a sudden decrease in kidney function, resulting in the retention nitrogenous waste products and in the disturbance of extracellular volume and electrolytes.

Definitions of AKI are based on serum creatinine values and urine output. The Kidney Disease: Improving Global Outcomes (KDIGO) definition of AKI is the most widely accepted definition and is increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 micromol/L) within 48 hours, or increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior seven days, or urine volume < 0.5 mL/kg/hour for six hours. Any one of these criteria if met will define AKI. This is used in the clinical settings as well as in research (4). Based on the serum creatinine and urine output KDIGO has put out a staging system as stage 1 being an increase in serum creatinine to 1.5 to 1.9 times baseline, or increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 micromol/L), or reduction in urine output to < 0.5 mL/kg/hour for 6 to 12 hours. Stage 2 is an increase in serum creatinine to 2.0 to 2.9 times baseline, or reduction in urine output to < 0.5 mL/kg/hour for ≥ 12 hours. Stage 3 is an increase in serum creatinine to 3.0 times baseline, or increase in serum creatinine to ≥ 4.0 mg/dL (≥ 353.6 micromol/L), or reduction in urine output to < 0.3 mL/kg/hour for ≥ 24 hours, or anuria for ≥ 12 hours, or the initiation of kidney replacement therapy, or, in patients < 18 years, decrease in estimated glomerular filtration rate (eGFR) to < 35 mL/min/1.73 m² (4).

Although this definition and staging system has worked well in epidemiologic studies it is not without its shortcomings. This definition and staging does not take into account what the diagnosis of the patient is as AKI is not a disease entity by itself. In clinical practice the multiple etiologies causing AKI have different approaches and this definition does not incorporate this. This definition needs a baseline creatinine for comparison to see the increase in this biomarker making it one of the major limitations of using this definition. KDIGO have added that after defining and staging AKI the physician should make every attempt to diagnose the underlying cause of the AKI and that the clinician should always use caution when interpreting the biomarker creatinine as it could vary due to different conditions. Despite these, this definition is still very important and is being used as a standard to practice and has shown strong association with its staging being proportional to the severity of AKI, odds of mortality and remains remarkably consistent across every clinical condition and environment in which it has been studied (4,5).

2.2. Prevalence of AKI

Using the current definition of AKI and its common understanding (standardization) has aided in epidemiological studies that have analyzed the magnitude of this condition. A study that tried to

assess the world incidence of AKI and to describe geographic variations according to countries, regions, and their economies conducted a meta-analysis. The study included retrospective and prospective cohort studies that analyzed the incidence of AKI in both adults and children. It also included studies that tried to see the associated outcomes including the need for dialysis, recovery of renal function and mortality both in the hospital during admission or long term mortality. The study evaluated 312 papers which fulfilled eligibility criteria making the number of patients evaluated close to 50 million from over 40 countries worldwide. Most of these studies were from North and South America about 49% followed by Europe, Asia, Australia and New Zealand and Africa, highlighting the disproportionate representation of certain countries in the scientific literature. The studies mainly originated from high income countries, about 82.7%. Using this study the pooled rate of AKI was 10.7%. The study also saw that using the 154 studies that used KDIGO for the definition of AKI, the pooled rate of AKI was 23.2% and adult only pooled rate was 21.6%. The all-cause mortality rate was 23% and increased with higher stages of severity (6).

A hospital based study from the US had tried to analyze the incidence of AKI in patients that were hospitalized and the association of AKI with in patient mortality. The study found that the incidence of AKI was 22.7%. The study used the Acute Kidney Injury Network (AKIN) to identify AKI and to stage it. Based on this staging the incidence of stage1 was 15.8%, stage 2 2.7% and stage 3 was 4.2%. With regards to mortality rate it was 10.8% as compared to 1.5% for cases without AKI (14).

A retrospective cohort study from Sudan that analyzed the pattern and outcome of AKI among adults evaluated 6,769 patient medical records and had found that the incidence of AKI using the KDIGO definition was 5.7%. The major causes of AKI identified were sepsis, volume depletion, obstructive uropathy, heart failure, acute glomerulonephritis and severe malaria. Mortality rate was 31.2%. As compared to studies done in the west and a studies that tried to analyze prevalence of AKI in the world, this study showed a lower incidence of AKI, which is thought to be because of underrepresentation but is actually believed to be much higher, but the mortality rate is higher as compared to other studies done in high and middle income countries (21).

A study done in University of Gondar Hospital tried to investigating the prevalence, characteristics and impact of AKI in patients admitted to the hospital using the AKIN criteria.

The study noted that 32% of the patients admitted had no record of renal function tests and that majority of renal function tests were done in the medical ward of the hospital as opposed to the surgical ward. The study found that none of the patients in the surgical ward at the time of the study had renal function test derangement. In the medical ward the prevalence of AKI was 17.2%. The causes for renal impairment; from the most common etiology to the least common were sepsis, cardiac disease, obstetric complication and intrinsic renal disease which were pyelonephritis, post streptococcal glomerulonephritis, nephrotic syndrome and renal vein thrombosis. The study had also found in line with other studies done in developing countries that age was a major risk factor for AKI and that relative to other studies the ages of the patients was relatively young. The study also found that comorbidities like cardiac illness and hypertension were associated with AKI (10).

2.3. Risk factors and outcome of AKI

A multicenter prospective cohort study conducted in 17 Chinese ICUs from January 2014 to August 2015 showed Hypertension, sepsis, Coronary artery disease, SOFA score, APACHEII score, use of vasopressors, use of nephrotoxic drugs, chronic live disease were the factors associated with an increases risk of new onset AKI. The study concluded that new onset AKI is common in ICU patients and that it is associated with higher 28-day mortality. The study also revealed Persistent AKI (non-renal recovery within 48 hours) had strong association with the 28-day mortality while Transient AKI (renal recovery within 48 hours) which was more than half of the new onset AKI had no significant relationship with the 28-day mortality (22).

An observational prospective study conducted in South Africa, in Livingston Hospital ICU from January 3 2017 to January 3 2018 showed of 849 admissions, the most common admission which was trauma (26%), 58.5% of cases developed AKI. Independently associated factors to AKI were Vasopressor drugs, sepsis, length of stay, illness severity, male gender. Patients with AKI had a higher mortality rate of 31.8 % than those patients without AKI which was 7.23%. The rate of death had a significant increase in patients with active tuberculosis, sepsis, those on mechanical ventilation, vasopressor support, SAPS 3 score and increasing age. 12.7 % of patients with stage 3 AKI developed CKD which was not dialysis dependent (23).

A study done in Zimbabwe which included 253 patients to assess the risk factors for the development of AKI in hospitalized patients found that 14.2% of the patients had developed AKI

and that being male, having hypertension and chronic kidney disease were significant risk factors for the development of AKI in these hospitalized patients (24).

A study in Ethiopia assessing the risk factor recognition of AKI in three teaching hospitals; namely Addis Ababa University, College of Health Sciences Tikur Anbessa Hospital, Gondor University Hospital and Hawassa University Hospital; recruited 366 patients admitted to these hospitals and found that renal function tests were most frequently evaluated in the internal medicine department and that there was a significant relationship between patients having comorbidities and having their renal status checked while there was not a significant relation found between the use of nephrotoxic medication and evaluation of renal status. The authors concluded that there was a variability in which physicians recognized the presence or risk factors for the development of AKI and that failure to identify these risk factors represent a lost opportunity to identify patients at high risk of developing renal injury (25).

A study from Jimma which tried to evaluate the clinical characteristics and outcome of 160 AKI patients who were hospitalized used a prospective observational study. The study involved all adult patients with the diagnosis of AKI admitted in Jimma Medical Center. The researchers found that the most common cause of AKI was hypovolemia followed by sepsis and pyelonephritis. 85% of the study participants had prolonged hospital stay which was defined by the study to be more than 7 days. They found that the presence of AKI and its complications and prolonged AKI (AKI more than 7 days) were associated with prolonged hospital stay. They also found that the presence of preexisting CKD and stage 3 AKI were significantly associated with 30 day readmission. Other outcomes of the study were renal replacement therapy in 7% of the patients, hospital mortality in 6% of the patients and renal recovery in 75% of the patients at discharge (26).

3. Conceptual framework

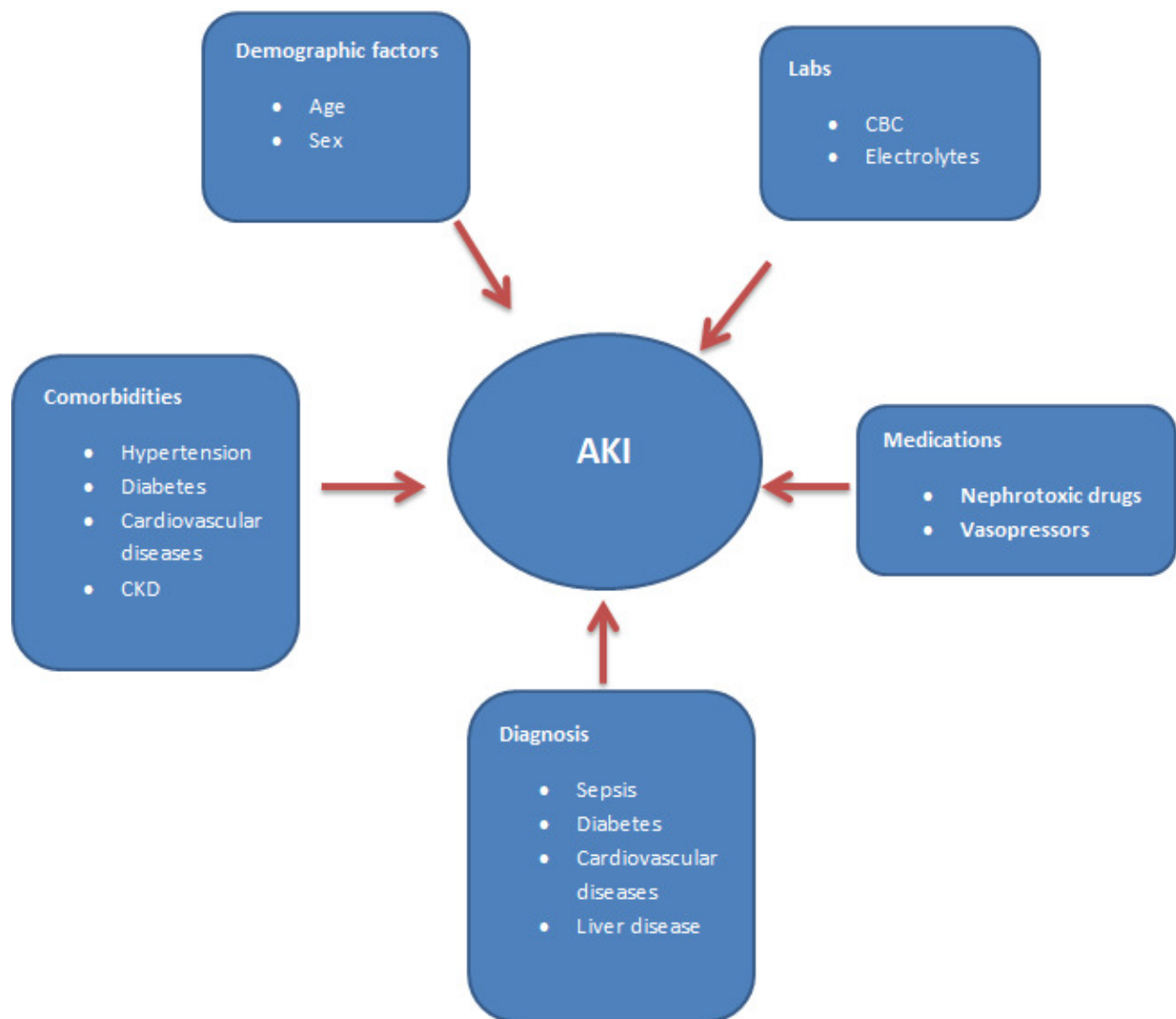


Fig. 1 Conceptual framework of risk factors for developing AKI is adopted from similar literatures (22,27,28)

4. Objectives

4.1. General objectives

To assess the prevalence of AKI and its associated factors among patients admitted to medical ward of St. Paul's Millennium Medical College in Addis Ababa, Ethiopia, from July 2019 to December 2021.

4.2. Specific objectives

To determine the prevalence of AKI among patients admitted to medical ward of St. Paul's Hospital Millennium Medical College.

To identify factors associated with the development of AKI in patients admitted to the medical ward of St. Paul's Hospital Millennium Medical College.

5. Methodology

5.1. Study area and period

The study was conducted from September 10, 2022 –September 30, 2022 at St. Paul’s Hospital Millennium medical college (SPHMMC) in Addis Ababa, Ethiopia. It is a federal hospital that was initially established in 1968 by Emperor Haileselasie but since 2008 have been reestablished as a medical college giving both undergraduate and postgraduate programs. The hospital is one of the biggest hospitals in the country treating an average of about 1200 patients daily as emergency and outpatients. It has over 700 beds for inpatient treatment. Of these the medical ward has 47 beds. The medical ward admits around 840 patients per year. St. Paul’s Hospital is also the only hospital in the country with a renal transplant unit.

5.2. Study design

A retrospective chart review study design was used for this study. Medical records and charts of patients admitted to the medical wards from July, 2019 to December, 2021 were reviewed.

5.3. Population

5.3.1. Source population

All patients admitted to the medical wards from July, 2019 to December, 2021 at St. Paul’s Hospital Millennium Medical College.

5.3.2. Study population

Patients admitted to St. Paul’s Hospital Millennium Medical College who are selected by using systematic sampling who fulfill the inclusion criteria.

5.3.3. Inclusion and exclusion criteria

5.3.3.1. Inclusion criteria

All patients admitted for more than 24 hours

Patients without diagnosed end stage renal disease (ESRD) on dialysis

5.4. Sample size determination and sampling technique

5.4.1. Sample size determination

The sample size for the descriptive objective was determined by using single population proportion formula. Prevalence was calculated from a similar study done in University of Gondor.

$$n = (Z \alpha/2)^2 p (1-p) / d^2$$

Where: -

n = is calculated sample size

Z = statistic corresponding to level of confidence [95%] is 1.96

p = prevalence AKI in patients admitted to the medical ward 17.2%(10)

d = precision 0.05

$$n = (1.96)^2 \times 0.172 [1-0.172] / 0.05^2 = 218.842$$

The sample size for the inferential objective or the associated factor is calculated using Epi Info

Table 1: Sample size calculation using Epi Info (16)

	Factors	Power	Confidence level	Odds ratio	% of controls exposed	% of cases exposed	Total sample size
1	Diabetes	80%	95%	2.562	18	36	277
2	CKD	80%	95%	3.709	18.8	46.2	130
3	Sepsis	80%	95%	3.493	18%	43.4	146

Based on these calculations the largest sample size calculated was 277. With the addition of 25% non-response, the final sample size is 347.

5.4.2. Sampling technique

To select the study participants to be included in the study, a systematic random sampling technique was used. Patients admitted to the medical ward in the past year was listed and found to be 760. Then it was divided by 347 to determine the K.

$$K = 760/347 = 2.19$$

Accordingly, every 2nd patient was part of the study population.

5.5. Variables of the study

5.5.1. Dependent variable

Acute kidney injury (AKI)

5.5.2. Independent variables

Demographic variables

Age

Sex

Patient's co morbidity

Patient's admission diagnosis

Patient's medications

Laboratory values

Admission white blood cell (WBC) count

Admission hemoglobin

Admission serum sodium

Admission serum potassium

Admission serum chloride

Admission random blood sugar

5.6. Operational definitions

Base line creatinine: The biochemical measurement of creatinine that is the lowest, most recent, or the median value over the preadmission period. (29)

AKI: based on KDGO definition, increase in serum creatinine by ≥ 0.3 mg/dl within 48 hours or increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the previous 7 days. (30)

AKI recovered: Return of creatinine to normal range or return of creatinine to baseline.

5.7. Data collection procedures

Pretested data abstraction tool that consisted of all the relevant variables was developed and used to collect the necessary data from patient's medical chart and registers. The data collected was written in English language and contained age, sex, patient's co morbidity, patient's admission diagnosis, patient's medications, base line creatinine, lab results, diagnosis of sepsis and outcome. Training on how to use the data collection tool was given by the principal investigator for the designated data collectors for one day, on September 8, 2022. Data was then collected from September 10- 20, 2022 by trained doctors. The collected data was checked for its consistency and completeness by principal investigator before any attempt to enter code and analyze it.

5.8. Data quality assurance

The data was collected at St. Paul's Hospital Millennium Medical College starting from September 10, 2022. Data collection tool was pretested on 5% of randomly selected patient chart and documentation after which necessary amendment to the data collection tool was made. Any irregularities were rechecked by the principal investigator. Before the start of data collection there was a day long training session for the data collectors on the components of data collection tool and how to enter it on Google forms. During the data collection there was daily supervision by the supervisors and the principal investigator. The collected data was then checked for its consistency and completeness before any attempt to enter code and analyze it.

5.9. Data Management and Data Analysis

The data collected using the data collection tool prepared using Google Forms. Data was transferred to Google Sheets; it was cleaned and exported to Statistical Product and Service Solutions (SPSS) version 25 for coding and analysis. Descriptive statistics was computed and presented using frequencies, percentages and measures of central tendency. The association between the independent variables and AKI was analyzed using binary logistic regression model. Univariable binary logistic regression was run at 25% level of significance to screen out potentially significant independent variables. Multivariable binary logistic regression model was run by including the significant independent variables from the Univariable binary logistic regression model. To measure the presence and strength of association between the independent variables and AKI adjusted odds ratio (AOR), P-value of 95% CI for AOR was used. For the final model, variables with p-value ≤ 0.05 were considered to be significantly associated with AKI.

The basic assumption of binary logistic regression model, multicollinearity and outlier were checked using variance inflation factor and box-plot respectively. The VIF value for all numeric independent variables are <10 (1.217, 1.108, 1.270, 1.095, 2.043 and 1.084) satisfying the no multicollinearity assumption. Finally, the multivariable binary logistic regression model was tested for model adequacy using Hosmer and Lemeshow test for AKI result analysis and showed a good fit to the data at p-value of 0.773.

5.10. Ethical Considerations

The study was conducted after obtaining ethical clearance from St. Paul's Hospital Millennium Medical College Review Board. Medical record number was used for the data collection and patient identities was not be used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the study.

6 Result

6.1 Demographic and Clinical Characteristics of study participants

A total of 341 clients were enrolled in this study with mean age of 46.2 ($\pm$ SD =18.3). Out of these participants, majority of the clients were young adults ranging from 12-39 years of age which accounted for 138 (40.5%) and males accounting for 186(54.5%). From the study 226 (66.3%) participants had one or more comorbidities. The majority had hypertension (46%) followed by type 2 diabetes mellitus (19.1%). Chronic lung disease and cardiovascular comorbidities which accounted for 27(7.9%) and 21(6.2%) respectively were combined as cardiopulmonary comorbidities. Comorbidities such as cerebrovascular diseases, malignancy, Connective tissue disease and autoimmune disease which accounted for 5 (1.5%), 12(3.5%), 6 (1.7%) respectively were categorized under other comorbidities.

The most common cause of admission was pneumonia (34.9%) and heart failure (23.2%). Admission diagnosis such as GI infection, upper GI bleeding and gastric/duodenal ulcer which accounted for 13(3.8%), 11 (3.2%) and 7 (2.1%) respectively were categorized under GI luminal disease. Hematologic diseases (17(5%)) and deep vein thrombosis (DVT) / pulmonary embolism (PE)/ Hypercoagulable states (46 (13.5%)) were categorized under Hematologic diseases while CNS infections (19(5.6%)) and stroke (33(9.7%)) were categorized under CNS diseases. Malignancy, COPD, genitourinary infections, obstetric complications, connective tissue disease and autoimmune disease which accounted for 5 (1.5%), 10 (2.9%) 5 (1.5%), 16 (4.7%), 2 (0.6%), and 8 (2.3%) respectively were categorized under other diagnosis.

During admission patients were taking or started on cephalosporin (77%), antihypertensive medications (41.6%) and diuretics (41.3%). In the study; from the lab results at admission the median WBC was 8,300/mcl (IQR=5.45), median hemoglobin was 13 mg/dl (IQR=4.23), median serum sodium was 137mEq/l (IQR=8.0), median serum potassium was 4.1mEq/l (IQR=1.20), median serum chloride was 98mEq/l (IQR=9.75) and median random blood sugar (RBS) was 120 mg/dl (IQR=42).

Table 2: Socio-demographic and Clinical Characteristics of the study population, Addis Ababa, Ethiopia, 2022 (N=341)

Variables	Frequency	Percentage
Age in groups		
12-39 years	138	40.5%
40-59 years	105	30.8%
>60 years	98	28.7%
Sex		
Male	186	54.5%
Female	155	45.5%
Comorbidities		
Hypertension	157	46%
Diabetes	65	19%
CKD	19	5.6%
HIV	17	5%
Cardiopulmonary Diseases	46	13.5%
Psychiatric Condition	18	5.3%
Other Comorbidities	23	6.7%
Admission Diagnosis		
Sepsis	44	12.9%
Heart failure	79	23.2%
Pneumonia	119	34.9%
TB	26	7.6%
Hepatitis	25	7.3%
GI luminal disease	26	7.6%
CNS diseases	52	15.2%
Hematologic diseases	62	18.2%
Other diagnosis	46	13.5%
Medications during admission		
Cephalosporin	2265	77%

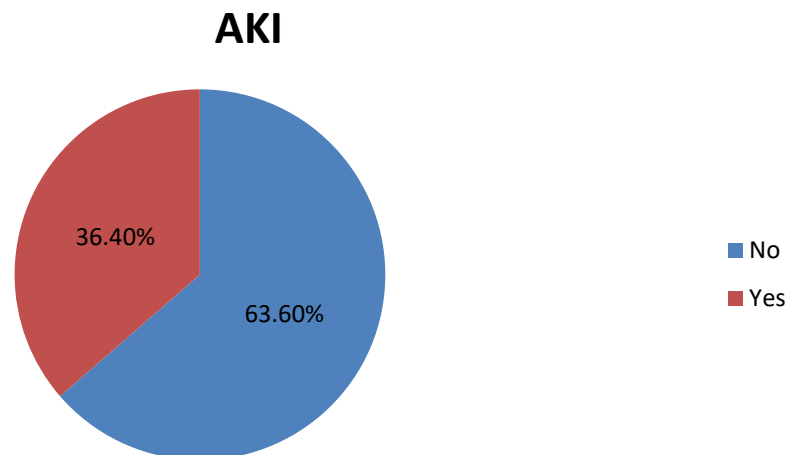
Macrolides	48	14.4%
Vancomycin	135	39.6%
Anti TB	31	9.1%
Other antibiotics*	111	32.6%
Antihypertensive	142	41.6%
Antiplatelet	20	5.9%
PPIs	213	62.5%
Anticoagulants	182	53.4%
Steroids	104	30.5%

*other antibiotics include Penicillin, Aminoglycoside, Metronidazole, Quinolone, Imipenem, Carbapenem,

6.2 Prevalence of AKI and outcome

Over all prevalence of AKI was 36.4% (124), of these 100 (80.6%) patients had community acquired AKI and 24 (19.4%) had hospital acquired AKI. Mean creatinine among patients with AKI was 3.8 ($\pm$ SD =3.5) compared to patients without AKI which was 0.67 ($\pm$ SD =0.20). Among the study participants, majority were discharged improved 173 (50.7%) and 41(12%) patients died. Among patients with AKI, 51 (41.1%) were discharged after full recovery from their kidney injury.

Figure 2: Prevalence of AKI among the study population Addis Ababa, Ethiopia, 2022 (N=341)



6.3 Factors associated with AKI

Univariable analysis at 25% level of significance was run to select to fit into the multivariable binary logistic regression model and the following variables were found to be significant; hypertension, diabetes mellitus, sepsis, pneumonia, hematologic diseases, cephalosporin, macrolides, diuretics, ACEI/ARBs, anticoagulants, steroids, WBC count, hemoglobin, serum sodium, serum potassium, serum chloride and random blood sugar.

On the multivariable binary logistic regression model; after adjusting for other covariates; Hypertension as a comorbidity, cardiopulmonary diseases, sepsis, pneumonia, hematologic diseases, diuretics, hemoglobin and potassium were found to have statistically significant relationship with AKI at a 5% level of significance.

The study showed that in patients with hypertension the odds of AKI was 2.11 times higher as compared to those who did not have hypertension (AOR=1.903, 95% CI 1.019,3.554). The odds of AKI was also 2.67 times higher in among patients diagnosed to have sepsis as compared to those who did not have sepsis (AOR=2.672 95% CI 1.207,5.915). The study also showed that patient taking diuretics had 4.75 times higher odds of having AKI as compared to patients that were not taking diuretics (AOR= 4.755 95% CI 2.730,8.284). In patients that had abnormal hemoglobin the odds of AKI was 2.64 times higher than those who had normal hemoglobin (AOR=2.413 95% CI 1.346,4.328). The odd of AKI was also 2.03 times higher in those who had abnormal potassium as compared to those with normal potassium (AOR=2.030 95% CI 1.117, 3.688). In addition to this the study found a significant relationship with pneumonia and hematologic diseases showing reduced odds of AKI in those having the conditions as compared to those who do not (AOR=0.364 95% CI 0.162,0.818) for pneumonia and (AOR=0.432 95% CI 0.226,0.825) for hematologic disease respectively.

Table 4: Factors associated with AKI among patients admitted to the medical ward, Addis Ababa, Ethiopia, 2022 (N=341)

Variables	Does patient have AKI?		COR (95% CI)	AOR (95% CI)	P-Value
	No (n=217)	Yes (n=124)			
Age in years					
12-39	87	51			
40-59	70	35	0.853 (0.501,1.453)	0.854 (0.423,1.723)	0.659
Above 60	60	38	1.080 (0.634,1.842)	1.068 (0.502,2.270)	0.865
Hypertension					
No	134	50			
Yes	83	74	2.389 (1.522,3.752)	1.903 (1.019,3.554)	0.044*
Diabetes Mellitus					
No	179	97			
Yes	38	27	1.311 (0.755,2.277)	1.032 (0.494,2.158)	0.933
Sepsis					
No	196	101			
Yes	21	23	2.125 (0.122,4.024)	2.672 (1.207,5.915)	0.015*
Pneumonia					
No	130	92			
Yes	87	32	0.520 (0.320,0.844)	0.432 (0.226,0.825)	0.011*
Hematologic diseases					
No	167	112			
Yes	50	12	0.358 (0.182,0.702)	0.364 (0.162,0.818)	0.014*
Cephalosporin					
No	54	22			
Yes	163	102	1.536 (0.883,2.673)	1.290 (0.620,2.684)	0.496
Macrolides					
No	169	106			
Yes	48	18	0.598 (0.330,1.083)	0.571 (0.278,1.172)	0.127
Diuretics					
No	158	42			
Yes	59	82	5.228 (3.244,8.426)	4.755 (2.730,8.284)	0.000*
ACEI/ARBs					
No	177	89			
Yes	40	35	1.740 (1.034,2.928)	1.753(0.876,3.507)	0.113
Anticoagulants					
No	96	63			
Yes	121	61	0.768 (0.494,1.196)	0.892 (0.512,1.556)	0.688
Steroids					
No	158	79			
Yes	59	45	1.525 (0.951,2.447)	1.695 (0.927,3.100)	0.087

WBC count					
Normal	139	73			
Abnormal	78	51	1.245 (0.792,1.958)	1.127(0.642,1.980)	0.676
Hemoglobin					
Normal	100	34			
Abnormal	117	90	2.262 (1.405,3.643)	2.413(1.346,4.328)	0.003*
Serum Sodium					
Normal	143	60			
Abnormal	74	64	2.061 (1.314,3.234)	1.354 (0.763,2.403)	0.300
Serum Potassium					
Normal	167	79			
Abnormal	50	45	1.903 (1.173,3.086)	2.030 (1.117,3.688)	0.020*
Serum Chloride					
Normal	135	57			
Abnormal	82	67	1.935 (1.237,3.027)	1.415 (0.791,2.530)	0.242
RBS					
Normal	90	45			
Abnormal	127	79	1.244 (0.789,1.961)	1.628 (0.911,2.909)	0.100

7. Discussion

The study aimed to assess the prevalence of AKI and associated factors in the medical ward of St. Paul's Millennium Medical College in Addis Ababa. Using a hospital based retrospective chart review the study found that the prevalence of AKI was 36.4%.

The standardization with regards to defining what AKI is has brought forth a common understanding and greatly aided in studies that analyze its epidemiologic significance (4). Using the KDIGO definition this study has found the prevalence of AKI in medical ward patients, non-critical care patients, to be 36.4%. Although studies have shown that there are differences in the prevalence of AKI in different regions of the world depending on different factors especially socio-economic status, the prevalence of AKI in this study is high (6). A meta-analysis that evaluated 312 papers and close to 50 million patients from over 40 countries had found the pooled rate of AKI to be 23.2% which is lower as compared to this study (6). In the same study when the rate of AKI was classified based on economic status as low, middle and high income, low income pooled rate of AKI was 38.1 which is comparable to this study (6). A study done in University of Gondar Hospital found the prevalence of AKI in medical ward patients to be 17.2% which is much lower than this study, which may be a reflection of SPHMMC being one

of the largest referral centers in the country and having one of the largest nephrology units in the country (10).

Study also showed that hypertension, sepsis, pneumonia, hematologic diseases, diuretics, hemoglobin and potassium were factors that were significantly associated with AKI. This study showed that in patients with hypertension the odds of AKI were 1.9 times higher as compared to those who did not have hypertension. Hypertension is a known a recognized risk factor for AKI, and this has been demonstrated in different studies including studies done in Africa (22,24). For instance hypertension was said to increase the odds of AKI by 3.2 fold as compared to those without hypertension in a study done in Zimbabwe assessing the risk factors for development of AKI in hospitalized patients (24). It is important to keep in mind that hypertension is seen in patients with AKI and studies have shown AKI to be a factor in the development of hypertension (31,32). But this study was not designed to differentiate between hypertension as a risk factor for AKI or vice versa.

This study also showed that patients that were diagnosed with sepsis were at higher odds of developing AKI, 2.67 times higher, as compared to those without sepsis. This finding was consistent with previous findings (22,23,26). For instance a study that aimed to identify risk factors for AKI in critically ill patients found that the septic patients had 2.57 times higher odds of developing AKI as compared with non-septic patients which is comparable with this study (22).

This study also found that patients who were on diuretics were associated with 4.75 times higher odds of having AKI as compared with those that were not taking diuretics. A study out of china tried to assess the association between the use of diuretics and AKI, specifically hospital acquired AKI and found that the rate of AKI among patients taking loop diuretics was 1.61 times higher than those that were not on diuretics and among patients taking other diuretics rate of AKI was 1.09 times higher than those not on these diuretics (33). But interpretation of this study's result must be tempered with the knowledge that diuretics, which increase urine output, are commonly prescribed as part of the management of AKI (33,34).

Among patients with deranged hemoglobin and the electrolyte potassium, a significant association was found with AKI. The odds of having AKI were 2.41 times higher in those with

deranged hemoglobin as compared with patients with normal hemoglobin values. The contribution of deranged hemoglobin especially anemia to AKI is likely multifactorial ranging from these patients having subclinical renal disease which increases the chances of renal disease to the presence of low hemoglobin predisposing to renal hypoxia and oxidative stress (35,36). A study assessing anemia and AKI found that the odds of having AKI was 1.5 times higher in those who were anemic than those that were not and the study also showed that the severity of anemia correlated with the AKI requiring renal replacement therapy (37). With regards to potassium, the odds of having AKI were 2.03 times higher in those with deranged potassium as compared with patients with normal potassium values. This finding is consistent with the knowledge that patients with AKI are associated with impaired potassium homeostasis (38).

This study also showed a significant association with pneumonia and hematologic disease, although not the expected association as patients with these diseases were at lower odds of AKI than those that did not have them. Other studies do not support this; a study assessing the relationship between pneumonia, specifically pneumococcal pneumonia, and AKI found that there was a 1.1 fold increased risk of developing AKI compared with a comparison cohort (39). Another study showed that even in patients diagnosed with non-severe pneumonia, 25% had developed acute kidney injury. But in both studies the patients with AKI were older and had more comorbidity as compared to this study's patients with pneumonia (40). With regards to hematologic disease, most of the patients in this category are young (<39 years) and only few had comorbidities or electrolyte disturbances.

7. Strength and Limitation of the study

7.1 Strengths

- The study of AKI in ward setting, noncritical care setting, is limited in sub-Saharan countries. More so there is no published study assessing the prevalence and associated factors in a tertiary center where there is a comprehensive renal treatment center in Ethiopia.
- The study involved patients admitted over the past two years to the medical ward of SPHMMC.

7.2 Limitations

- Since the study was based on chart review several social and behavioral factors such as smoking, alcohol intake, illicit drug use and dietary habits could not be explored, which could better characterize the findings of the study.
- Factors such as hypertension, which is a known factor for AKI at the same time AKI being a factor for the development of hypertension, could not be further explored in this study due to its design.

8. Conclusion

Prevalence of AKI was high among patients admitted the medical ward of St. Paul's Hospital Millennium Medical College as compared to other studies done in Ethiopia and elsewhere. The study showed that hypertension, sepsis, diuretics, hemoglobin and potassium value derangements were significantly associated with AKI. This study contributes to the better characterization of AKI and its risk factors in non-critical, medical ward admitted patients.

9. Recommendation

- Clinicians should be vigilant to identify patients with the above significant factors as these patients are at higher odds of having AKI.
- With a prevalence of AKI this high, there is a need for additional research aimed at further characterization of risk factors for AKI to better predict the risk of AKI.

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Annex 1

Information Sheet

My name is Nahom Dessalegn working in St. Paul's Hospital Millennium Medical College. I am conducting a research on Risk Factors and Outcome of Acute Kidney Injury Patients Admitted to the Medical Ward of St. Paul's Hospital Millennium Medical College, Addis Ababa Ethiopia. The research will benefit patients as a whole as well as the hospitals to know the risk factors and outcomes of AKI in admitted patients and manage accordingly for better outcome.

For this reason I would like to ask a permission to conduct this research. I assure you that the name of the clients is not mentioned on the data collection tool and confidentiality will be kept.

Annex 2

Data collection tool

	Question	Response	
1	MRN		
2	Age		
3	Sex	Male	Female
	Comorbidity	Yes	No
4	Hypertension		
5	Diabetes		
6	CKD		
7	HIV		
8	Cardiovascular disease		
9	Chronic lung disease		
10	Cerebrovascular disease		
11	Malignancy		
12	Connective tissue disease		
13	Autoimmune disease		
14	Psychiatric condition		
15	Other co-morbidity		
	Admission Diagnosis	Yes	No
16	Sepsis		
17	Heart failure		
18	Pneumonia		
19	TB		
20	COPD		
21	Malignancy		
22	Hepatitis		
23	GU infection		
24	GI infection		
25	Upper GI bleeding		
26	Gastric / duodenal ulcer		
27	CNS infection		
28	Stroke		
29	DVT / PE / Hypercoagulable state		
30	Hematologic disease		
31	Obstetric complication		
32	Connective tissue disease		
33	Autoimmune disease		
	Medication patient is taking	Yes	No
34	Cephalosporin		
35	Penicillin		
36	Macrolides		
37	Quinolones		

38	Vancomycin		
39	Anti TB		
40	Other antibiotics		
41	Diuretics		
42	ACI / ARBs		
43	Antihypertensive		
44	Antiplatelet		
45	PPI		
46	Anticoagulants		
47	Steroids		
	Date of admission		
48	Day/month/year		
	Labs at admission		
49	WBC		
50	Hemoglobin		
51	Sodium		
52	Potassium		
53	Chloride		
54	RBS		
	Abdominal Ultrasound		
55	Creatinine		
56	Baseline creatinine		
	Creatinine nadir		
	AKI	Yes	No
57	Does the patient have AKI		
58	Date of AKI diagnosis dd/mm/yy		
	Out come	Yes	No
59	Died		
60	Discharged improved/		
61	AKI recovered		
62	Discharged without improvement /		
63	Discharged without full renal recovery		
64	Date of outcome dd/mm/yy		

Annex 3

Declaration

I the undersigned resident declare that this thesis is my original work, in partial fulfillment of the requirement for certificate of specialty in Internal Medicine. I also declare that it has never been presented in this or any other higher institution and all the resources and materials used in the research work have been duly acknowledged.

Name of the Resident: Dr. Nahom Dessalegn

Signature: _____

Date: _____

Approval of Advisors

This research work has been submitted for examination with my approval

Name of Public Health Advisor: Mrs. Fana Adugna

Signature: _____

Date: _____

Name of Clinical Advisor: Dr. Abel Mureja

Signature: _____

Date: _____