

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE
DEPARTMENT OF EMERGENCY MEDICINE AND CRITICAL CARE**



**CLINICAL PROFILE AND OUTCOME OF ACUTE
KIDNEY INJURY IN TIKUR ANBESSA SPECIALIZED
HOSPITAL, ADDIS ABABA, ETHIOPIA**

RESEARCH THESIS

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DOCTOR ADDISU MELKIE (INTERNIST, AND CONSULTANT NEPHROLOGIST)

A THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCE,
DEPARTMENT OF EMERGENCY AND CRITICAL CARE FOR THE PARTIAL FULFILLMENT OF
THE REQUIREMENT IN SPECIALITY PROGRAM.

August, 2019

Addis Ababa, Ethiopia

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Name of Advisor(s)	Professor Aklilu Azazh Dr. Sofia Kebede Dr. Addisu Melkie
Full title of the research project	Pattern and outcome of Acute Kidney Injury in Tikur Anbessa specialized hospital
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ABBREVIATION

AKI- Acute Kidney Injury
AKIN- Acute Kidney Injury Network
AOR- Adjusted odd's ratio
ATN- Acute Tubular Necrosis
AGN-Acute Glomerulonephritis
ARF- Acute renal failure
Ca.- Cancer
CI-Confidence interval
COR- Crude odd's ratio
Df- Degree of freedom
DNS- Dextrose in normal saline
KDIGO-Kidney Disease: Improving Global outcomes
LOS- Length of stay
NS- Normal saline
PI- Principal investigator
RL- Ringer's lactate
SD- Standard deviation
SE- Standard error
TASH- Tikur Anbessa Specialized Hospital
TLS-Tumor lysis syndrome
WBC- White blood Cells

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ABSTRACT

Background

Acute kidney injury (AKI) is a major health problem, causing morbidity in 13 million people annually, among which, 85% occur in developing countries. It is therefore one of important issue in Africa where there is resource limitation at large, and appreciation of its pattern can help understand it's causes, complications and outcome better which are determinants for its early prevention and management.

Objective

To evaluate Patterns and outcome of AKI patients who are admitted in Tikur Anbessa specialized hospital(TASH) Adult Emergency Unit, Addis Ababa, Ethiopia

Methodology

Prospective Crossectional study was done from August 1, 2018 to May 1, 2019.:The research was done at TASH adult ED. SPSS software version 25 was used for analysis. The area selected for this research was TASH adult emergency unit, Addis Ababa, Ethiopia where the sample was collected from the patients who fulfill the inclusion criteria. SPSS software was used for analysis. Binary logistic regression was done for identification of mortality predictors. Patients' laboratory results on admission and discharge were compared by paired samples T-test. Survival time was estimated by Kapan- Meier and log rank test with a 95% CI. A P-value of <0.05 was considered to denote statistical significance.

Result

A total of 144 cases of AKI were included in the study. The mean age of presentation at a younger age of 46.16 ± 16.6 . The most common causes of AKI were Sepsis (43.2%), volume depletion (25%), cardio renal syndrome-1(16%) and obstructive uropathy (16%). Uremic encephalopathy, sepsis and hyperkalemia were factors that were identified as mortality predictors in overall AKI patients. AKI patients with sepsis were found to have lower hospital survival than those without sepsis. From the laboratory findings, there was significant difference between creatinine values on admission and discharge.

Conclusion

As sepsis was the dominant cause of AKI as well as mortality predictor and cause of lower hospital survival, early initiation of antibiotics in the Emergency unit would be beneficial in order to improve the in hospital outcome of patients with AKI.

1. INTRODUCTION

1.1. Background

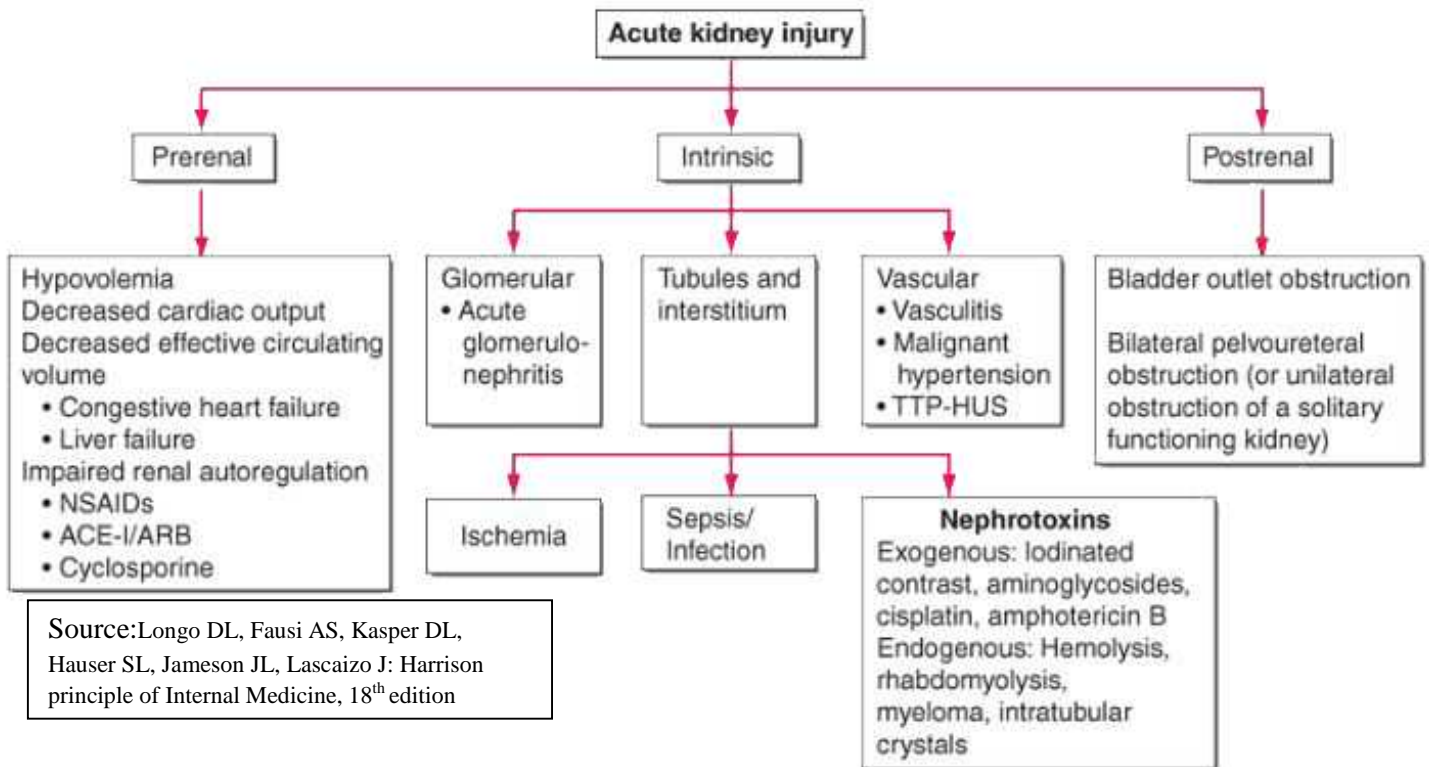
Acute kidney injury is defined as decline in renal function over hours or days resulting in the accumulation of toxic wastes and the loss of internal homeostasis(1)

Acute kidney injury (AKI) is one of the major health problems, adversely affecting patient morbidity occurring in more than 13 million people every year, 85% of whom accounts for developing countries.(2)Several studies reviewed risk factors attributed to AKI, in terms of in-hospital mortality, progression to end stage renal disease, accelerating progression of established chronic kidney disease (CKD), and increased cardiovascular risk(3).Yet there are quite few data addressing the epidemiology and causes of AKI in Low Resource Settings(4)(5)(6). AKI with its related features accounts for around 3% of admissions in general health-care facilities(7).

In developing countries, the distinction between community acquired and hospital acquired AKI is important because AKI is commonly caused by community-acquired diseases such as dehydration secondary to acute gastroenteritis and malaria which can be easily prevented by community-based interventions like oral hydration(8).

The etiology of AKI is classified into pre-renal, Intrinsic Renal and Post Renal. Figure 1 illustrates the possible underlying causes of these three types of AKI

Figure 1: Causes of Acute kidney injury



1.2. Statement of the problem

It is known that AKI accounts for significant morbidity and mortality in the world, particularly in Africa. Yet there is insufficient data regarding its clinical profile in Emergency unit in tertiary center of Ethiopia. Therefore, it will be of paramount importance to do a research on AKI which can clearly explain existing burden, common causes and risk factors, complications, practices of Management and outcome. This can be acquired through acknowledging previous studies; determine the knowledge gap; and then filling the gap and provide guidance by proving options in the way that healthcare professionals work.

1.3. Significance of the research

AKI is a one of important issue in Africa particularly Ethiopia where there is resource limitation at large, and appreciation of its local pattern can help inform policies on its early prevention and management.

This research is going to be helpful in understanding common causes, complications, practice of management and outcome of patients with AKI in our context by filling the knowledge gap on the area. Moreover, it will be one of the complements forwarded in solving problems regarding practices of management of AKI as it is going to have important implication regarding health promotion for better life.

2. LITERATURE REVIEW

2.1. Epidemiology of AKI

AKI is one of the common worldwide problems being responsible for an estimated 1.4 million deaths per year(9). And there are no trustworthy data regarding incidence of AKI in Africa. According to regional publications, the incidence has been estimated at 150 per million population(10).

According to a systematic review (2004-2012) of large cohort studies conducted the pooled incidence rates of AKI were 21.6% in adults concluding that 1 in 5 adults worldwide experience AKI during a hospital episode of care(6). However, most studies originated from North America, Northern Europe, and Eastern Asia, from high-income countries, and from nations that spent 5% of the gross domestic product on total health expenditure.

Study done in France on Five hundred patients with ARF, 227 males and 237 females ranging in age from 7 to 81 years (average age: 46 years), the etiologies or predisposing causes of ARF were surgical (50%), traumatic (52%), obstetrical (15%) and medical origins (46%)(11).

Incidence of AKI in Low income countries is not completely understood the proposed reasons being late presentation of patients to tertiary centers, underreporting, and a reduced capacity to provide intensive care to severely ill patients(12).

According to the study of Phillips and associates regarding the relationship between AKI risk factor recognition and monitoring of renal function in three hospitals in Ethiopia, Male patient dominate in the majority of Medical and surgical centers and almost all patients in surgical wards underwent surgery during their admission. The majority of surgical procedures were performed electively. The proportion of patients from the O&G wards categorized as obstetric cases varied between the three (13)

Another research done in same country by Zewdu and colleagues showed contradiction with study of Phillips et al. As of his study on the causes and clinical course of 136 cases of acute renal failure (ARF) treated in the Renal Unit of TASH, Ethiopia there were 106 women and 30 men with mean age of 26.9 +/- 7.2 and 40.7 +/- 14.9 years respectively(14).

2.2. Causes

Seedat et al. did a study on 150 patients in South Africa with ARF of which medical causes were 65%, followed by gynecologic 17%, surgical 10%, and Obstetric 7.3% (15).

A retrospective study on the patterns of ARF was carried out in a general nephrology referral center in Sudan during the period from February 2003-February 2004. 64% cases were males and mean age was 39 +/- 19.4 years) fulfilled the criteria for the diagnosis of advanced renal failure. Acute tubular necrosis (ATN) was diagnosed in 56% patients; 66% ATN patients had renal failure as a complication of volume depletion, fulminant infections (particularly malaria and typhoid fever) or snakebites and 13.4% patients ingested paraphenylenediamine (PPD) (hair/Henna dye) in suicidal attempts. 9% patients of the total study group had glomerular diseases and 12.3% had obstructive uropathy associated with ARF; the cause of ARF could not be determined in 19% patients(16).

2.2.1. Sepsis

According to the study done in Australia, 32.4% of patients with AKI had Sepsis.(17) There was a study done in Uganda which evaluated the relationship between sepsis and AKI. According to cross-sectional study of sepsis-related AKI on the adult medical wards of Mulago National Referral Hospital 387 patients recruited out of which 55.6% were male with an average age of 37 years. Among these patients, AKI secondary to sepsis occurred in 16.3%. The 3 factors that significantly associated with AKI were Age >59 years, a postural drop in systolic blood pressure of >9 mmHg and a white blood cell count >12,000 cells/mL(18).

2.2.2. Volume Depletion

On the other hand, Ahmed et al. studied 151 cases AKI requiring dialysis in Saint Paul's Hospital Millennium Medical College (SPHMMC). The patients were found younger with a mean age of 36.7 years. The most common causes of AKI were hypovolemia accounting for 22.5%, followed by acute glomerulonephritis (AGN), 21.9% and pregnancy related causes 18.5% (19) as opposed to Zewdu's study which showed that septic abortion was the leading cause of ARF, 71% followed by falciparum malaria, 29% and nephrotoxic agents 12% (14).

2.2.3. Cardiorenal syndrome-1(CRS-1)

According to a metaanalysis done by Wim Vandenberghe and associates, the median occurrence of AKI defined was 24.4%, and the higher occurrence of AKI was recorded in those with acute heart failure(20)

And as per retrospective study done in USA by Zehra Eren et al., majority of the CRS-1(50.7%) are caused by ACS followed by Acute decompensated heart failure(21)

2.2.4. Obstructive uropathy(OUP)

OUP is one of the common causes of AKI which accounts 6-20% of cases of AKI in Africa. (22) A study done in tertiary referral center in Khartoum, Sudan, found that the incidence of OUP from patients admitted to the hospital with a diagnosis of AKI was 23% with male predominance(17.5%).(23)

2.2.5 Acute glomerulonephritis(AGN)

A report from Pakistan showed that glomerular diseases contribute only 4.19% of total AKI admitted.(24) Yet according to local study done in St. Paul hospital, the incidence of dialysis requiring AGN was as high as 21.9% of patients with AKI(19)

2.2.6 Hypertensive Crisis

As reported by Scott T. Benken and colleagues, only with 1-3% of patients with hypertension presents with hypertensive emergency. And regarding Acute Target-Organ Damage, neurologic system is the commonest system affected in hypertensive crisis followed by cardiac. Kidney is the third commonest organ damaged during hypertensive crisis accounting for <10% of the cases of hypertensive crisis(25)

2.2.7. Nephrotoxic drugs

A study done on critically ill adults revealed that AKI was caused by nephrotoxins in 28.0% of patients having AKI (26). Another study done in Cape Town demonstrated that clinically acute tubular necrosis was the most common underlying cause of AKI, in 272 (72.1%) patients which was due to exogenous nephrotoxins in 137 (37.4%) patients(27)

2.2.5. CKD related AKI

Another strong risk factor associated with AKI is Underlying CKD. Hsu et al. did comparison of 1,746 hospitalized adult members of an integrated health care delivery system who developed dialysis-requiring AKI with 600,820 hospitalized members who did not, and showed that the adjusted odds ratios were significantly and progressively elevated from 2.0 for those with baseline eGFR 45–59 ml/min/1.73m² up to 40.1 for those with baseline eGFR <15 ml/min/1.73m², when compared to referent patients with baseline eGFR ≥ 60 ml/min/1.73m²(28).

And as of incidence in Ethiopia, Ahmed et al. found that 16.9 % of patients had AKI superimposed on CKD and the most common cause of CKD was Hypertension, 51.9 %. From the study, Diabetes and hypertension accounted for a combined 56 % of causes of underlying CKD and 22 % had no immediately identifiable cause(19).

2.3. Complications of AKI

2.3.1. Electrolyte Abnormalities

2.3.1.1. Hyperkalemia

Hyperkalemia is a life-threatening electrolyte abnormality that can render cardiac arrhythmia which has fatal consequence. In majority of cases, Symptomatic hyperkalemia presents when levels are > 7 mEq/L. Indications for immediate treatment of hyperkalemia include EKG findings of narrow, peaked T-waves, shortened QT interval followed by widened QRS, lengthening of PR interval, and low amplitude P waves(29). Electrolyte abnormalities like hyperkalemia has been very well known complications of AKI for about half a century(30)(31)(32). In various countries around the world, it's even the predominant indication of dialysis(33)(34)

In tropics, Hyperkalemia is strongly associated with falciparum malaria, Leptospirosis, chemical poisons like copper which are used in leather industries and formic acid used in rubber plantations(35)

2.3.1.2. Hyponatremia

Hyponatremia is reported to account 25% to 60% of patients with AKI secondary to Falciparum Malaria the possible mechanisms being hemodilution and sodium wasting before the onset of oliguria. However, an increase of serum antidiuretic hormone is unlikely to play a major role(35). However, there is no clear association between hyponatremia and AKI in other risk factors other than Falciparum Malaria

2.3.2. Neurologic Complications

Study in Germany showed that the central nervous system (CNS) symptoms of kidney failure as a complication of uremic encephalopathy, such as cognitive deficits, somnolence, or seizures, uremic encephalopathy has become less frequent with the advancement in techniques of renal replacement therapy. These neurologic manifestations are possibly explained by presence of endogenous guanidines such as creatinine, guanidine, methylguanidine, and guanidine succinic acid(36). But in third world countries like Ethiopia where there is no easy access for renal replacement therapy, the incidence of uremic encephalopathy is several, yet not studied well.

2.3.3. Gastrointestinal complications

Gastrointestinal complications like vomiting and Gastroduodenal bleeding can be both risk factor as well as complication of AKI(1). As a risk factor, they cause decreased circulating volume and as a complication they come as a direct effect of uremia or indirectly being associated with diseases like cancer and malaria(37)(38).

2.4. Dialysis and Outcome of Patient with AKI

According to a study done in tertiary hospital in Rwanda, pulmonary edema and uremic encephalopathy were the leading indications of dialysis accounting for 54.9% and 50% , respectively.(39)Comparable result was entertained in local tertiary hospital which showed that refractory fluid overload and uremic signs and symptoms accounting for 89% and 61.6% of the dialyzed patients. (19)

AKI affects up to 13.3 million cases per year, 11.3 million of which are in low- to middle-income countries and it accounts for approximately 1.4 million deaths per year. In addition, AKI-related problems account for up to 3% of hospital admissions in general health care facilities in Low Resource Settings(40).

Study done in Cape Town on 145 patients dialyzed in ICU showed that, there were 49% deaths at 3 month follow up. And from those patients on follow up serum creatinine, 79.8% had full renal recovery, and 3.4% had end-stage renal disease. Mechanical ventilation was associated with 3-month mortality (OR 2.46, p-value 0.019, 95% CI 1.41–4.03). Sepsis had a borderline significant association (OR 1.83, P-value 0.066, 95%CI 1.02–3.27), as did prolonged time to dialysis (OR 1.93, p-value 0.08, 95% CI 0.93–4.03) and HIV did not affect outcome(3). However, it has low sample size which is just 119 and difficult to infer to the general population. The other limitation is that it didn't include Patients who have stayed in the Emergency with the diagnosis of AKI and died in the Emergency unit before admission. The third point is that majority of the patients are AKI stage 3 and above as the hospital was tertiary center.

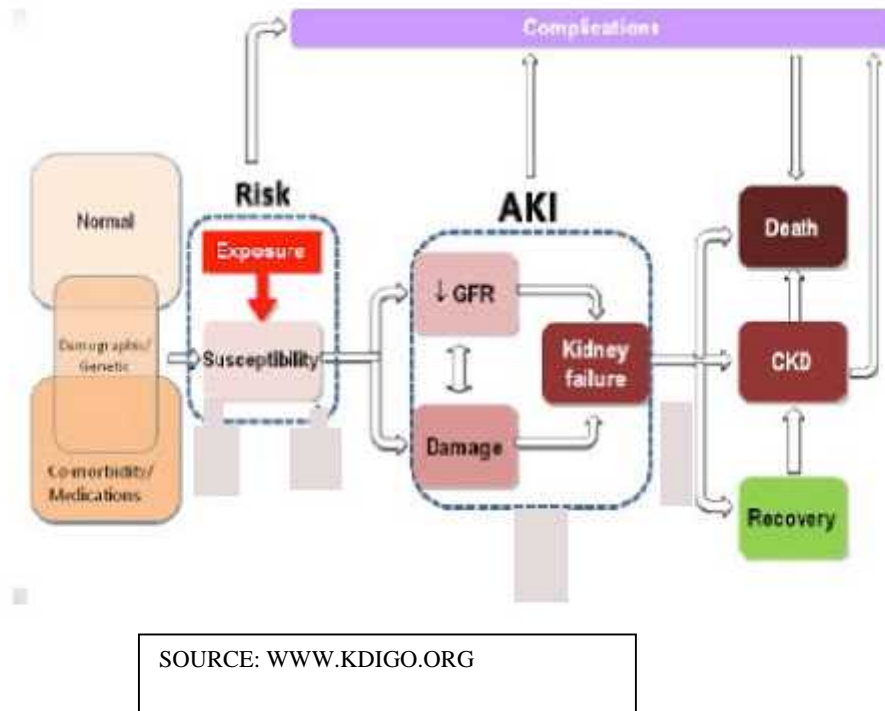
And local study done in patients with AKI in dialysis unit showed that averageLOS was 20.7 days, with range of 1–92 days. From the total 151 patients, 53 % were discharged improved, and 29.1 % died, with the remaining absconding 10.6 % or progressing to end stage renal disease 7.3 %.(19)

According to a study done on Sudanese patients was analyzed with binary logistic regression to identify independent predictors of mortality among AKI patients; Mortality significantly associated with the increase in patients' age, presence of chronic liver disease, and the severity of AKI as per the KDIGO staging.(16)

Patients with CKD have been reported in some studies to have lower in-hospital mortality than patients without CKD who develop AKI. As of the done by Waikar SS et.al, 22% of AKI on CKD patients died in hospital, whereas, as high as 30% of patients died who are AKI without CKD.(41)

3. Conceptual framework

Figure 2: Conceptual framework



4. OBJECTIVES OF THE STUDY

4.1. General Objective

To evaluate patterns, and outcome of AKI in Tikur Anbessa specialized Hospital(TASH), Addis Ababa, Ethiopia

4.2. Specific Objectives

- . To assess for causes of AKI in TASH, Addis Ababa, Ethiopia
- . To identify AKI related complications in TASH, Addis Ababa, Ethiopia
- . To explore management practice for patients with AKI in TASH, Addis Ababa, Ethiopia
- . Evaluate disposition of patients with AKI in TASH, Addis Ababa, Ethiopia
- . To compare laboratory values on admission and discharge
- . To assess predictors of mortality in patients with AKI in TASH, Addis Ababa, Ethiopia

. To identify determinants of survival of patients with AKI in TASH, Addis Ababa, Ethiopia

5. METHODOLOGY

5.1. Study Setting

It was conducted in TASH Adult, Addis Ababa, Ethiopia. TASH is one of the largest, ~700-bed, teaching hospital for Addis Ababa University, School of Medicine in Ethiopia which is visited by approximately 370,000- 400,000 patients a year (42). Currently it is estimated that 50-60 patients visit our Emergency unit on a daily basis making monthly visit of 15,000-18,000. TASH currently has 4 nephrologists with 2 functional dialysis machines. It is tertiary hospital which approaches patients from all walks of life and all over the country. The Adult Emergency unit in TASH is a site where all AKI patients visit in the first place regardless of the underlying cause.

5.2. Study time

It was conducted from September, 2018 to May, 2019

5.3. Study design

A prospective cross-sectional study was used for the study.

5.4. Source population and study population

5.4.1. Source Population

Patients that came to TASH adult Emergency unit during the study period

5.4.2. Study population

Patients seen at TASH Adult Emergency Unit with the diagnosis of AKI

5.5. Inclusion criteria and Exclusion criteria

5.5.1. Inclusion criteria

All AKI patients with age ≥ 13

5.5.2. Exclusion criteria

Patients who opt out are excluded from the study

Patients with CKD without superimposed AKI

5.6. Sample Size Determination

According to a systematic review (2004–2012) of large cohort studies done to estimate the world incidence of AKI and its stages of severity and associated mortality there were 312 studies identified ($n=49,147,878$), primarily in hospital settings. Among the 154 studies ($n=3,585,911$) that adopted a KDIGO-equivalent AKI definition, the pooled incidence rates of AKI were 21.6% in adults (95% Confidence interval [95% CI], 19.3 to 24.1). The proportion we will be using in this research will be 20%.

$$n = \frac{Z_{\frac{\alpha}{2}}^2 P (1 - P)}{d^2}$$

Where;

n = required sample size

Z /2 = critical value for normal distribution at 95% confidence interval= 1.96 (= 0.05).

P = Proportion = 20%

d = margin of error= 5%

So, $n = \frac{(1.96)^2 * (0.2) (1-0.2)}{(0.05)^2} = 246,$

Therefore, the total required sample size is 246 and with adjustment for non-response rate (5%) and the final required sample size was 258. Yet due to time constraint, we failed to achieve that sample size with in the data collection period which was from September,2018 to May,2019. Therefore, we were obliged to use convenience sampling method.

5.7. Sampling Procedure

The area was selected which was TASH adult Emergency unit where the sample was collected from the patients who fulfilled the inclusion criteria.

5.8. Method of data collection

Data was collected 24 continuous hours for total of 9 months. The principal investigator took the role of training a nurse on data collection tailored for this study. The training lasted for three days during the piloting process. It was focused on how to fill the questionnaire. Piloting of the questionnaire was done on 10 patients, one week prior to the actual data collection. After piloting method misunderstanding on some terminologies by data collector was identified after which the decision was made to make periodical check on the data completeness and validity.

5.9. Study variables

5.9.1. Independent variables:

Sociodemographic variables

Causes

Complications

Treatments modalities: Fluid therapy: NS, RL, DNS

Dialysis

Drug treatment

5.9.2. Dependent variables: Death

Survival time

All the data of independent variables were collected from the patient chart by PI and data collector. Any missed laboratory data was communicated to PI who then checked in the laboratory documentations and computer for the missing data.

5.10. Operational definitions

AKI is defined as: Increase in Serum Creatinine by 0.3 mg/dl (26.5 μmol/l) within 48 hours; or Increase in Serum Creatinine 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days(43)

CKD is defined ,with structural criteria, as the presence of kidney damage **or** decreased kidney function for 3 months(43)

5.11. Data collection

The form consisted of information regarding sociodemographic data, causes, AKI related complication, practice of management and disposition of patients with AKI.

Data was collected by PI and data collector and collected data was stored. Appropriate explanation was given on definition of some terms, purpose and importance of the research.

5.12. Data Quality Control

As the data was collected by the PI and the data collector, completeness and validity was checked meanwhile, by the principal investigator.

5.13. Data Analysis

The data was checked for completeness and inconsistency, and then it was Processed and analyzed using SPSS software version 25. Categorical data were compared with chi-squared test. Mortality predictors were analyzed using binary logistic regression. Laboratory tests on admission and discharge were compared using paired samples T-test. Kaplan- Meier estimator and Log Rank test with a confidence interval of 95% were used to assess survival of AKI patients with sepsis; who underwent dialysis; and those with underlying CKD. Time to discharge of each types of AKI was analyzed using Kaplan-Meier curve. P-value < 0.05 was considered significant.

5.14. ETHICAL CONSIDERATION

The study was done in conformity with the ethical guidelines. Ethical clearance for the study was asked from Addis Ababa University medical faculty(AAUMF), and department of Emergency Medicine. This study holds no feasible risk for the participant. Participants will get no financial benefit. All participants' right, privacy and autonomy will be respected. Participation is voluntary.

5.15. DISSEMINATION OF THE RESULTS

The research will be communicated to, FMOH, Ethiopian Kidney association. Effort will be made to publish the paper in scientific journals.

6. RESULT

6.1. Socio-demographics

There were a total of 144 patients diagnosed to have AKI in TASH EOPD from August, 2018- May, 2019 of which there was a slight predominance of male, 79 (54.9%) and the rest were female.

The mean age of the patients was 46.6 ± 16.6 and around 40% of the patients are found in the age group between 30-50 years.

Although patients came from all around Ethiopia, nearly half of them (49.3%) came from Addis Ababa and more than quarter of the patients came from Oromia (27.8%).

Table 1 Socio demographic characteristics of patients with AKI, TASH, Addis Ababa, May 2019

Sociodemographic variable	Sub-variable	Frequency	Percent
Sex	Male	79	54.9
	Female	65	45.1
	Total	144	100
Age	<21	9	6.3
	21-30	20	13.9
	31-40	28	19.4
	41-50	29	20.1
	51-60	28	19.4
	61-70	18	12.5
	>70	12	8.3
	Total	144	100
Region	Addis Ababa	71	49.3
	Oromia	40	27.8
	SNNPR	16	11.1
	Amhara	9	6.3
	Others	6	4.2
	Total	142	98.6
	Missing	2	1.4

6.2. Clinical characteristics of AKI

The commonest cause of AKI identified was sepsis (43.8%), The remaining others are summarized in **Table 2** below

39(27.1%) of the patients were found to have preexisting CKD. The main underlying cause of CKD was extra renal OUP which included 1/4th of the cases (25.6%) followed by hypertension (23.1%) and diabetes (20.5%). The mean baseline creatinine was 9.8 ± 6.6 . The majority of deaths in AKI on CKD patients was found in those with extra renal OUP most of which are due to cervical ca. (38.5%). The others are listed on **Table 2**

More than half, 52.8%, of the patients with AKI had complications. Of these, the commonest complication identified was uremic encephalopathy which occurred in 42.1%, followed by anemia (40.8%) and hyperkalemia (28.9%).

A Chi-square test of independence was calculated comparing the frequency of clinical characters in men and women. A significant interaction was found in men with nephrolithiasis as compared with women.

Table 2 Clinical characters and proportion of death of patients with AKI, TASH, Addis Ababa, 2019

Causes of AKI	Clinical characteristics ^a	Frequency N (%)	Male N(%)	Female N(%)	P- Value	Proportion of death(%)
	Sepsis	65(43.2)	36(55.4)	29(44.6)	0.854	25(56.8)
Volume depletion	36(25)	19(52.8)	17(47.2)	0.805	12(27.3)	

Causes Of underlying CKD	CRS-1	23((16)	13(56.5)	10(43.5)	0.835	3(6.8)
	OUP	23(16)	11(47.8)	12(52.2)	0.480	9(20.5)
	AGN	8(5.6)	5(63)	3(37)	0.642	3(6.8)
	Hypertensive crisis	7(4.9)	4(57.14)	3(42.86)	0.887	2(4.5)
	Drug	5(3.5)	3(60)	2(40)	0.803	0(0)
	TLS	4(2.8)	1(25)	3(75)	0.229	2(4.5)
	Others	3(2)	3(100)	0(0)	0.194	1(2.3)
	Extra renal OUP	10(25.6)	4(40)	6(60)	0.349	5(38.5)
	Hypertension	9(23.1)	6(66.7)	3(33.3)	0.462	3(23.08)
	Diabetes	8(20.5)	5(62.5)	3(37.5)	0.655	3(23.08)
Complications of AKI	Nephrolithiasis	5(12.8)	5(100)	0(0)	0.039	0(0)
	Others	7(18)	4(57.14)	3(42.86)	0.901	2(15.38)
	Uremic encephalopathy	32(42.7)	20(13.9)	12(8.3)		23(52.3)
	Anemia	31(41.3)	15(10.4)	16(11.1)		8(18.12)
	Hyperkalemia	22(29.3)	10(6.9)	12(8.3)		11(0.25)
	Fluid overload	11(14.7)	7(63.64)	4(36.36)		6(13.64)
	Uremic gastropathy	11(14.7)	6(54.55)	5(45.45)		3(6.82)
	Uremic pericarditis	3(4.0)	3(100)	0(0)		1(2.27)

^aSum is more than 100 % as most patients had more than one cause and complication

6.3. Laboratory values

The patients had complete blood count and renal function test during admission and upon discharge. The mean white cell count is $13,138.8 \pm 9558.1$ and 11810 ± 6520.7 on admission and discharge respectively. There is, as well decrement of creatinine upon discharge from mean of 5.7 ± 5.4 to 4.9 ± 4.9 . The rest are shown on **Table 3**.

Table 3: Selected laboratory values of patients with AKI, TASH, Addis Ababa, 2019

Laboratory values	Point in time	Mean \pm Standard deviation
Urea	Admission	122 \pm 76.3
	Discharge	116.2 \pm 82.4
Creatinine	Admission	5.7 \pm 5.4
	Discharge	4.9 \pm 4.9
WBC count	Admission	13138.8 \pm 9558.1
	Discharge	11810 \pm 6520.7
Hemoglobin	Admission	11.1 \pm 3.3
	Discharge	10.8 \pm 2.9
Platelet count	Admission	212887.4 \pm 127867.3
	Discharge	269042.5 \pm 138420.506

6.4. Treatment practice and outcome of patients with AKI

More than 3/4th of the patients (82.6%) took drug treatments for the variety of causes of AKI including cardiac, Septic ATN, hypertension and AGN. On the other hand, around half of the patients took fluid treatment for the AKI.

Figure 3: Treatment practice of patients with AKI, TASH, Addis Ababa, 2019

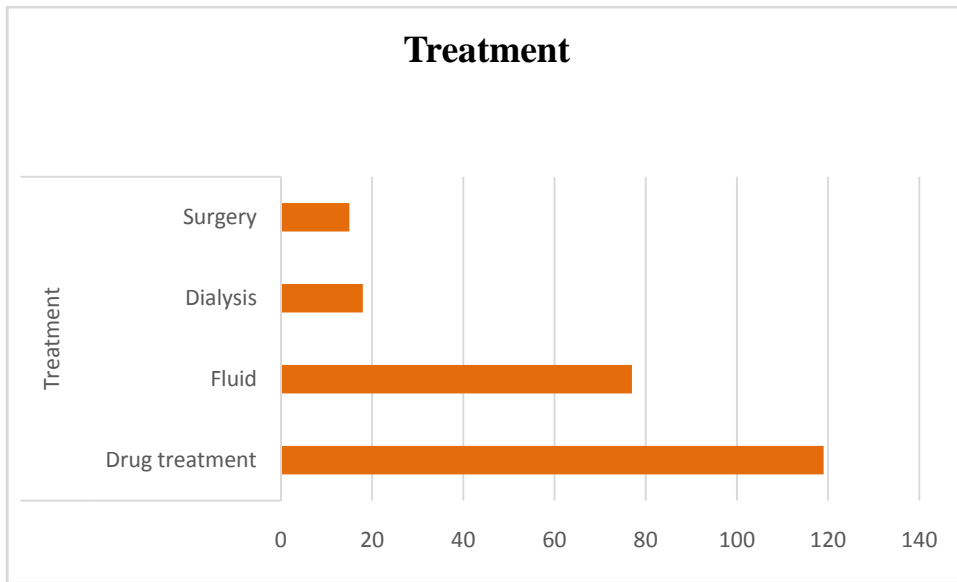
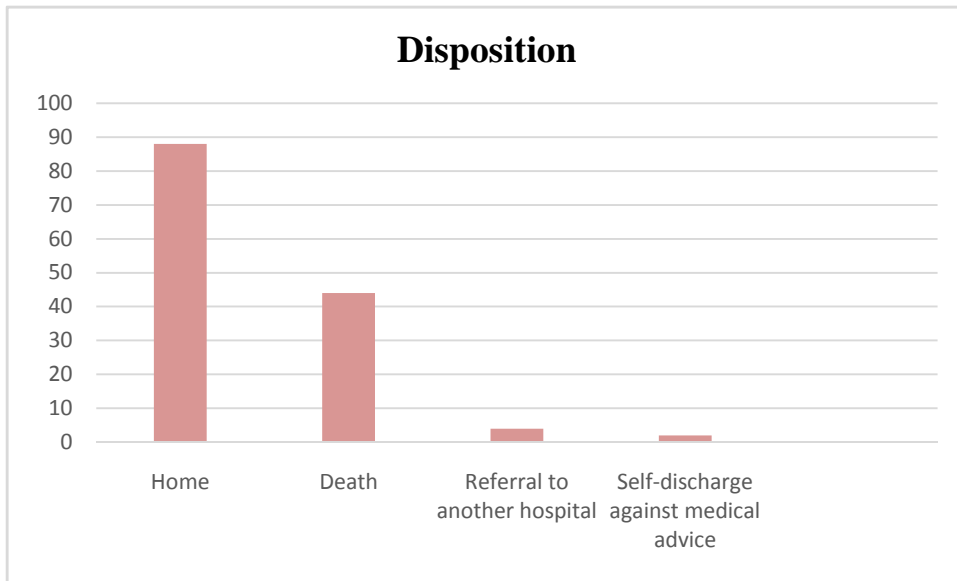


Figure 4: Disposition of patients with AKI, TASH, Addis Ababa, 2019



18 patients (12.5%) underwent dialysis. Indications for dialysis are shown in Table 5. The commonest indication identified was uremic encephalopathy (72.2%) followed by hyperkalemia (27.8%) and refractory fluid overload (22.2%).

The rest minority underwent surgical management, percutaneous nephrostomy being the commonest surgical procedure. Cervical ca. was the cause in most cases of obstructive uropathy.

Average duration of hospital stay was 7.2 days, the minimum being 2 days and the maximum being 36 days, with a range of 34 days. The average length of stay in each type of AKI is shown the **Table 6**. More than half of the patients (61.1%) were discharged home. And nearly 1/3rd (30.6%) of the patients died. 4 patients were referred to another centers the reason being lack of bed and two patients self-discharged

Indications for dialysis		Dialysis ^b			Death ^b	
		Yes(%)	No(%)	Total(%)	Yes(%)	No(%)
Refractory fluid overload	Yes(%)	4(22.2)	7(5.6)	11(7.7)	6(60)	4(40)
	No(%)	14(77.8)	117(94.4)	131(92.3)	38(29.7)	90(70.3)
Hyperkalemia	Yes(%)	5(27.8)	17(13.7)	22(15.5)	11(55)	9(45)
	No(%)	13(72.2)	107(86.6)	120(84.5)	33(28)	85(72)
Uremic encephalopathy	yes(%)	13(72.2)	18(14.5)	31(21.8)	23(74.2)	8(25.8)
	No(%)	5(27.8)	106(85.5)	111(78.2)	21(19.6)	86(80.4)

against medical advice.

Table 4: Indication for dialysis of AKI patients, TASH, Addis Ababa, 2019

^bSum is more than 100 % as most patients had more than one indication for dialysis

Types of AKI	Mean hospital LOS±SE
Prerenal	6.50±6.65
Intrinsic renal	7.84±8.18
Post renal	8.39±6.73
Mixed	6.40±4.85

Table 5: mean hospital LOS in each types of AKI, TASH, Addis Ababa, 2019

LOS: Length of stay (In days) **SE:** Standard deviation

Common complications leading to deaths encountered were uremic encephalopathy, fluid overload and hyperkalemia. From the death records, nearly 3/4th (74.2%) had uremic encephalopathy; where as in 60% of deaths, there were complications of fluid overload. And more than half of the deaths (55%) had hyperkalemia. These results are well summarized in **Table 5**.

6.5. Predictors of mortality

6.5.1. Binary logistic regression

Binary logistic regression was implemented further to determine the independent predictors of mortality among AKI patients with and without CKD; In overall AKI patients (those AKI regardless of presence or absence of CKD) mortality was significantly correlated with presence of Uremic encephalopathy [OR,0.061; 95 %CI (0.019,0.198); P=<0.001] and hyperkalemia which was marginally significant

[OR,0.283; 95 %CI (0.077,1.046); P=0.058]. This, as well as, the finding for factors in AKI patients without underlying CKD is shown in Table 7

Table 6: Binary logistic regression analyses for correlation between different factors and death in Overall as well as pure AKI (Without underlying CKD), TASH, Addis Ababa, 2019

		Death			
		COR(95%CI)	P-value	AOR(95%CI)	P-Value
factors in AKI	Fluid Overload	3.55(0.95,13.3)	0.060	1.743(0.28,10.68)	0.548
	Hyperkalemia	3.15(1.19,8.29)	0.02	5.06(1.291,19.87)	0.020
	Sepsis	2.46(1.18,5.16)	0.017	3.151(1.23,8.07)	0.017
	Uremic encephalopathy	11.8(4.6,30)	<0.001	13.71(4.32,43.5)	<0.001
	Creatinine on admission	0.952(0.893,1.014)	0.128	1.049(0.954,1.154)	0.320
Factors In AKI without underlying CKD	Fluid overload	3.12(0.67,15.32)	0.144	1.189(0.090,15.627)	0.895
	Hyperkalemia	6.32(1.51,26.44)	0.012	0.124(0.017,0.905)	0.039
	Sepsis	2.31(0.96,5.54)	0.062	0.378(0.124,1.152)	0.087
	Uremic encephalopathy	30.93(6.4,149.19)	<0.001	0.033(0.006,0.190)	<0.001
	Creatinine on admission	0.90(0.811,0.999)	0.047	1.036(0.887,1.211)	0.653

AKI: Acute kidney Injury **CKD:** Chronic kidney injury **COR:** Crude odd's ratio **AOR:** Adjusted odd's ratio

6.6. Paired samples T-test

A paired-samples t-test was conducted to compare selected laboratory values of patients with AKI upon admission and discharge. There was a significant difference between creatinine values upon admission (M=5.14, SD=4.9) and discharge (M=4.87, SD=4.85) conditions; $t(46) = 3.243$, $p = 0.002$. This results showed that there was real improvement on creatinine after the patient finished course in the hospital. This result is illustrated in the table 8

Table 7: Paired-samples T-test for selected laboratory values of patients with AKI, TASH, Addis Ababa,2019

Laboratory values on admission and discharge	Mean	SD	SE mean	95%CI of the difference		t	df	Sig.(2-tailed)
				Lower	Upper			
Urea	15.561	52.164	9.369	-3.573	34.695	1.661	30	0.107
Creatinine	1.067	2.256	0.329	0.405	1.730	3.243	46	0.002
WBC	1862.750	7816.859	1235.954	-	4362.703	1.507	39	0.140

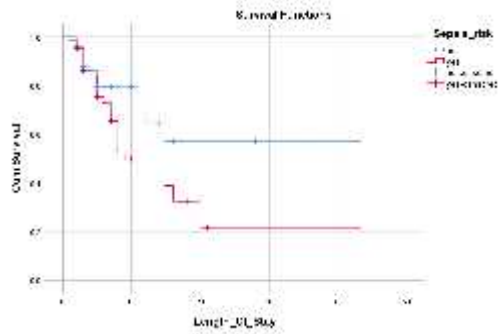
Hemoglobin	-0.0111	2.953	0.479	-1.081	0.860	-	37	0.819
						0.231		

SD: Standard deviation, **SE:** Standard Error, **CI:** Confidence interval, **df:** Degree of freedom

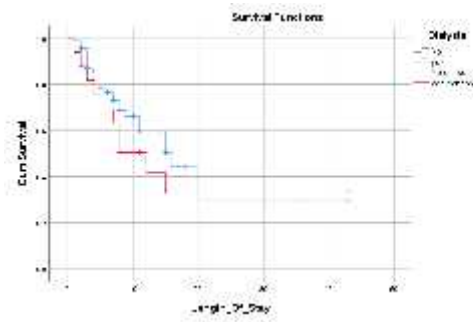
6.7. Survival of AKI patients

Probability of survival of AKI patients who have sepsis, who underwent dialysis and who had underlying CKD estimated using Kaplan-Meier curves. A lower survival of all AKI patients with sepsis over the hospital stay period was found with marginally significant P-value (Mean survival AKI with sepsis=16.967; SE= 3.169 vs without sepsis=28.105; SE 3.413; P = 0.056). The comparison between AKI patients with CKD, time to death didn't not significantly differ from those who haven't underlying CKD. For those patients who underwent dialysis, as well, no significance with regards to survival in hospital stay. Finally, time to discharge was assessed between each types of AKI and there was no significant difference found. The illustration is depicted on Figure 5 below.

A



B



C

D

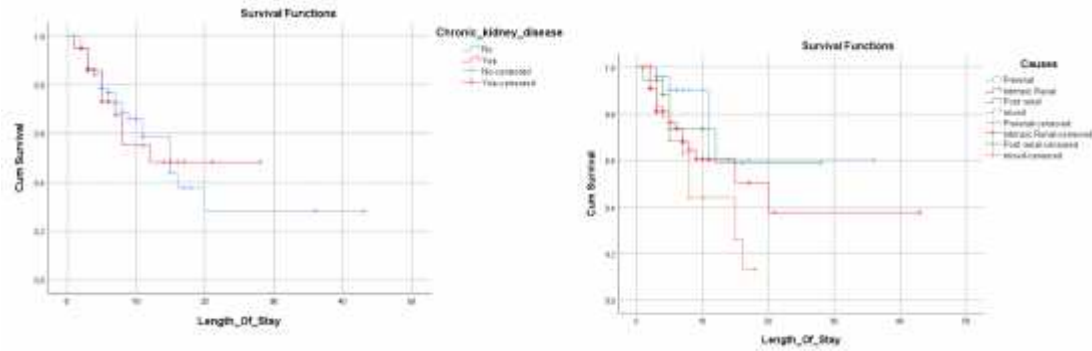


Figure 5: Kaplan-Meier curves A. Time to death in AKI patients with sepsis B. Time to death in AKI patients who underwent dialysis; C. Time to death in AKI patients who had underlying CKD; D. Time to discharge in each types of AKI

7. DISCUSSION

This study elucidated the epidemiology, causes, complication practice of management and outcomes of patients with AKI. The presentation of the patients at a younger age coincided with results from Europe, African countries as well as those done in Ethiopia(11)(19)

Although patients coming from different corners of the country, more than half of the patients came from Addis Ababa and Oromiya. This coincides with another literature done in St. Paul hospital which is found in the same area where TASH is found.(19) This can be explained by the Geographical proximity of the patients living in Addis Ababa and Oromiya to TASH.

In line with the study done in sub-Saharan country(16), ATN was the leading cause of AKI in this study, followed by gastrointestinal loss(diarrhea or vomiting), cardiac and obstructive uropathy. In contrast, recent local literature from Saint Paul's Hospital Millennium Medical College showed that the predominant causes were hypovolemia, acute glomerulonephritis and pregnancy related causes(19)

Sepsis related AKI was top cause for on the list in this study. This went in harmony with the study done across Australia which showed that nearly 1/3rd of patients with AKI had sepsis(17) However, the study done in Uganda showed considerably lower number of septic related AKI cases which was 16.3%.(18)

This study showed that CRS-1 is still one of the major causes of AKI which was also strengthened by a systematic review and meta-analysis.(20) Yet, there is a difference regarding dominant cause of CRS-1 which in this study is acute heart failure in contrast to single-center retrospective study done in USA which showed that acute coronary syndrome to be the dominant cause of CRS-1. (21) This dissimilarity can be explained by the higher incidence of valvular heart disease in Ethiopia as compared to western setup.

OUP was also found to be one of the major causes of AKI which corresponds to reports from other African countries. And the major cause of OUP were women with cervical ca. which is still consistent with other developing countries.(22)

AGN accounted for 5.6% of all AKI cases admitted to the hospital with higher mortality of 37.7% as compared to other causes and this closely correlated with the report from Pakistan which showed 4.19% which also unfolded that the morbidity was higher in comparison with other causes(24)

Counter to the data from Capetown which demonstrated that exogenous nephrotoxins accounted for more than 1/3rd (37.4%) of AKI patients(27), this study showed that they were one of the rare causes of AKI

In this study, more than half of the patients with AKI were discharged and nearly 1/3rd died, both findings being consistent with other local literatures done recently in tertiary hospital(19)

The top indication for dialysis was uremic encephalopathy followed by Hyperkalemia. In contrast, other literatures from Africa in general and Ethiopia in particular showed that it was rather the refractory fluid overload which is the commonest indication for dialysis followed by uremic symptoms and signs(19)(39)

This study showed uremic encephalopathy, hyperkalemia and sepsis significantly predicted mortality for patients with AKI. According to a study done on Sudanese patients was analyzed with binary logistic regression to identify independent predictors of mortality among AKI patients; Mortality significantly associated with the increase in patients' age, presence of chronic liver disease, and the severity of AKI as per the KDIGO staging(16)

Those AKI patients with underlying CKD had not shown to have decreased in-hospital survival. This corresponds with other studies including the one which was done by waikar and associates which even showed that there was lower in-hospital mortality of AKI patients with underlying CKD as compared with patients without CKD who develop AKI.(41)

8. CONCLUSION

As sepsis was the dominant cause of AKI as well as mortality predictor and cause of lower hospital survival, early initiation of antibiotics in the Emergency unit would be beneficial in order to improve the in hospital outcome of patients with AKI.

9. LIMITATIONS OF THE STUDY

The research, however, is subject to some limitations:

In CKD patients it was difficult to find whether hypertension and diabetes were causes or complications. Additionally, there was also another challenge in finding creatinine and urea of some patients due to unavailability of reagents. Additionally, the term 'drug treatment' used in the study was too non-specific which encompassed all the medications used to treat sepsis, CRS-1, Hypertension, AGN, TLS and others. So, it made it difficult to analyze each medication types. Moreover, it should have been better if AKI was staged in order to entertain differences among each stages with regards to different parameters.

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Annexes

Annex I: Check list

1. Socio demographic
 - a. Age.....
 - b. Sex.....
 - C. Region.....
2. Causes
 - 2.1 Infection Yes No
 - 2.2 Cardiac Disease Yes No
 - 2.3 Volume defletioion due to diarrhea, vomit, blood loss..Yes No
 - 2.4 Hypertensive crisis Yes No
 - 2.5 OUP yes No
 - 2.6 Obstructive Uropathy- Yes No
 - 2.7 Others.....
- 3.Chronic Kidney Disease Yes No
 - If 'YES', answer the questions below. If 'NO' jump to question 2.2.
what is the underlying cause?
 - 3.1 Hypertension
 - 3.2 Primary Glomerulonephritis
 - 3.3 Diabetes
 - 3.4 Nephrolithiasis
 - 3.5 Others.....
 - 3.6 No identifiable cause
4. AKI related complications
 - 4.1. Pulmonary Edema
 - 4.2. Electrolyte

- 4.2.1. Hyperkalemia
 - 4.2.2. Hyponatremia
 - 4.2.3. Others.....
- 4.3. Cardiovascular
 - 4.3.1 Pericardial Effusi
 - 4.3.2. Pulmonary Embolism
 - 4.3.3. Hypertension
 - 4.3.4 Others.....
- 4.4. Neurologic
 - 4.4.1. Uremic encephalopathy
 - 4.4.2. Seizure
- 4.5. Gastrointestinal Tract
 - 4.5.1. Intractable Vomiting
 - 4.5.2. Gastroduodenal bleeding
 - 4.5.3. Others.....
- 4.6. Hematologic
 - 4.6.1. Anemia
 - 4.6.2. Hemorrhagic Diathesis
 - 4.6.3. Others.....
- 4.7. Infectious
 - 4.7.1. Sepsis
 - 4.7.2. Urinary Tract Infection
 - 4.7.3. Others.....
- 5. Laboratory values on admission and discharge
 - 5.1 Urea on admission..... On Discharge.....
 - 5.2 Creatinine on Admission..... On Discharge.....
 - 5.3 WBC on admission..... On discharge.....

5.4 Hemoglobin on admission..... On Discharge.....
5.5 Platlet on admission..... On Discharge.....

6. What was done for the patient

5.1.Fluid Normal Saline Ringer's Lactate Dextrose with Normal Saline

5.2. Dialysis

5.3. Drug Treatment

5.4.Surgery

7. Length of stay.....

8. Disposition

Home

Ward

Referral to another hospital

Death

Annex II: Curriculum vitae, 2019

Name: Merahi Kefyalew Merahi

Sex: Male

Date of Birth: October 13/1989

Country of Citizenship: Ethiopian

Contact Information

Mailing Address: Merahi K. Merahi, P.O.Box 34587, Addis Ababa, Ethiopia

Telephone

Mobile Phone: +251-910881699

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Degrees

November/2016: Doctorate, Medical Doctorate, Addis Ababa University

Degree Status: Completed

February/2017-Ongoing: Post-doctorate, Postgraduate Residency in Emergency Medicine and Critical Care, Addis Ababa University, Degree Status: Ongoing

Employment

Feb/2017-Ongoing: Emergency Medicine and Critical Care Residency, School Of Medicine, AAU

Public Education In Media

Addis TV- Yegna Guday-Media Public awareness and education on Emergency Cases(2018)

Quality Improvement Activity

On provision and Application of Perfusers in Department of Emergency Medicine And Critical Care(2017)- Succeeded

Undergraduate Research, Addis Ababa University, School of Medicine (August 2014)

Anthropometric assessment of under 5 children of Ziway area, Edom Gojola Kebelle

Proposal

Knowledge, attitude and practice of Orthopedic Patients In Tikur Anbess Hospital, Addis Ababa Unibersity, Ethiopia, about traditional bonesetter and Impact On Treatment

Skills

- Microsoft Skills: Word, Excel Access, PowerPoint
- Language: Fluent in Amharic, fluent in Geez and fluent in English
- Adobe Photoshop
- Communication skills
- Time management
- Teamwork and leadership

Training And Certificate

- Prevention and management of HIV and Co-Infections (May 2016) by Addis Ababa University, School of Medicine

Social Activities

- Member of Iyakem wo Hana Orthodox church and Gola Michael church (as a deacon) in giving service for the people with the aim of wide spreading fraternity and brotherhood
- Advanced Chess player
- Soccer and table tennis player

Annex III: Assurance of investigator

I, the undersigned candidate agrees to accept responsibility for the scientific and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the Addis Ababa university

Name of investigator: Merahi Kefyalew

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Date_____

Approval of the advisors

Advisors Name: Professor Aklilu Azazh

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(Internist, Professor of Emergency Medicine)

(Assitant professor of Emergency and critical care)

Signature: _____

Date: _____
