TREATMENT OUTCOME AND ASSOCIATED FACTORS AMONG HOSPITALIZED CHRONIC KIDNEY DISEASE PATIENTS AT JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, OROMIA, ETHIOPIA

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Treatment Outcome and Associated Factors among Hospitalized Chronic Kidney Disease Patients at Jimma University Medical Center, Southwest Ethiopia: Prospective Cohort Study

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ABSTRACT

Background: Chronic kidney disease (CKD) is an increasing public health problems worldwide and greatly impact patients' quality of life. Understanding the most prominent risk factors and treatment outcomes is essential to identify patients at high risk for adverse outcome like mortality. In Ethiopia, the treatment outcome of CKD as well as its predictors are not well studied.

Objectives: To assess treatment outcomes and associated factors among hospitalized CKD patients attending Jimma University Medical College (JUMC) in Jimma from April 23 to September 25, 2018.

Method and participants: A prospective cohort study was conducted among 130 CKD patients admitted to renal unit of JUMC. Patients with Acute Kidney Injury (AKI) on CKD diagnosis were categorized as exposure while CKD only group were considered as non-exposed ones. Relevant patient information was collected using data abstraction format. Data was entered into Epidata manager version 3.1 and analyzed using SPSS version 21. Data were summarized using univariate analysis. After selecting candidate variables in bivariate analysis at p-value <0.05 and p-value <0.20 for in-hospital and 30 day mortality, the final multivariable cox-proportional hazard model was fitted and variables with p-values were considered predictors of treatment outcome of CKD. The hazard ratio was used as a measure of strength of association.

Result: Among 130 CKD patients followed, 92(70.8 %) were males with male: female ratio of 2.42:1. The rate of in hospital and within 30 day mortality were 16.9% and 30.0% respectively. Khat use (AHR: 3.37, 95% CI: 1.27-8.96), type of diagnosis at admission (AHR: 3.02, 95% CI: 1.21-7.54) and presence of proteinuria at admission (AHR: 0.11, 95%CI: 0.02-0.55) were significant predictors for in-hospital mortality. Whereas, sex of the patients (AHR: 2.66, 95% CI: 1.21-5.88), family history of hypertension (AHR: 0.29, 95% CI: 0.10-0.85), diagnosis at admission (AHR: 2.46, 95% CI: 1.26-4.78), and complication related to CKD (AHR: 5.38, 95% CI: 1.64-17.72) were the significant independent predictors of 30 days mortality in the patients with CKD during the study period. The mean length of survival after hospital admission was 16.41±6.86 days for patients who died within 30 days.

Conclusion and recommendation: CKD accompanied to higher rate of medical admissions, in hospital as well as 30 day mortality. Hypertension, anemia and heart failure were the common risk factors identified in CKD patients. As such a comprehensive public health awareness creating campaign on risk prevention, involvement of multidisciplinary sectors, better and affordable dialysis and Kidney transplantation center were some of the efforts expected from professional, government and stakeholders to improve the outcome of CKD patients.

Keywords: Chronic Kidney Disease, treatment outcome, risk factors, JUMC

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TABLE OF CONTENTS

Contents

ABSTRACT I

ACKNOWLEDGEMENT II

TABLE OF CONTENTS III

List of Tables VI

List of Figure VII

ABBREVIATIONS AND ACRONYMS VIII

1. INTRODUCTION 1

1.1. Background 1

1.2. Significance of the Study 3

1.3. Statement of the Problem 4

2. LITERATURE REVIEW 6

2.1. Risk Factors of CKD 6

2.2. Treatment Outcome of CKD 7

2.3. Conceptual Framework 10

3. OBJECTIVES 11

3.1. General Objective 11

3.2. Specific Objectives 11

4. METHOD AND PARTICIPANTS 12

4.1. Study Area and Period 12

4.2. Study Design 12

4.3. Source Population 12

4.4. Study Population 12

4.5. Inclusion and Exclusion Criteria 12

4.6. Sample Size and Sampling Method 13

4.7. Study Variables 13
4.7.1. Independent Variables 13
4.7.2. Dependent Variables 14
4.8. Outcome and Validation Methods of Data Analysis 14
4.9. Data Collection Instrument and Procedures 15
4.10. Data Quality Assurance 16
4.11. Data Processing and Analysis 16
4.12. Plan for Dissemination of Findings 17
4.13. Ethical Consideration 17
4.14. Operational and Definition of Terms 17
5. RESULTS 20
5.1. Baseline Socio-demographic Characteristics of Patients 21
5.2. Disease Related Factors 22
5.3. Laboratory Data/Biochemical Parameters of the Patients 25
5.4. Drug Related Factors 27
5.5. Outcomes and Discharge Condition of the Patients 29
5.6. 30 Day Mortality Follow up Outcome 31
6. DISCUSSION 34
7. CONCLUSION 40
8. RECOMMENDATION 41
REFERENCES 42
Annex 1: Information Sheet 49
Annex 2: Consent Form 50
Annex 3: Data Collection Tools 51
Annex 4: Amharic Version of Informed Consent 57
Annex 5: Oromic Version of Informed Consent 58

Annex 6: Amharic Version of Adherence Measurement Tool 59

Annex 7: Oromic Version of Adherence Measurement Tool 60

List of Tables

Table 1. Baseline socio-demographic characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018, Ethiopia. 21
Table 2. Risk factors and Clinical characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 24
Table 3. Etiology and Clinical characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 25
Table 4. Laboratory data/ biochemical parameters of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 26
Table 5. Drug related factors of CKD among Adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 28
Table 6. Outcome and discharge conditions of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 31
Table 7. Predictors of in-hospital mortality among adult CKD patients admitted to renal unit of JUMC from April 23 to August 23, 2018. .....**Error! Bookmark not defined.**
Table 8. Predictors of 30 day mortality among adult CKD patients admitted to renal unit of JUMC from April 23 to August 23, 2018. 33

List of Figure

Figure 1. Conceptual Framework Adopted from previous Literatures (1,16,17,39) 10

Figure 2. Selection of eligible study population of CKD patients admitted to renal unit of JUMC. 20

Figure 3. Kaplan-Meier analysis for the cumulative probability of in-hospital mortality based on the two cohort type of diagnosis at JUMC, Ethiopia from April 23 to August 23, 2018. 30

Figure 4. Kaplan-Meier analysis for the cumulative probability of 30 days mortality based on the two cohort type of diagnosis at JUMC, Ethiopia from April 23 to August 23, 2018. . 32

ABBREVIATIONS AND ACRONYMS

ACEI/ARB: Angiotensin Converting Enzyme Inhibitors/ Angiotensin Receptor Blocker
AIDS: Acquired Immunodeficiency Syndrome
AKI: Acute Kidney Injury
BMI: Body Mass Index
CG: Cockroft-Gault
CKD: Chronic Kidney Disease
DM: Diabetes Mellitus
eGFR: Estimated Glomerular Filtration Rate
ESA: Erythropoiesis-stimulating Agents
ESRD: End Stage Renal Disease
GFR**:** Glomerular Filtration Rate
HIV: Human Immune Virus
JUMC: Jimma University Medical Center
KDIGO: Kidney Disease Improving Global Outcomes
K/DOQI: Kidney Disease Outcomes Quality Initiative
MAP: Mean Arterial Pressure
MDRD: Modification of Diet in Renal Disease
MMAS: Morisky Medication Adherence Scales
RRT: Renal Replacement Therapy

1. INTRODUCTION

1.1. Background

Chronic kidney disease (CKD) is an increasing public health problems worldwide with growing incidence and prevalence, poor outcome and high costs (1,2). It is an ongoing abnormalities of kidney structure or function, present for a period of ≥ 3 months, with implications for health. It also include a patients with a glomerular filtration rate (GFR) of < 60 mL/(min·1.73 m2), as well as those with GFR > 60 mL/(min·1.73 m2) but with some evidence of kidney lesions (urinary abnormalities such as glomerular hematuria and/or micro-albuminuria/proteinuria, or alterations on kidney imaging examination) (3,4). The symptoms of CKD are not specific, and might include feeling generally unwell and experiencing a reduced appetite. Usually, CKD is diagnosed as a result of screening of people known to be at risk of kidney problems. Further, it may also be identified when it leads to one of its recognized complications. CKD frequently identified by a blood test for creatinine, which is a breakdown product of muscle metabolism and imaging techniques. Higher levels of creatinine indicate a lower glomerular filtration rate and as a result a decreased capability of the kidneys to excrete waste products (5,6).

To facilitate assessment of CKD severity, the National Kidney Foundation as part of its Kidney Disease Outcomes Quality Initiative (NKF KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines stratify CKD into 5 stages by choosing glomerular filtration rate (GFR) of 60 ml/min/1.73 m2 as a cutoff point (3,4). Among that, stage 1 and 2 are ascertained by proteinuria that shows the presence of kidney damage and reduced GFR as well. A clinically significant CKD also known as 'moderate' stages is referred by many authors to be stage 3 (GFR 30-59 ml/min/1.73m^2), stage 4 (GFR 15- 29ml /min/1.73 m^2) and stage 5 also called end stage renal disease (ESRD) is characterized by GFR below 15 % with < 60ml/min/ 1.73 m^2 chosen as a cutoff because it represents loss of about 50 % of normal renal function. While > 90 ml/min/1.73m^2 being the normal GFR (6,7).

The major adverse outcomes of CKD include progression to kidney failure and complications of decreased kidney functions which often develop when patients reach stage 3 CKD. Among these complications following CKD, the main includes: hypertension, dyslipidemia, anemia, electrolyte

abnormalities and metabolic abnormalities. Moreover, CKD is associated with frequent admission, prolonged length of hospital stay and serious adverse outcomes including increased mortality rate if its progression were not halted early. Progression of kidney disease to ESRD can be slowed if kidney disease is recognized and treated in its earlier stages (5,8,9).

Acute Kidney Injury (AKI) is defined as an increase in serum creatinine (SCr) by ≥ 0.3 mg/dl (≥ 26.5μmol/l) within 48 hours; or increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume < 0.5 ml/kg/h for 6 hours. AKI is among the most important complications observed in hospitalized patients with underlying CKD. Furthermore, some studies stated that AKI is associated with high mortality rates which is another mechanism contributing to the high mortality rates observed among patients with CKD (10–12).

Some of the studies identified older age, prevalent atherosclerotic cardiovascular disease (ASCVD), lower albumin, high CKD stage, cholesterol, proteinuria, lower GFR, poor medications compliance, cardiovascular disorders, hematological disorders, respiratory disorders, hypertension and diabetes mellitus (DM) as the common risk factors associated with CKD (5,7,13,14).

Even though a single therapy is not available for CKD, the management mainly target reducing its progression and treating associated complications besides increasing the prevention approaches toward modifiable risk factors associated with it. Hence, the management CKD complications like anemia, hypertension, hyperlipidemia and others have indispensable value in improving the quality of life in CKD patients worldwide as well as for low income country like Ethiopia were Renal Replacement Therapy (RRT) is totally an affordable for majority. However, the late presentation, absence of frequent screening, under-diagnose of CKD patients, unavailability of medications and lack of data on CKD outcome reduce the virtue of these available interventions (2,15–17).

1.2. Significance of the Study

Nowadays, with the increased prevalence in risk factors such as diabetes, hypertension, and cardiovascular disease in an aging population due to sedentary way of living and life style changes, the prevalence and burden of CKD are also expected to increase in parallel. However, there has been very limited studies undertaken to investigate and document the risk factors and treatment outcome of CKD in hospitalized patients as per the investigator's knowledge.

This study will assist in identifying the independent risk factors associated with CKD and determine its treatment outcomes. Recognizing these helps hospital set up to device strategy that mitigate illness and death related to CKD by maximizing patient care. The finding of this study will have the paramount importance to empower health care teams and CKD patients to give due attention on preventing and halting CKD progression to complicated outcomes by strengthening follow up plan & take actions on modifiable risk factors timely. The information generated would shed light on burden of CKD and be helpful as an input for health care system decision and resource allocation so that effective strategy will be developed to minimize the mortality and morbidity associated with CKD and save health care costs associated with kidney transplantation and dialysis. Moreover, with better identifying risk factors and outcome of hospitalization in CKD early and devising applicable preventive plan, the disease progression may be delayed and patients with CKD may enjoy healthier and more productive lives. Finally, the findings from this study will also serves as baseline for future studies on related topics.

1.3. Statement of the Problem

CKD is a common condition affecting numerous people along with increasingly recognized as a leading public health issue globally. An estimated 200 million people have diagnosed with CKD and the prevalence is anticipated to be 8 to 16 % worldwide (18,19). In addition, it has been recognized as a risk factor not only for a progressive kidney failure but also for cardiovascular morbidity and mortality. Furthermore, CKD is a well-known predictor of hospitalization, non-cardiac and all-cause mortality along with association with numerous complications (12,13,20).

According to the 2010 Global Burden of Disease study, CKD ranked 27th in the list of causes of total number of deaths worldwide in 1990 rose to 18th in 2010. Low or middle-income countries have the greatest burden of CKD, accounting for 80% of all cases of CKD globally. Although its prevalence is not fully studied in depth recently in Africa, its estimated to be 13.9 % in Sub-Saharan Africa (21,22). Some studies (18,23–25) have been described the prevalence of CKD among adults in Sub-Saharan Africa. On distribution, the prevalence of CKD is 83.7% in Tanzania (23), 13.5% in Botswana (24), 11.0% in Cameroon (25) and 60% in Ethiopia (1). Likewise, an adverse outcome of CKD is high for low income country probably due to late arrival of patients for diagnosis and screening or low awareness about the disease and limited diagnostic resources for routine checkup in Sub-Saharan Africa (21,22,26).

In developing countries, such as Ethiopia, chronic disease is a growing problem. Like many other chronic diseases, the incidence of CKD in Ethiopia is rising because of increased risk factors such as high blood pressure and diabetes mellitus (1,18,23). In Ethiopia, one study revealed that the prevalence of CKD is 18.2% and 23.8% as per Modification of Diet in Renal Disease (MDRD) and Cockroft-Gault (CG) equations (27), respectively while other study done at Ayder Referral and Teaching Hospital in Mekelle increase the prevalence to 60 % (25).

Even though CKD becoming prevalent in Ethiopia, I didn't come across a published researches regarding the outcomes of CKD and mortality rates in general and among hospitalized patients in particular. Additionally, determinant risk factors for CKD like aging, diabetes, obesity and cigarette smoking are highly increasing globally as well as in case of Ethiopia (27–29).

Moreover, in patients with CKD stage 5 the five-year survival rate was 38%, less than that of acquired immune deficiency syndrome (AIDS) and many cancers, which account only 18% for patients more than 65 years. Further the annual mortality rate of these patients is approximately 16% (1,16). Hence, CKD progression to ESRD and complications can be prevented or slowed by clearly drawing its major predictors and associated risk factors for their adverse outcome and planning early intervention to reduce deterioration at individual level and economic wastage at country level. Therefore, it is crucial and has a vital importance to conduct a study on the treatment outcome of CKD and its associated factors among admitted patients who attend Jimma University Medical Center (JUMC) in Jimma.

2. LITERATURE REVIEW

CKD is a global health burden with a high economic cost to health systems and is related to a series of complications of which anemia, hypertension, hyperlipidemia, metabolic bone disease (hypocalcaemia, hypophosphatemia) are the major ones which has been linked to higher morbidity and mortality and CKD progression. The global and Ethiopia related literatures on risk factors and treatment outcomes of CKD are summarized as follows:

2.1. Risk Factors of CKD

A study done in California by CY Hsu et al revealed that proteinuria, hypertension and DM were the common risk factors in patients with AKI on underlying CKD. The study involved 1,746 participants with a mean age of 65.4±14.1 in AKI on CKD patients. Further the study exposed that presence of AKI in CKD patients was associated with high mortality rates predicting the high mortality rates observed among patients with CKD (11).

A historical prospective cohort study done in United States exposed that 245 patients died and 195 patients started dialysis out of the 440 patients who reached the composite end point. Patients with time-averaged hemoglobin of < 110 g/l had highest hazard ratio for all-cause mortality (2.06) and for ESRD (2.96) compared to the group with time-averaged hemoglobin > 130 g/l. The study also revealed that older age, prevalent ASCVD, lower mean arterial pressure, lower albumin, lower cholesterol, lower proteinuria, and lower GFR were associated with higher risk of all-cause mortality while younger age, prevalent DM, higher proteinuria and lower GFR were significantly associated with higher risk of ESRD (30).

A prospective cohort study done in UK revealed that older age, current smokers; presence of baseline cardiovascular disorder, lower hemoglobin, serum albumin, baseline eGFR levels, and higher serum phosphate level were the identified predictive risk factors for CKD mortality. In addition, the study exposed that use of renin-angiotensin blocker and statins was associated with a decreased hazard ratio for death. Furthermore, the study indicated that patients with CKD stage 5 at inception into the study had a 2.5 times increased risk of death as compared to those at stage 3a (31).

A study done on the data from the Observation of Cardiovascular Risk Factors in Luxembourg (ORISCAV-LUX) exposed that hypertension and DM were independently associated with more than 3-fold and 4-fold higher risk of CKD. The study further showed that increased physical activity, high-density lipoprotein cholesterol, and gender remained independently associated with lower odds of CKD (32).

A facility based cross sectional study conducted in Butajira, southern Ethiopia revealed that older age, longer duration of diabetes, family history of kidney disease, and poor glucose control were the risk factors identified in CKD patients. Moreover, the study exposed that female sex ($p<0.008$) and obesity ($p<0.038$) were the independent risk factors for CKD.

2.2. Treatment Outcome of CKD

A prospective cohort study done by J.-P. Lafrance et al in Canada involving 6862 patients exposed that AKI on CKD patients were associated with a higher risk of in-hospital death (RR = 2.32, 95% CI = 2.04, 2.64) as compared to those without AKI. The mean age of the study population was 69.8 years and the proportion of females was 46.0%. AKI on CKD accounted 44.9% of study population. AKI on CKD was associated with both a higher risk of death (adjusted RR = 2.32, 95% CI = 2.04, 2.64) and an increased risk of dialysis (adjusted RR = 2.33, 95% CI = 2.07, 2.61). In addition, the study revealed that 18.0% of AKI on CKD cases and 13.0% of CKD only patients were died during follow up period (11).

A study on three major health insurance schemes in Thailand involving 128338 CKD patients revealed that elder age, level of care, presence of ESRD, presence of comorbidities like sepsis, respiratory failure, stroke, pneumonia, heart failure, DM and presence of CKD complications like metabolic acidosis, hyperkalemia were the predictors of in hospital mortality. Further the study stated that the common complications associated with CKD patients were anemia (30.2%), hyperkalemia (14.9%), volume overload (11.9%), and metabolic acidosis (8.2%) (19).

A prospective observational study involving 312 patients done in Manipal, India on management and treatment outcome of complications of CKD revealed that anemia and hyponatremia were the major observed complications representing 255 (81.7%) and 192 (61.5%) patients respectively. The study's maximum number of patients was in the age group of 46-60 years and it showed male

predominance (77.6%). Moreover, the study stated that metabolic acidosis (53.21%), hypophosphatemia (46.2%), hypocalcaemia (38.1%), hyperkalemia (33.7%), hyperuricemia (26.6%), and secondary hyperparathyroidism (16.67%) were the other complications. Anemia was managed by oral and parenteral iron products, erythropoietin and by blood transfusions. Furthermore, the study showed an average length of hospital stay to be 7.34 ± 4.89 days. Monotherapy or combinations of drugs like nebulisation albuterol, insulin with glucose and sodium polystyrene sulfonate was used for the management of hyperkalemia (16).

A prospective cohort study done on the prognosis of CKD patients in Italy revealed that an estimated rates (per 100 patient-years) of death and ESRD were 5.9 (95% CI: 5.2 to 6.6) and 8.3 (95% CI: 7.4 to 9.2) respectively. Further, the risk of death increased progressively from stages 3 to 5. The study cohort was characterized by advanced age (67±14 years) (33).

A prospective cohort study done in United Kingdom involving 1,325 patients with CKD stages 3-5 and mean age of 65.1 years revealed that 20% died (9.6 deaths/100 patient-years) during a median follow-up of 26 months. While 13% reached the end point of Renal Replacement Therapy (RRT) (5.1 events/100 patient-years). Further, a Markov model projections suggested a steady decrease for proportions with stages 3 and 4; a steady increase for death and RRT; and a biphasic pattern for (non-RRT) stage 5, with a plateau in the first 2 years followed by a steady decrease (31).

A prospective observational cohort study done on a potential for improved outcomes from AKI on pre-existing CKD revealed that patients with prior CKD had lower in-hospital mortality rates as compared to those with AKI only (31 versus 40%). The study involved 618 patients of which majority were male (58%) and older age were more prevalent in AKI on CKD patients. The median length of hospital stay was shorter in AKI on CKD groups as compared to AKI only group (14.7 versus 19.3 days). Furthermore, the study stated that hypertension, DM, heart failure, and coronary artery disease were more common among AKI on CKD group than AKI only group (9).

A longitudinal follow up study done in large managed care organization revealed that mortality rate were 19.5%, 24.3%, and 45.7% for patients with CKD stage 2, 3, and 4 respectively. This study also revealed that congestive heart failure, coronary artery disease, DM, and anemia were

the most prevalent conditions associated with those who died. Furthermore, the study showed that hypertension were distributed similarly over the stages (34).

2.3. Conceptual Framework

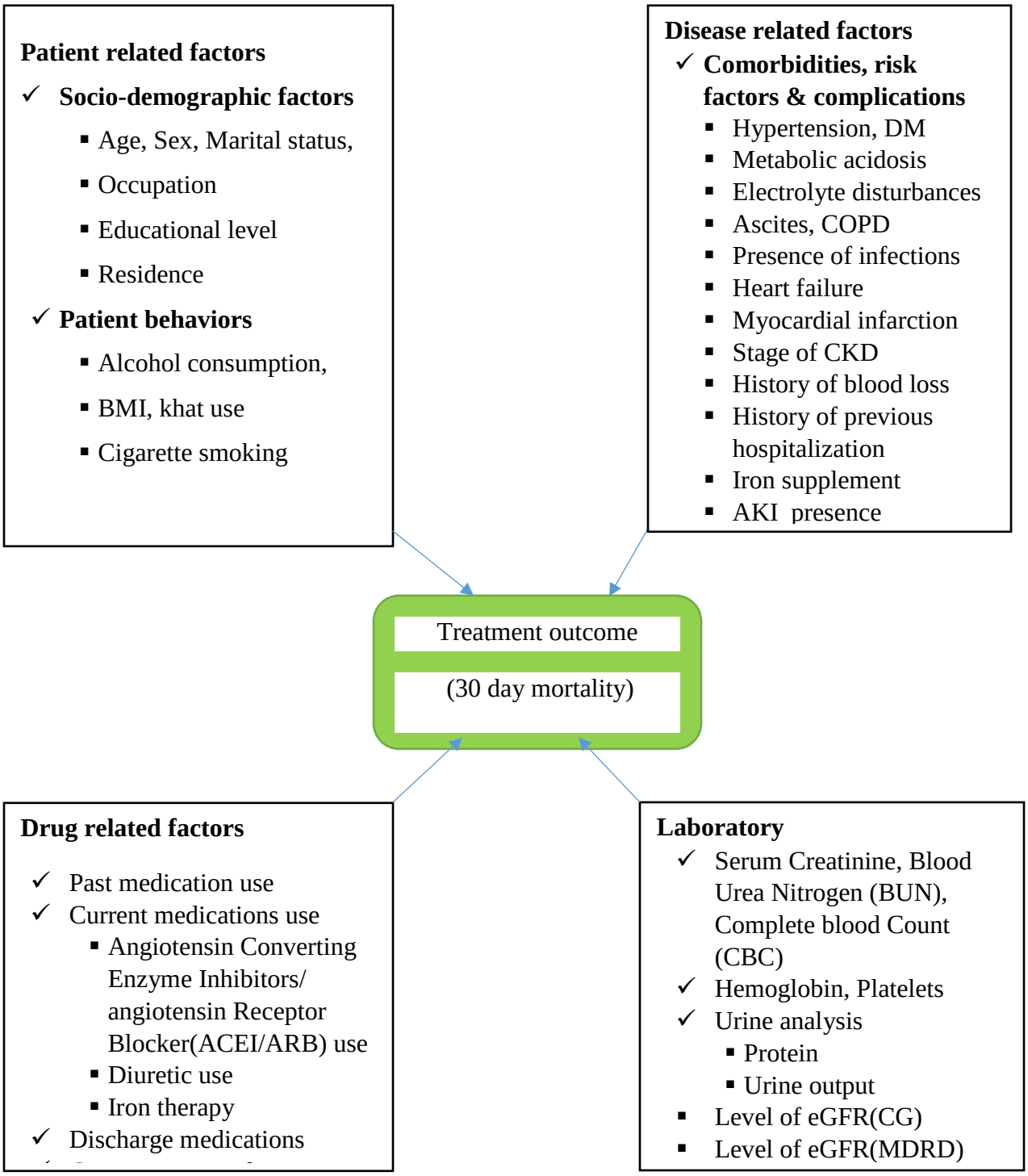

Figure 1. Conceptual framework adopted from previous literatures (2,7,9,12)

3. OBJECTIVES

3.1. General Objective

To assess treatment outcome of CKD and associated factors among hospitalized patients attending JUMC in Jimma.

3.2. Specific Objectives

- To determine the treatment outcome of CKD among admitted patients attending JUMC.
- To determine survival status of patients with CKD attending JUMC.
- To identify predictors of treatment outcome of CKD among admitted patients attending JUMC.

4. METHOD AND PARTICIPANTS

4.1. Study Area and Period

The study was conducted at JUMC, which is located in Jimma town; Jimma zone, Oromia region, Southwest Ethiopia. JUMC is the only teaching and referral medical center in the southwestern part of Ethiopia. The medical center is found in Jimma town about 352km southwest from capital city of Ethiopia, Addis Ababa. It provides specialized health services for inpatient, outpatient, emergency cases and deliveries in a year coming to the medical center from the catchment population of about 15 million people (35). The medical center also deliver renal related care in its own renal unit which own one senior specialist trained in the area and many medical interns besides medical residents working at both internal medicine and renal unit. The study was conducted from April 23 to August 23, 2018 at renal unit of JUMC.

4.2. Study Design

An institutional based prospective cohort study was conducted.

4.3. Source Population

All hospitalized CKD patients attending JUMC.

4.4. Study Population

All hospitalized patients with CKD attending medical and renal unit of JUMC during study period and fulfill the inclusion criteria.

4.5. Inclusion and Exclusion Criteria

Inclusion Criteria

All patients diagnosed with CKD and admitted to medical and renal unit of JUMC during the study period whose age was 18 years and above who were willing to participate in the study were included.

Exclusion Criteria

All patients with psychiatric problem that made them unable to respond consciously were excluded.

4.6. Sample Size and Sampling Method

The sample size was calculated using open Epi info version 3, statistical package. The exposed group was AKI on CKD group and non-exposed group was CKD only patients based on the outcome status of previous study. With this regard, a 5% level of significance, a power of 80% and 1:1 ratio of unexposed to exposed were used. The estimated proportion of mortality was 18.0 % for AKI on CKD group and 13.0% for CKD only group from previous study (12). With Epi info, the minimum sample size calculated was 180 patients. But in this study all eligible study participants hospitalized during the study period, 130 CKD patients (64 AKI on CKD and 66 CKD only patients) were included consecutively. Eligible study participants were selected by convenience sampling technique.

4.7. Study Variables

4.7.1. Independent Variables

☑ Patient Related Factors

- ✓ Socio-demographic factors
  - Age, sex, marital status
  - Educational level,
  - Occupation
  - Residence
- ✓ Behavioral factors
  - Alcohol consumption, obesity
  - Cigarette smoking,
  - Khat use

☑ Drug related factors

- ✓ Past medication use
- ✓ Current medications use
  - ACEI/ARB use
  - Diuretic use
  - Iron therapy
- ✓ Discharge medications

- ✓ Concomitant medications
- ✓ Adherence to medications

☑ Disease Related Factors

- ✓ Comorbidities, risk factors & complications
  - Hypertension, DM, Heart failure
  - Metabolic Acidosis, Ascites, COPD
  - Electrolyte disturbances, Stage of CKD
  - Presence of infections, Myocardial infarction
  - History of blood loss
  - History of previous hospitalization
  - Iron supplement, AKI presence

☑ Laboratory result

- ✓ Serum Creatinine, BUN, WBC, Hemoglobin, platelets, urine PH, urine protein, Serum electrolytes, level of eGFR (CG), level of eGFR (MDRD)

4.7.2. Dependent Variables

Treatment outcome:

- ➢ 30 day all-cause mortality

4.8. Outcome and Validation Methods of Data Analysis

In this study, CKD was diagnosed based on markers of kidney damage like presence of proteinuria/albuminuria (>300 mg/d) (albumin excretion > 30 mg/24 hour), elevated serum creatinine or presence of electrolyte & other tubular abnormality or structural abnormality detected by imaging test (renal ultrasound), or suggestive clinical sign & symptoms or history. Similarly, AKI was diagnosed mainly based on an abrupt decline of renal filtration which is evidenced by increased level of creatinine or blood urea nitrogen or renal ultrasound. After patients were diagnosed, those who had AKI on CKD were considered as exposure group while CKD only group were taken as non-exposed group in our study. The study participants were followed until the events occur or end of study period.

Mortality (in hospital and 30 days) after hospital admission of the patients was considered the outcome of the study. Hence, the patients were followed from hospital admission until death or lost from follow up or 30 day after admission or until end of study period. All patients were prospectively followed for about 4 months. The discharged participants were followed for about 30 day starting from their admission. Death ascertainment for those who died during hospitalization was based on physician on duty note. Within admission of 30 day mortality was assessed by close interview of patient family or care giver through telephone. Since most patients were died in their home without any death certificate, death of the patients was confirmed only by the information obtained from patient family or care giver.

Complication related to CKD were ascertained by different measurements. As such hypertension was confirmed in CKD patients if office blood pressure was consistently >130 mm Hg systolic or >80 mm Hg when urine albumin excretion 30 mg/24 hours. Similarly anemia was ascertained in CKD patients when hemoglobin concentration is <13.0 g/dl (<130 g/l) in males and <12.0 g/dl (<120 g/l) in females. Hyperkalemia was defined when patients serum potassium was greater than 5.5 mmol /l in study population while hyponatremia is defined as a plasma sodium concentration of <135 mmol/l.

Estimated GFR was calculated based of laboratory result of individual creatinine level for at least two times (during admission and discharge) to stratify the CKD patients into respective stages. For the purpose of this study, we calculated eGFR by MDRD equation: 186 × [serum creatinine (mg/dl)] $^{-1.154}$ × (age)$^{-0.203}$ × (0.742 if female) x (1.21, if black in race).

4.9. Data Collection Instrument and Procedures

The data collection tools was adapted from different published sources and modified to the local context. It was prepared in English, Afan Oromo and Amharic languages with the intention that the respondents understand and provide an accurate response. A Morisky Medication Adherence Scales (MMAS) was utilized to collect information regarding patient's medication adherence. Interview was used to obtain patient Socio-demographics, patient's medication experience, disease duration and adherence. The facilitator was principal investigator and he had to announce what and how of the study. The data collectors were well trained pharmacy professionals at JUMC.

Data collection tool included socio-demographic factors, CKD risk factors, CKD stage category, laboratory/ biochemical tests, approaches to the management, complication associated with CKD, outcome of the patients and length of hospital stay.

4.10. Data Quality Assurance

To ensure the quality of data, preceding data collection, training of data collectors was carried out for one day by the principal investigator on the objective, relevance of the study and confidentiality of information. Moreover, the applicability of the tool was tested on 5 % of the study population. After data was collected, its quality management analysis was undertaken by sorting either as completely filled or incompletely filled. The supervisor had the responsibility of supervising data collectors and facilitating the daily activities. Then the incompletely filled checklists were discarded and only those completely filled were used for evaluations.

4.11. Data Processing and Analysis

Data was first entered with Epi-data version 3.1. After cleaning and coding was undertaken, Statistical Package for Social Sciences (SPSS) version 21.0 was used for data analysis. Descriptive statistics such as frequency, mean, standard deviation and percentage were calculated to describe the socio-demographic characteristics, risk factors, management approaches, and discharge conditions among CKD patients admitted to renal unit of JUMC.

Chi square test and Fisher's exact test were used to determine significance of associations between categorical variables and Kolmogorov-Smirnov test was used to assess the distribution of variables. From the collected variables, to select candidate variables associated with AKI on CKD and CKD only groups for multivariable regression initially binary regression at $P<0.25$ was planned to be considered. But because of adequate variables were obtained at $P<0.05$, this was considered as cut off point for candidate selection and those identified variables at $P<0.05$ on binary cox regression were subjected to multivariable cox regression to identify predictors of mortality at hospital and 30 days period. Multivariable cox regression was run using Forward Wald method to identify paramount independent predictors of mortality of in-hospital and 30 day period.

In hospital and 30 days mortality rate was calculated by the Kaplan-Meier method. Independent predictors of CKD mortality at hospital and 30 days were investigated with the cox regression to estimate the hazard ratio of explored predictors. Interaction between covariates and AKI on CKD and CKD only group were tested. Finally, predictors with probability value (p-value) less than 0.05 was considered statistically significant.

4.12. Plan for Dissemination of Findings

The result of the study will be disseminated to Jimma University, Institute of Health, School of Pharmacy and different institutions. Further, the result will be presented for all concerned and interested bodies for utilization. Final attempt will be made to publish on reputable and well-reviewed journal.

4.13. Ethical Consideration

Ethical clearance letter was initially obtained from research ethical committee. The support letter was obtained from chief executive officer of JUMC to get permission. Further, data collectors briefed about the study to the participants stating its main objective and purpose as well as any unclear points related to the study and consent was obtained from each participant with respecting of their withdrawal at any time.

4.14. Operational and Definition of Terms

Baseline data: was a measurement occurring closest to the date of admission or on admission by clinicians.

Survival time to in-hospital mortality: is the time (days) between hospital admission and occurrence of the death as documented by the physician at duty or patient care giver or family.

Previous drinker: ex drinker (being drinker) for more than one year in the past.

Current drinker: drinking alcohol within the nearest 3 months.

Smoker: on average 2 cigarettes per day in men and 1 per day for females.

- **Non- smoker**: person who abstained from smoking for greater than 1 year.
- **Current smoker**: smoking within 1 year.

Obesity: according to the WHO, Body Mass Index (BMI) greater than or equal to 30kg/m^2.

Hypertension: previously receiving anti-hypertensive medication or when the patient was previously diagnosed with hypertension or detecting blood pressure which was consistently >130 mm Hg systolic or >80 mm Hg when urine albumin excretion 30 mg/24 hours.

Diabetes mellitus: if the patient is previously on oral hypoglycemic agents /insulin treatment or had the diagnosis of any type of DM or fasting blood glucose greater than or equal to 126 mg/dl or had a documented random blood sugar greater than or equal to 200 mg/dl or glycosylated hemoglobin of greater than or equal to 6.5 %.

Length of hospital stay: is the time gap the patient admitted to medical ward until patient discharged/ transferred to other ward, lost to follow up or died in the hospital.

Co-morbidity: presence of any two or more of morbid condition or disease that occur in one person at the same time.

Adherence: the extent to which a person's behavior taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a health care provider.

High adherence: patients who score 0 for MMAS-8 was considered as highly adherent to CKD associated medications.

Medium adherence: patients who score 1-2 for the MMAS -8 was considered to have medium adherence to CKD associated medications.

Low adherence: patients who scored ≥ 3 for the MMAS-8 was considered to have low adherence to CKD associated medications.

Elevated serum creatinine: Reduction in functional state of the kidney, which is defined with elevated serum creatinine >0.3mg/dl above standard normal level (female (0.5-0.9mg/dl: male (0.6-1.2mg/dl).

CKD and CKD classifications: CKD is an abnormalities of kidney structure or function, present for >3 months, with implications for health. It classified into 5 CKD stage based on eGFR (3,4).

AKI: an abrupt reduction in kidney function as evidenced by changes in, serum creatinine (serum creatinine), blood urea nitrogen (BUN), and urine output.

AKI on CKD patients: are patients diagnosed having acute kidney injury on already existing chronic kidney disease.

CKD only patients: are patients who diagnosed as having chronic kidney disease in the absence of acute kidney injury.

CKD complications: are the complication associated to CKD or occur due to CKD like anemia, hypertension and electrolyte disturbances as per KDIGO guideline.

Treatment outcomes: are events like death, improvement and worsened which occur during hospital stay or discharge or after discharge within 30 days (3).

Self-discharge: patients that were discharged by him/herself against medical advice or lost from follow up.

Event: patient who were died in hospital or after discharge within 30 days.

Censored: patients who were lost to follow up, self-discharge, transferred/ referred to other set up or did not experience the event during follow up period.

5. RESULTS

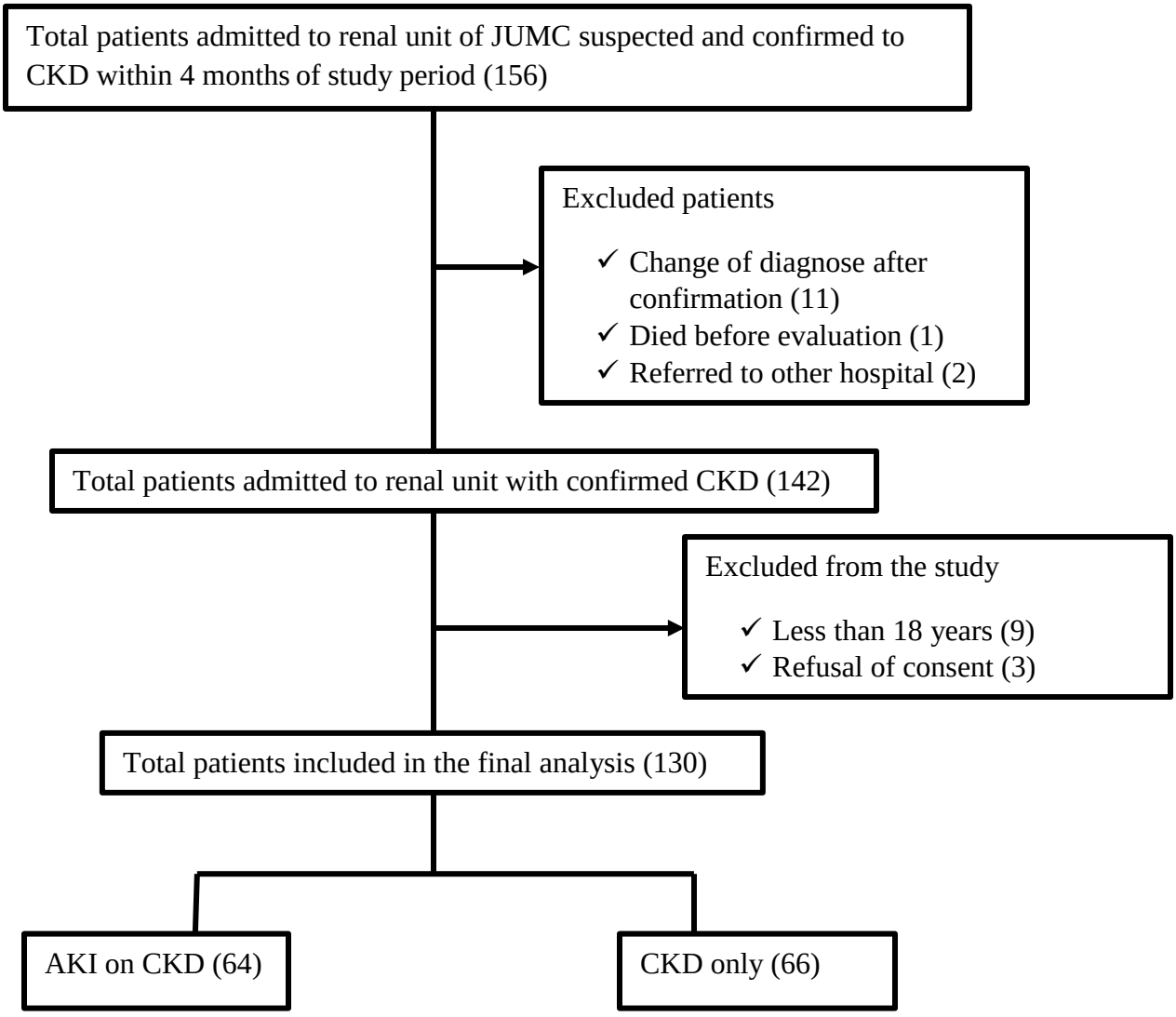

Figure 2. Selection of eligible study population of CKD patients admitted to renal unit of JUMC.

There were a total of 660 medical admissions with 128 in hospital mortality. Out of 142 CKD admissions in-hospital mortality was recorded in 22 patients. Hence, CKD accounted 21.5% of total medical admissions and 17.2% of the total cases of in-hospital mortality during the study period. One hundred forty two patients were admitted to renal unit with suspected diagnosis of CKD and 12 patients were excluded from the study for various reasons during the follow up period (figure 2). Consequently, 130 study participants obtained during the study period were included in the final analysis.

5.1. Baseline Socio-demographic Characteristics of Patients

One hundred thirty patients participated in the study, of which 92(70.8 %) were males. The mean (±SD) age of the patients was 40.00(±15.67) years and the incidence of CKD was high in the age group of greater than forty years which comprised of 65(50.0%) followed by those less than twenty nine years old 39 (30.0%). Young AKI on CKD (18-29years) comprised of 30.0% of all patients. Mean age of patients with AKI on CKD was 42.44±17.430 years as shown in table 1.

109(83.8%) were from rural area and 63(48.5%) subjects had no basic education (unable to read and write). Equal participants 25(19.2%) had informal education (able to read and write) and elementary school history. Only 5(3.8%) of them attended college and above education. More than half of the participants were farmers 79(60.8%) followed by merchant 20(15.4%) and students 14(10.8%). About 82(63.1%) were Muslim by religion and 109(83.8%) subjects were married as shown in table 1.

Table 1. Baseline socio-demographic characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018, Ethiopia.

Socio-demographic and other patient related factors		**Total patients**	**CKD only**	**AKI on CKD**	**P-value**
Sex	Male	92 (70.8%)	47 (71.2%)	45 (70.3%)	0.910
	Female	38 (29.2%)	19 (28.8%)	19 (29.7%)	
Age (years)	Mean ± SD	40.00±15.67	37.64±13.457	42.44±17.430	0.230
Age (years)	18-29	39 (30.0%)	20 (30.3%)	19 (29.7%)	0.079
	30-39	26 (20.0%)	18 (27.3%)	8 (12.5%)	
	≥40	65 (50.0%)	28 (42.4%)	37 (57.8%)	
Residence	Rural	109 (83.8%)	53 (80.3%)	56 (87.5%)	0.265
	Urban	21 (16.2%)	13 (19.7%)	8 (12.5%)	
Level of education	Unable to read	63 (48.5%)	30 (45.5%)	33 (51.6%)	0.851
	Able to read	25 (19.2%)	15 (22.7%)	10 (15.6%)	
	Elementary	25 (19.2%)	12 (18.2%)	13 (20.3%)	
	Secondary	12 (9.2%)	6 (9.1%)	6 (9.4%)	
	College & above	5 (3.8%)	3 (4.5%)	2 (3.1%)	
Occupational status	Farmer	79 (60.8%)	38 (57.6%)	41 (64.1%)	0.958
	Merchant	20 (15.4%)	11 (16.7%)	9 (14.1%)	

	Student	14 (10.8%)	8 (12.1%)	6 (9.4%)	
	Employed	4 (3.1%)	2 (3.0%)	2 (3.1%)	
	Unemployed	13 (10.0 %)	7 (10.6%)	6 (9.4%)	
Religion	Orthodox	36 (27.7 %)	21 (31.8%)	15 (23.4%)	0.311
	Muslim	82 (63.1 %)	41 (62.1%)	41 (64.1%)	
	Protestant	12 (9.2%)	4 (6.1%)	8 (12.5%)	
Marital status	Single	18 (13.8%)	9 (13.6%)	9 (14.1%)	0.126
	Married	109 (83.8%)	54 (81.8%)	55 (85.9%)	
	divorced	3 (2.3%)	3 (4.5%)	0 (0.0%)	
Income (monthly)	< 500ETB	62 (47.7%)	27 (40.9%)	35 (54.7%)	0.116
	≥ 500ETB	68 (52.3%)	39 (59.1%)	29 (45.3%)	
Tobacco use	Past smoker	30 (23.1%)	12 (18.2%)	18 (28.1%)	0.327
	Current smoker	5 (3.8%)	2 (3.0%)	3 (4.7%)	
	Non-smoker	95 (73.1%)	52 (78.8%)	43 (67.2%)	
Khat use	Yes	62 (47.7%)	33 (50.0%)	29 (45.3%)	0.593
	No	68 (52.3%)	33 (50.0%)	35 (54.7%)	
Alcohol use	Past drinker	9 (6.9%)	2 (3.0%)	7 (10.9%)	0.174
	Current drinker	21 (16.2%)	12 (18.2%)	9 (14.1%)	
	Never	100 (76.9%)	52 (78.8%)	48 (75.0%)	
Physical inactivity	Yes	75 (57.7%)	57 (86.4%)	18 (28.1%)	<0.001
	No	55 (42.3%)	9 (13.6%)	46 (71.9%)	
BMI	< 18.5	16 (12.3%)	8 (12.1%)	8 (12.5%)	0.465
	18.5-25	107 (82.3%)	56 (84.8%)	51 (79.7%)	
	≥25	7 (5.4%)	2 (3.0%)	5 (7.8%)	

*ETB: Ethiopian Birr, BMI: Body Mass Index, SD: Standard Deviation

5.2. Disease Related Factors

Out of 130 CKD patients, 74(56.9%) were known CKD patients and 12 (9.2%) patients were diagnosed before three years. 64(49.2%) of patients were diagnosed as AKI on CKD while 66(50.8%) of cases were diagnosed as CKD alone. Common risk factors reported in AKI on CKD patients include ascites 56(87.5%) followed by previous hospitalization 42(65.6%), and family history of CKD 13(20.3%). Previous hospitalization 51(77.3%), heart failure 22(33.3%) and DM 20(30.3%) were the common risk factors reported in CKD only patients as shown in table 2.

Fifty three (82.8%) patients from AKI on CKD group and 45(68.2%) of CKD only patients were in CKD stage 5 as MDRD equation on admission. Following this, stage 4 and 3b were the next prevalent stage as MDRD equation accounting 16(12.3%) and 8(6.2%) respectively. Ninety three (71.5%) of patients had prior history of admission and 21(16.2%) had other kidney disease comorbidity.

Concerning distribution of co-morbidity and risk factors, ascites 71(54.6%), heart failure 35(26.9%), and DM 30(23.1%), were the leading co-morbidity and risk factors identified among all the participants. Among the participants, 28(21.5%) had family history of CKD while 24(18.5%) had family history of HTN as shown in table 2.

The predominant primary etiology of CKD was Diabetes Nephropathy 12(9.2%) followed by Glomerulonephritis 6(4.6%) and hypertension/renovascular 3(2.3%). 101(77.7%) of the participants had at least one CKD associated complications at admission. Out of these, anemia 93(71.5%), hypertension 66(50.8%), and electrolyte disturbance 41(31.5%) were the most frequent complications associated with CKD as shown in table 3.

Table 2. Risk factors and Clinical characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Disease related factors			**Total patients**	**CKD only**	**AKI on CKD**	**P-value**
Risk factors and Co-morbidities	Ascites		71 (54.6%)	15 (22.7%)	56 (87.5%)	<0.001
	Heart failure		35 (26.9%)	22 (33.3%)	13 (20.3%)	0.094
	Diabetes mellitus		30 (23.1%)	20 (30.3%)	10 (15.6%)	0.047
	MI		22 (16.9%)	15 (22.7%)	7 (10.9%)	0.073
	Blood loss		14 (10.8%)	8 (12.1%)	6 (9.4%)	0.615
	COPD		2 (1.5%)	0 (0.0%)	2 (3.1%)	0.240
	Family history of CKD		28 (21.5%)	15 (22.7%)	13 (20.3%)	0.738
	Family history of HTN		24 (18.5%)	13 (19.7%)	11 (17.2%)	0.712
	Other kidney disease		21 (16.2%)	12 (18.2%)	9 (14.1%)	0.523
	Previous hospitalization		93 (71.5%)	51 (77.3%)	42 (65.6%)	0.141
	CKD status	New	56 (43.1%)	30 (45.5%)	26 (40.6%)	0.578
		Known	74 (56.9%)	36 (54.5%)	38 (59.4%)	
	CKD duration status	<1 month	56 (43.1%)	31 (47.0%)	25 (39.1%)	0.565
		b/n 1-6 month	27 (20.8%)	13 (19.7%)	14 (21.9%)	
		b/n 6 months-3 years	35 (26.9%)	18 (27.3%)	17 (26.6%)	
		≥3 years	12 (9.2%)	4 (6.1%)	8 (12.5%)	
	Stage of CKD at admission (MDRD)	Stage 1	1 (0.8%)	1 (1.5%)	0 (0.0%)	0.145
		Stage 2	3 (2.3%)	1 (1.5%)	2 (3.1%)	
		Stage 3a	4 (3.1%)	2 (3.0%)	2 (3.1%)	
		Stage 3b	8 (6.2%)	4 (6.1%)	4 (6.3%)	
		Stage 4	16 (12.3%)	13 (19.7%)	3 (4.7%)	
		Stage 5	98 (75.4%)	45 (68.2%)	53 (82.8%)	

*COPD: Chronic Obstruction Pulmonary Disease, HTN: Hypertension, MI: Myocardial Infarction, MDRD: Modification of Diet in Renal Disease, CG: Cockcroft-Gault, AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease.

Table 3. Etiology and Clinical characteristics of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Disease related factors			**Total patients**	**CKD only**	**AKI on CKD**	**P-value**
Primary cause of renal disease		glomerulonephritis	6(4.6%)	5(7.6%)	1(1.6%)	0.036
		Hypertension /renovascular	3(2.3%)	2(3.0%)	1(1.6%)	
		diabetes nephropathy	12(9.2%)	9(13.6%)	3(4.7%)	
		interstitial nephritis	2(1.5%)	2(3.0%)	0(0.0%)	
		Unknown	107(82.3%)	48(72.7%)	59(92.2%)	
CKD related complication	CKD Complication		101(77.7%)	51(77.3%)	50(78.1%)	0.907
	Anemia	Mild	12(9.2%)	1(2.1%)	11(23.9%)	<0.001
		Moderate	29(22.3%)	6(12.8%)	23(50.0%)	
		Severe	52(40.0%)	40(85.1%)	12(26.1%)	
	Hypertension		66(50.8%)	34(51.5%)	32(50.0%)	0.863
	Electrolyte disturbances		41(31.5%)	21(31.8%)	20(31.3%)	0.944
	Metabolic acidosis		17(13.1%)	14(21.2%)	3(4.7%)	0.005
	Dyslipidemia		4(3.1%)	3(4.5%)	1(1.6%)	0.321

* AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease.

5.3. Laboratory Data/Biochemical Parameters of the Patients

Regarding renal function tests, majority of the participants had elevated serum creatinine 129(99.2%) and blood urea nitrogen level 124(95.4%) at baseline. The elevated serum creatinine had no significant difference between AKI on CKD and CKD only groups (P=0.508).The mean of eGFR of the participants was found to be 12.56(SD ±11.39) ml/min per 1.73 m^2 by Cockcroft Gault and 14.58(SD±15.60) per modification of diet for renal disease (MDRD) equation. There is no significant difference between AKI on CKD and CKD only groups on mean eGFR by CG and MDRD, (P=0.270 and P=0.151) respectively as shown in table 4.

At baseline, majority of the participants had normal Calcium, Chlorine, Potassium, Sodium, and PH level. More than three fourth of the participants had low hemoglobin level 105(80.8%) while

23(17.7%) were within normal range. Concerning white blood cell count, those within normal range, leukocytosis and leukopenia were account 47.7%, 36.9%, and 15.4% respectively. The mean urine output for CKD only and AKI on CKD group were 711.82± 302.497 and 705.08±438.368 respectively, with no significant difference between the groups (P=0.129).

Table 4. Laboratory data/ biochemical parameters of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Laboratory parameters			**Total patients**	**CKD only**	**AKI on CKD**	**P-value**
Renal function tests	Serum Creatinine	Normal	1(0.8%)	1(1.5%)	0(0.0%)	0.508
		Elevated	129(99.2%)	65(98.5%)	64(100.0%)	
	BUN or Urea	Normal	6(4.6%)	3(4.5%)	3(4.7%)	0.645
		Elevated	124(95.4%)	63(95.5%)	61(95.3%)	
	eGFR (CG)	Mean ± SD	12.56±11.39	13.9485±11.36	11.1388±11.35	0.270
	eGFR (MDRD)	Mean ± SD	14.58±15.60	16.6171±17.43	12.4804±13.28	0.151
Complete blood count with differential cell count	White blood cells/ microliter	Normal	62(47.7%)	27(40.9%)	35(54.7%)	0.279
		Leukocytosis	48(36.9%)	27(40.9%)	21(32.8%)	
		Leukopenia	20(15.4%)	12(18.2%)	8(12.5%)	
	Hemoglobin (g/dl)	Low	105(80.8%)	52(78.8%)	53(82.8%)	0.831
		Normal	23(17.7%)	13(19.7%)	10(15.6%)	
		Elevated	2(1.5%)	1(1.5%)	1(1.6%)	
	MCV	Normocytic	35(26.9%)	19(28.8%)	16(25.0%)	0.626
		Microcytic	95(73.1%)	47(71.2%)	48(75.0%)	
	Platelet counts	Normal	118(90.8%)	61(92.4%)	57(89.1%)	0.453
		Thrombocytopenia	11(8.5%)	5(7.6%)	6(9.4%)	
		Thrombocytosis	1(0.8%)	0(0.0%)	1(1.6%)	
Serum electrolytes done	Sodium	Normal	110(84.6%)	59(89.4%)	51(79.7%)	0.125
		Low	20(15.4%)	7(10.6%)	13(20.3%)	
	Potassium	Normal	93(71.5%)	45(68.2%)	48(75.0%)	0.661
		Low	4(3.1%)	2(3.0%)	2(3.1%)	

		Elevated	33(25.4%)	19(28.8%)	14(21.9%)	
	Calcium	Normal	113(86.9%)	57(86.4%)	56(87.5%)	0.848
		Low	17(13.1%)	9(13.6%)	8(12.5%)	
	Chlorine	Normal	102(78.5%)	50(75.8%)	52(81.3%)	0.521
		Low	5(3.8%)	2(3.0%)	3(4.7%)	
		Elevated	23(17.7%)	14(21.2%)	9(14.1%)	
	PH	Normal	113(86.9%)	57(86.4%)	56(87.5%)	0.848
		Low	17(13.1 %)	9(13.6%)	8(12.5%)	
Urine analysis	Blood		50(38.5%)	23(34.8%)	27(42.2%)	0.390
	Glucose		7(5.4%)	6(9.1%)	1(1.6%)	0.062
	Protein		124(95.4%)	62(93.9%)	62(96.9%)	0.355
	Urine output	Mean ± SD	708.50 ± 374.12	711.82± 302.49	705.08±438.37	0.129

*SD: Standard deviation, MCV: Mean Corpuscular Volume, BUN: Blood Urea Nitrogen, eGFR: estimated Glomerular Filtration Rate, MDRD: Modification of Diet in Renal Disease, CG: Cockcroft-Gault, AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease.

5.4. Drug Related Factors

Of the total patients included in the study, 99 (76.2%) had at least one past medication. The most common past medication was ACEIs/ARBs 23 (17.7%) followed by anti-ulcer 20 (15.4%) and diuretics 17(13.1%). Past medication history were more apparent in CKD only group (54.5%) as compared to AKI on CKD group (53.1%) but statistically not significant (P=0.871). All the past medications were used by both AKI on CKD patients as well as CKD only patients.

During hospitalization, all patients both AKI on CKD and CKD only patients had received at least one medication. The most common medication given for the patients was furosemide, 99 (76.2%) followed by ceftriaxone, 76 (58.5%), and amlodipine, 58 (44.6%). Nifedipine, norfloxacillin, anti-pains were solely given to CKD only groups while captopril was given to AKI on CKD group. Enalapril was mainly given for CKD only patients, but 2 patients with AKI on CKD were received this medication since the diagnosis was changed later. Seventy patients (53.8%) had received at least one medication during discharge. Out of these, 54.5% were CKD only patients while 53.1% were AKI on CKD patients. Ferrous sulphate 49 (37.7%), amlodipine 31(23.8%) and furosemide 13 (10.0%) were among mostly given medications during discharge as shown in table 5.

As it was assessed by MMAS, majority of the patients were low adherence to their medication which accounts 111 (85.4%) while 9 (6.9%) showed to have high adherence level and the rest were scored medium adherence level to each of the prescribed medication they were taking during study period. High adherence level was apparent in CKD only groups as compared to AKI on CKD group but the difference was not statistically significant as shown in table 5.

Table 5. Drug related factors of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Management protocols			**Total patients**	**CKD only**	**AKI on CKD**
Past medication history (n=99)	ACEIs/ARBs		23 (17.7%)	21(31.8%)	2(3.1%)
	Anti-ulcer		20 (15.4%)	7(10.6%)	13(20.3%)
	Diuretics		17 (13.1%)	6(9.1%)	11(17.5%)
	Unknown medications ✯		15 (11.5%)	3(4.5%)	12(18.8%)
	Others ★		16 (12.3%)	8(12.1%)	8(12.5%)
Medication given during hospitalization	Diuretics	furosemide	99 (76.2%)	47(47.5%	52(52.5%)
		hydrochlorothiazide	4 (3.1%)	3(75.0%)	1(25.0%)
	ACEIs	Enalapril	41 (31.5%)	39(59.1%)	2(3.1%)
		Captopril	3 (2.3%)	3(4.5%)	0(0.0%)
	CCB	Amlodipine	58 (44.6%)	32(48.5%)	26(40.6%)
		Nifedipine	2 (1.5%)	0(0.0%)	2(3.1%)
	Anti-microbials	Ceftriaxone	76 (58.5%)	40(60.6%)	36(56.3%)
		Azithromycin	16 (12.3%)	10(15.2%)	6(9.4%)
		Other anti-microbials ✖	9(6.9%)	6(9.1%)	3(4.7%)
		Anti-ulcer	50(38.5%)	23(34.8%)	27(42.2%)
		Other miscellaneous medications ▲	16 (12.3%)	9(13.6%)	7(10.9%)
Medications at discharge		Ferrous sulphate	49(37.7%)	26(39.4%)	23(35.9%)
		Amlodipine	31(23.8%)	15(22.7%)	16(25.0%)

	Furosemide/ Lasix	13(10.0%)	6(9.1%)	7(10.9%)
	Other discharge medications⁂	12(9.2%)	8(12.1%)	4(6.3%)
Adherence level	High	9(6.9%)	8(12.1%)	1(1.6%)
	Medium	10(7.7%)	5(7.6%)	5(7.8%)
	Low	111(85.4%)	53(80.3%)	58(90.6%)

*ACEIs: angiotensin converting enzyme inhibitors, ARBs: angiotensin Ⅱ receptor blockers/antagonist, BB: beta blockers, CCB: calcium channel blockers, KCL: potassium chloride, NPH: neutral protamine hagedorn

★Others: this were past medications given other than those mentioned above which had small frequency like aspirin, hydralazine, paracetamol, etc.

⍟Unknown medications: past medications which were reported by patients and not available at hand during period of data collection.

✖Other anti-microbial: those anti-microbial medications given during stay which had small frequency like cotrimoxazole, doxycycline, vancomycin, etc.

▲Other miscellaneous medications: those medications like bisocodyl, salbutamol, vitamin B complex, etc.

⁂Other discharge medications: those medications given during discharge other than those mentioned discharge medications which had small frequency like phenobarbital, digoxin, vitamin B complex, etc.

5.5. Outcomes and Discharge Condition of the Patients

A total of 108(83.1%) patients were discharged alive making hospital mortality rate of 22(16.9%). Out of those discharged alive, 69(53.1%) with improvement, 11(8.5%) with worsened/complicated and 28(21.5%) were self-discharged. More patients with CKD only were discharged with improvement compared to patients with AKI on CKD (57.6% versus 48.4%) as shown in table 6.

Fifty nine (45.4%) of the patients were at CKD stage 5 during discharge by MDRD equation followed by CKD stage 4 and stage 3b accounting 39 (30.0%) and 15 (11.5%) respectively. CKD stage 3a constituted 10 (7.7%) while stage 2 account 7 (5.4%). CKD stage 5 were more evident in AKI on CKD patients 41 (64.1%) as compared to CKD only patients 24 (36.4%).

The mean length of hospital stay among the study participants was 10.99 ± 8.17 which range from 1 to 41 days. AKI on CKD patients had 9.328±7.305 mean length of hospital stay while CKD only patients had 12.606±8.691 mean length of hospital stay. 46 (35.4%) patients were discharged within 7 days while 29 (22.3%) patients stayed for greater than two weeks as shown in table 6.

The mean length of survival after hospital admission for patients who died in hospital was 7.50±8.34 days (1.0-29.0 days). The mean length of survival after hospital admission for AKI on CKD and CKD only patients who died at hospital was 6.64±6.96 days and 9.00±10.70 days, respectively.

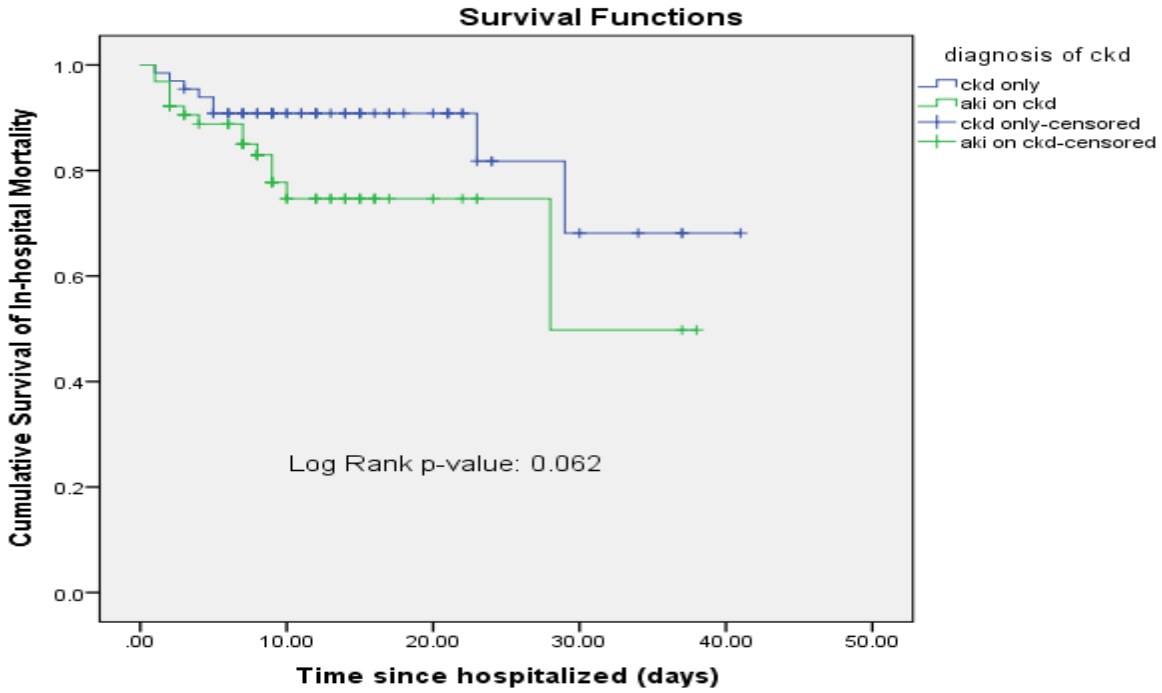

Figure 3. Kaplan-Meier analysis for the cumulative probability of in-hospital mortality based on the two cohort type of diagnosis at JUMC, Ethiopia from April 23 to August 23, 2018.

The survival time related to in-hospital mortality was compared graphically between the AKI on CKD and CKD only groups using Kaplan-Meier curve and statistically tested using Log-rank test. Kaplan-Meier analysis showed that there was no significant difference in survival time to in-hospital mortality between the two groups (P=0.062) as shown in figure 3.

Table 6. Outcome and discharge conditions of CKD among adult patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Outcome and discharge conditions		Total patients	CKD only	AKI on CKD	P-value
Status of the patients during discharge	Improved	69(53.1%)	38(57.6%)	31(48.4%)	0.492
	Dead	22(16.9%)	8(12.1%)	14(21.9%)	
	Self-discharge	28(21.5%)	14(21.2%)	14(21.9%)	
	Worsened/complicated	11(8.5%)	6(9.1%)	5(7.8%)	
CKD stage at discharge by MDRD	Stage 2	7(5.4%)	4(6.1%)	3(4.7%)	0.002
	Stage 3a	10(7.7%)	5(7.6%)	5(7.8%)	
	Stage 3b	15(11.5%)	13(19.7%)	2(3.1%)	
	Stage 4	39(30.0%)	24(36.4%)	15(23.4%)	
	Stage 5	59(45.4%)	20(30.3%)	39(60.9%)	
Length of hospital stay(days)	Mean ±SD(days)	10.992 ± 8.175	12.606±8.691	9.328±7.305	0.112
	≤ 7 days	46(35.4%)	20(30.3%)	26(40.6%)	
	8-14 days	55(42.3%)	25(37.9%)	30(46.9%)	
	≥ 15 days	29(22.3%)	21(31.8%)	8(12.5%)	

∗ CG: Cockcroft-Gault, MDRD: Modification of Diet for Renal Disease, SD: standard deviation.

5.6. 30 Day Mortality Follow up Outcome

At 30-day follow up, 91(70.0%) patients were still alive, 17(13.1%) patients were died. The 30 day total mortality in study population was 39(30.0%) making 23 (35.9%) for AKI on CKD and 16(24.2%) for CKD only group which was statistically significant (AHR: 0.456, 95% CI: 0.239-0.872, P=0.018).

The mean length of survival after hospital admission for patients who died within 30 days was 16.41±6.86 days (2.0-24.0 days). The mean length of survival after hospital admission for AKI on CKD and CKD only patients died within 30 days was14.00±7.60 days and 19.13±5.08 days, respectively.

Seven potential predictors of satisfactory outcome were selected to predict 30-days mortality at bivariate cox regression analysis using P<0.05. From socio-demographic characteristics, sex and age of the patients, from disease related risk factors, diagnosis at admission, presence of complication related to CKD, family history of CKD and HTN and from protocols of CKD management, ACEI usage were selected to be included in multivariate cox regression. Up on multivariate cox regression sex of the patients, family history of hypertension, diagnosis at admission, and complication related to CKD were the independent predictors of 30 days mortality in the patients with CKD during the study period.

As such, male patients are dying at the rate of 2.66 times greater than female patients throughout 30 days observational follow up period (AHR: 2.66, 95% CI: 1.21-5.88). In addition, the risk (rate) of death in patients who had family history of HTN have 71.0 % reduction than those patients without family history of HTN during 30 days follow up (AHR: 0.29, 95% CI: 0.10-0.85). Further, patients who were diagnosed as AKI on CKD at admission are dying at the rate of 2.46 times greater than those patients diagnosed as CKD only during 30 days observational follow up period (AHR: 2.46, 95% CI: 1.26-4.78). Moreover, patients who had CKD related complication are dying at the rate of 5.38 times greater than patients without CKD related complication throughout 30 days follow up period (AHR: 5.38, 95% CI: 1.64-17.72) as shown in table 8.

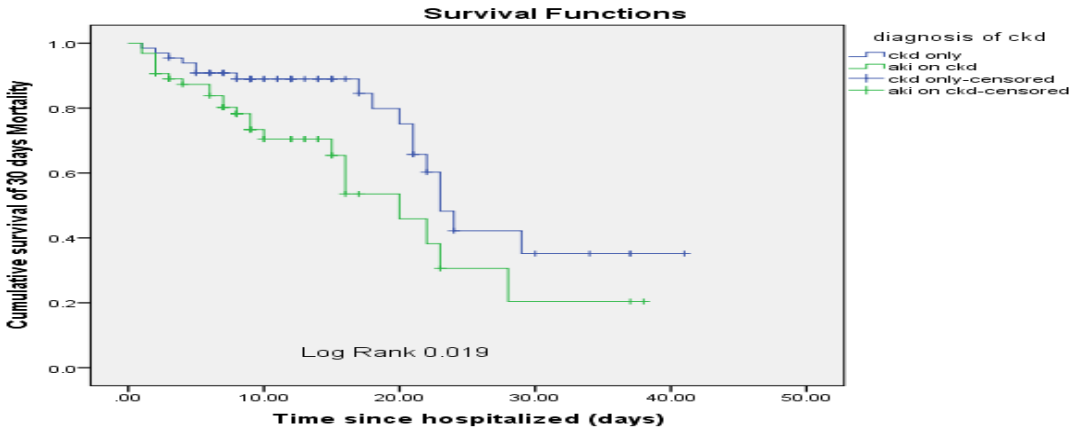

Figure 4. Kaplan-Meier analysis for the cumulative probability of 30 days mortality based on the two cohort type of diagnosis at JUMC, Ethiopia from April 23 to August 23, 2018.

The survival time related to 30 days mortality was compared graphically between the AKI on CKD and CKD only groups using Kaplan-Meier curve and Log-rank test for statistical significance.

Kaplan-Meier analysis showed that there was significant difference in survival time to 30 days mortality between the two groups (P=0.019) as shown in figure 4.

Table 7. Predictors of 30 day mortality among adult CKD patients admitted to renal unit of JUMC from April 23 to August 23, 2018.

Variables		**Mortality (at 30 day)**	**Censored**	**CHR 95% CI**	**P-value**	**AHR 95% CI**	**P-value**
Sex	Male	32	60	2.306(1.050-5.066)	0.037	2.66(1.21-5.88)	**0.015**
	Female	8	30	1.00			
Age	18-29	8	31	1.00			
	30-39	6	20	1.381(0.478-3.989)	0.551		
	40-90	26	39	2.341(1.059-5.175)	0.036		
Family history of CKD	Yes	3	25	0.284(0.087-0.923)	0.036		
	No	37	65	1.00			
Family history of HTN	Yes	36	70	0.325(0.115-0.919)	0.034	0.29(0.10-0.85)	**0.024**
	No	4	20	1.00			
Diagnosis at admission	AKI on CKD	23	41	2.089 (1.105-3.947)	0.023	2.46(1.26-4.78)	**0.008**
	CKD only	17	49	1.00			
ACEI	Yes	21	55	0.481(0.241-0.962)	0.038		
	No	19	35	1.00			
Complications of CKD	Yes	37	64	5.719(1.747-18.717)	0.004	5.38(1.64-17.72)	**0.006**
	No	3	26	1.00			

*AHR: Adjusted Hazard Ratio, AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease, HTN: Hypertension, ACEI: Angiotensin Converting Enzyme Inhibitors.

6. DISCUSSION

This is prospective cohort study conducted on CKD patients in JUMC, Ethiopia to identify treatment outcome and its determinants. The patients who develop event were 30.0 % while those censored were 70.0 % during the study period.

The mean age of CKD patients was 40.00±15.67 years, which was higher compared to study in Nigeria which was 28.3±9.7 years (22) and lower as compared to study in Philadelphia (36), Thailand (37) and Manchester, UK (31)**.** But it was similar to study in Ethiopia and Cameroon (25,38). Mean age for AKI on CKD was 42.44±17.43 years, which was differ from study by Nitin Khosla et al in California in which the mean age was 65.6 years (9). The differences in age specific incidence rates reflect etiological differences which could be explained by survival bias and development related life span difference between countries.

The incidence of CKD was maximum in the age greater than 40 years, this was in contrary to studies in Thailand and Philadelphia (17,36) in which majority of the patients were elderly, but similar to global trend as well as to studies in Nigeria and India (22,36). Difference in population distribution pyramid, awareness of risk factors and their control could be the possible explanation of this difference. Young CKD patients accounted more than one third (30.0%) of all patients which was higher than studies in Ethiopia and Philadelphia (1,36) but similar to study in Tanzania which was comprised 28 % (39). This gap may be explained as the difference of study population inclusion criteria among the studies as some include only diabetic patients while other include outpatients which is contrary to this study. This difference could be due to socioeconomic gap among different population and type of set up as being referral center could overestimate the youth age groups relative to other age categories.

The prevalence of CKD (21.5%) was lower than some studies (1,23) in Tanzania (83.7%) and Ethiopia (60%) but higher than other studies (25,27) in southern part of Ethiopia and Cameroon. This discrepancy could be explained as a difference in inclusion criteria of the study and type of setting in which some were the only referral at the area and includes specifically defined population with some comorbidities.

The most common primary etiology of CKD were Diabetes Nephropathy and Glomerulonephritis, which was consistent to worldwide trend & to studies in China, UK and Korea (40–42). Unlike this, other dominant primary etiology of CKD were revealed in study by Borja Quiroga et al (43). Genetic makeup population difference and awareness to common etiologic risk factors may the possible reason for this discrepancy.

The male predominance in CKD patients comply with other studies (16,27,38,44,45). But this was unlike to some studies where female patients were dominant (37,46,47). The possible explanation of the sex difference may be due to increased risk factors such as cigarette smoking, alcohol consumption in male and hormonal difference as well as increment of this practices in female nowadays beside sample size difference.

During hospitalization almost all of the patients had received at least one medication. Majority of the medications were given during hospitalization for the treatment of CKD related complications, underlying comorbid conditions and symptomatic relief. Accordingly, the most common medication given for the patient were furosemide for the symptomatic relief and comorbidities, which was contrary to the studies (37,41,48) in Thailand, UK and Pennsylvania (USA) in which other medications like ACEI and erythropoietin stimulating agents were common. This discrepancy may be due to the hypertensive and other risk factors prevalence difference and availability of the medications.

Majority of the CKD patients were classified in CKD stage 5,4 and 3b in decreasing order by MDRD equation, which was similar to some studies (15,16,31,49) but contrary to other studies (25,38). This discrepancy could be explained by our small sample size and single center based design of the study.

Ascites, heart failure and diabetes mellitus were the common comorbid risk factors identified in this study. This was in contrary to the studies (1,7,13) in which hypertension, DM, cigarette smoking, older age, obesity and overweight were the common identified risk factors. This is likely due to the variance in width of study subject inclusion and demographic difference in population at study. Moreover, it could be due to absence of vigorous follow up and checkup of the study population and less awareness for timely screening before admission.

The mean length of hospital stay of the patients was 10.99 ± 8.175 days which was shorter than other studies (9,50) in five academic medical centers and Taiwan. This could be explained as critical ill patients of the study population were rapidly self-discharged and go to other facility in search of better management. Other reason could be due to rapid discharge of patients with improvements with medical advice due to limited bed in renal unit of the center. This length of hospital stay was longer as compared to study by George et al in South Indian tertiary care hospital which 7.34 ± 4.89 days (16). This gap may be due to better management and care of the patients at the setup which might rapidly enhance improvement and discharge of the patients.

In this study, in-hospital CKD mortality rate was (16.9%) which was higher as compared to studies in India which is 0.96 % (16), 5.9 % in China (51) and 12.4% in Thailand (20). But, it was lower as compared to study by Hoefield et al in UK which was 20% (41) and by Nitin Khosla et al which is 31% (9). The difference in-hospital mortality rate could be explained by different way of diagnosis approach, risk factors identification, complications, in hospital patient care and population size included. Moreover, it could be due to difference inadequate management like absence of important medications and late arrival of study population at the hospital. The hospital mean survival time for patients who died in hospital was 7.50±8.34 days which was earlier as compared to study by Anutrakulchai et al (20). This may be due to late arrival of the patients to the facility and difference in hospital care.

The 30 day total mortality in study population was 30.0% which is lower than the study by Goswami et al (52) and the study by D. Juneja et al particularly in which the rate was 41.1 % (8). But it was higher than the study by Madero et al (53). This difference may be occur as variance in the study period and exclusion of important comorbidities in some of the study while not in the others. The 30 day mortality was high in AKI on CKD (35.9%) as compared to CKD only group (24.2%) which is similar to study by J.-P. Lafrance et al (12). This could be due to presence of more complication and additional contributory mechanisms of AKI effect on underlying CKD. Furthermore, AKI is a risk factor for development and accelerated progression of CKD which finally lead to more death.

Sex of the patients, family history of HTN, diagnosis at admission, and complication related to CKD were the independent predictors of 30 days mortality in the patients with CKD. But as to the

studies by Goswami et al and D. Juneja et al in which markers of 30 day mortality were Renal Replacement Therapy type, need for mechanical ventilation, vasoactive drugs and others (8,52). This difference could be understand as the gap in participants size between studies as well as the admission set up differences including of ICU patients. In addition, other study by Madero et al revealed uric acid as a predictor of mortality even if the study period was different as compared to this study (53). Furthermore, presence of AKI, older age, sex of the patients and eGFR were independent predictors of mortality in the other study by J.-P. Lafrance et al which was somehow different to our study although sex of the patient and presence of the AKI were significant at both study (12). The reason might be due to difference in both population size and study period which were larger as compared to this study.

In our study, male sex has been dying at the rate of 2.66 times greater than female patients throughout 30 days follow up period (AHR: 2.66, 95% CI: 1.21-5.88) which is similar to studies by J.-P. Lafrance et al and Borja Quiroga et al (12,43). Besides this, patients who were diagnosed as AKI on underlying CKD at admission were dying at the rate of 2.46 times greater than those patients diagnosed as CKD only during 30 days observational follow up period (AHR: 2.46, 95% CI: 1.26-4.78). This could be due to presence of AKI has been further deteriorate CKD and hasten its progression which finally lead to death. Moreover, patients who had CKD related complication were dying at the rate of 5.38 times greater than patients without CKD related complication throughout 30 days follow up period (AHR: 5.38, 95% CI: 1.64-17.72). This could be due to presence of complication further deteriorate CKD patients which may lead to higher mortality and morbidity.

Strength and limitation of the study

Strengths of the study

This study looked in to treatment outcome and various factors associated to CKD with a clinical follow up and provides baseline data which may shed some light on the need for early preventive strategy and to improve patient care and management.

The major strength of this study was its prospective study design and the enrollment of consecutive patients. This prospective cohort study allowed collection of accurate data on risk factors, socio-demographic, CKD related complications, treatment approaches and mortality.

To ensure a uniform data collection, we ascertained consistently established risk factors and obtained reliable information on the important ones. The study provides a preliminary database on mortality and clinical outcome which can inform CKD management strategies and interventions required to decrease mortality associated with CKD.

The eGFR of CKD was assessed by both CG and MDRD equations at admission and discharge unlike in other areas which provide further information on clinical practice evaluation. We have performed a detailed initiated assessment for clinical staging of CKD based of NKF KDOQI and KDIGO stratification on admission and at discharge allowing us to evaluate for determinants of outcome in series of patients with CKD. Further, we included AKI as a determinants in underlying CKD patients in which majority of studies excludes. In addition we used method of survival analysis for both in hospital and 30 day mortality which allow us to compare the risk difference between the two time periods.

Limitations of the study

As this study was hospital-based study rather than population based, it may be subjected to referral bias, as most of CKD patients' visit this hospital from the south western part of Ethiopia directly without any selection and severe cases may have died before reaching the hospital and mild cases may have not reported to hospital. These referral and selection biases as well as convenience sampling approach used might not reflect the true fatality of CKD in the community; hence our finding may not be generalizable. Thus extrapolations to the rest of the community should be done with caution. Further we used a single shot laboratory results for the determination of patient' clinical status due to limited and cost of testing resources. But this single shot test would have not been feasible for most patients if it were community-based. Similarly the mean age, male predominance, identified risk factors and other basic patient profile of our data like level of mortality were quite similar to other studies. Even though the study was hospital based, having this study as the only referral center might probably reflect the actual scenario of CKD in the country.

Since our study ascertained events over about 4-month period, we acknowledge the possibility of a contribution of seasonal variation in CKD events to our findings and were unable to time analyze event trends over time, as our study did not run for a complete 1 year period.

We followed up the patients discharged before 30 days by telephone based care giver interview. Thus, the detailed data of CKD related death could not be collected in this study and the accuracy of these reported events needs to be evaluated by further study.

In our study protocol, the primary etiology of CKD was not refined sufficiently enough as majority of them were undetermined due to infrastructure constraints, which may underestimate or overestimate some other etiologic factors. However, our main purpose was not the precise assessment of such etiologic risk factors.

The sample size of our study was small hampering the analysis of some prognostic indicators due to the short recruitment period. This is due to limited study period which was about 4 months and following the hospitalized patients alone in which large participants were attained only by elongating the study period which was not feasible to us. Indeed, in low to moderate income country setting, resources are not available for community-based cohort design as well as the urgent requirement of the result to help implementation of the intervention like prevention, acute care and patient management do not allow us to do this.

7. CONCLUSION

In this present study, CKD accompanied to higher rate of medical admissions and in hospital mortality. Majority of the patients were males, rural residents, uneducated and farmers with low socioeconomic status.

During discharge majority of the patients were alive and discharged from hospital with improvement. About half of the patients were in CKD stage 5 during discharge from the hospital. The mean length of hospital stay was short in study population. Similarly, the mean length of survival after hospital admission for patients who died in hospital was short. Khat chewing (use), diagnosis at admission and presence of proteinuria were the independent predictors of in-hospital mortality.

At 30-day follow up, majority of patients were still alive, about one third patients were died. The mean length of survival after hospital admission for patients who died within 30 days was 16.41±6.86 days. Sex of the patients, family history of HTN, diagnosis at admission, and complication related to CKD were the independent predictors of 30 days mortality in the patients with CKD up on multivariable cox regression. AKI on CKD patients had higher mortality at both in hospital and 30 days' time period unlike CKD only patients.

In general, the burden of death associated to CKD patients in this setting was high similar to other developing countries.

8. RECOMMENDATION

As CKD is a growing public health problem, comprehensive public health awareness creating campaign should be launched focusing on preventable risk factors and recognition of CKD-related symptoms. There should be aggressive information from social media, mass media and at political level of the country in the purpose of increasing awareness and understanding of risk prevention and devastating effect of the disease on individual level as well as at country's economy at further.

Increasing the involvement of community and NGO in public health education and training of the community health professionals on early detection of the disease and preventive strategies to reduce the adverse outcome and complications associated with CKD. In addition, the health system needs to be reoriented to encourage and promote identification of lifestyle related risk factors which includes regular screening and controlling of non- communicable disease like hypertension and DM.

Essential etiologic investigations infrastructure, trained man power as well as essential medications and renal replacement therapy center should be available by the government and stakeholders to fit the number of CKD patients visiting the hospital. In addition, ministry of health of the country should develop and implement generalized protocol guideline for in hospital and follow up management.

A prospective community-based CKD incidence and prevalence studies are required to define true socio-demographic risk factors and outcome of CKD in our population including the mortality and quality of life. Additionally, studies that attempts to assess delays for treatment and early complication and its management are advisable to address those issue further. To achieve these goals diagnostic tests capable of identifying primary etiologies and managing protocol is essential through smoothly functioning cooperation of all professionals involved for the prevention of early CKD related mortality.

Finally, there is a need to provide and future planning of a better and affordable dialysis and kidney transplantation center to minimize mortality and quality of life in CKD survivors.

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Annex 1: Information Sheet

Good morning /Good afternoon. This questionnaire is prepared for research work to be conducted on the treatment outcome of Chronic Kidney Disease and its associated factors in hospitalized patients at JUMC, Southwest Ethiopia. The research is conducted to fulfill the thesis requirement of MSc degree in Clinical pharmacy: Jimma University, School of Pharmacy, faculty of Health Sciences.

Dear respondents, I would like to interview you a few questions about you, your disease and adherence status, treatment you are getting and review your laboratory findings from medical chart. The study will provide information that might enable the health personnel and the government to get an insight into treatment Outcomes of hospitalization among CKD complications and its associated factors. I would like to take your time to respond to my interview questions and it will take approximately 15 minutes. I also request you to answer as truthfully as possible. Your answer will not be revealed to the health personnel or any other people, and the information you give will be treated anonymously and confidential. This research imposes no risk and therefore no compensation will be provided for your participation in this study. Your participation is totally voluntary and you can withdraw anytime or refuse to continue, and this will not influence the way you are treated in the health institution or in the community. I would like to express my heartfelt appreciation for your collaboration and thank you in advance. If you are not still discomfort with the interview, Please feel free to drop it any time you want. Do I have your permission to continue?

1 – If yes, continue
2 – If no, skip to the other participant

In case you need to contact the investigator you may use the following address:

Name: Eskinder Amin

Tel: 0910 68 66 40

Email: eskeamin4@gmail.com

Annex 2: Consent Form

I the selected participant heard the information in the study's information sheet and understood the purpose and benefits; and what is required from me as well. I understood that all the information regarding me like name and all answers given by me will never be transferred to a third party. So, I am willing to participate in the study.

Signature of Participant _____Date _____

Data Collector Name _____Signature _____ Data _____

Annex 3: Data Collection Tools

Card number_____ Code no_____ Bed no_____ Date_____

Instruction:

i. Select your answer for the questions by marking "✓" in the box provided
ii. If your answer is out of the choice provided; write it in the space provided

i. Demographic and general data of participants

Date of admission_____ Ward_____	**Sex:** ☐ Male ☐ Female	**Age**:_____ (yrs)	Kebele:_____ Woreda:_____ Region:_____	**Residence** ☐ Urban ☐ Rural
Education status ☐ Unable to read and write ☐ Able to read and write ☐ Elementary school (1-8) ☐ Secondary school (9-12) ☐ College/university or above		**Occupational-status** ☐ Employee ☐ Merchant ☐ Farmer ☐ Unemployed Other(specify)_____ _	**Religion** ☐ Orthodox ☐ Muslim ☐ Protestant ☐ Catholic ☐ Traditional belief Others_____	**Marital status** ☐ Single ☐ Married ☐ Divorced ☐ Widowed Other_____
Socio-economic status Average monthly income_____(ETB)	**Physical Condition** a. Weight ___ ___kg b. Height ___ ___cm c. BMI ___ ___kg/m^2	**Contact address** Phone no_____ Mobile no_____ Optional phone:_____		**Pregnancy status (if female)** ☐ Yes ☐ No
Tobacco use ☐ Never ☐ Past-smoker how long ago did you stop_____ ☐ Current smoker Average daily cigarette _____	**Alcohol intake** ☐ Never ☐ Past ☐ Present If presently drink, how often ☐ Socially ☐ Daily ☐ >3 days/week ☐ <3 days /week	**Khat chewing** ☐ Yes ☐ No		

ii. Disease Related Factors

Diagnosis			**Date of diagnosis of CKD** **Time to complication/event**	
Reason of current admission ☐ Anemia ☐ HTN ☐ Electrolyte disturbance ☐ Dyslipidemia ☐ CKD ☐ AKI Other(s):				
Infection/ Inflammation ☐ Yes ☐ No	**Diabetes Mellitus** ☐ Yes ☐ No If yes, duration____	**Heart failure** ☐ Yes ☐ No If yes, duration _____	**Hematologic disorder** ☐ Yes ☐ No	**Asthma** ☐ Yes ☐ No
Anemia ☐ Yes ☐ No	**Hypertension** ☐ Yes ☐ No If yes, duration _____	**Dyslipidemia** ☐ Yes ☐ No If yes, duration _____	**Metabolic acidosis** ☐ Yes ☐ No If yes, specify_____	**Electrolyte disturbances** ☐ Yes ☐ No If yes, specify_____
History of recent surgery ☐ Yes ☐ No If yes, how long_____	**AKI** ☐ Yes ☐ No If Yes, duration____	**HIV/AIDS** ☐ Yes ☐ No	**PAD** ☐ Yes ☐ No If yes, specify _____	**Other kidney disease** ☐ Yes ☐ No specify_____
Malnutrition ☐ Yes ☐ No	**Iron supplement** ☐ Yes ☐ No	**Vomiting** ☐ Yes ☐ No If yes, duration_____ Frequency/day____	**Diarrhea** ☐ Yes ☐ No If yes, duration_____	**Body weakness/Fatigue** ☐ Yes ☐ No
Previous hospitalization ☐ Yes ☐ No If yes, which disease_____	**Edema(body swelling)** ☐ Yes ☐ No If yes, which area_____	**Reduced skin turgor** ☐ Yes ☐ No	**Palm Pallor** ☐ Yes ☐ No	**Family history** ☐ HTN ☐ DM ☐ HF ☐ CKD ☐ Dyslipidemia Other_____ ☐ No
Amount of urine passed? ☐ As usual ☐ Increased ☐ Decreased If no, for how long_____	**CKD status** ☐ Newly diagnosed CKD ☐ Known CKD patient If known, time since diagnosis _____			
Estimated GFR (CG)			**Stage of CKD** ☐ Stage 1 ☐ Stage 2 ☐ Stage 3 ☐ Stage 4 ☐ Stage 5	
1^0 renal disease/cause ☐ Glomerulonephritis ☐ Hypertension/ renovascular ☐ Polycystic kidney disease ☐ Diabetes nephropathy ☐ Interstitial nephritis ☐ other specified ☐ Unknown				

iii. Medications

<table>
<tr><th colspan="4">Approaches/ protocol of CKD complications management</th></tr>
<tr><th>Past medication history</th><th colspan="2">Medication during hospitalization</th><th>Medication at discharge</th></tr>
<tr>
<td>☐ No previous medication
☐ Unknown medications
☐ Antibiotics
☐ Diuretics
☐ Iron therapy
☐ ACEI or ARB
☐ B-blocker
☐ CCB
☐ Statin
☐ Antidiabetics
☐ Anticoagulant
☐ Antiplatelet
☐ Other_____
_____</td>
<td>a. ACEI/ARB
☐ Enalapril
☐ Captopril
☐ Losartan
☐ _____
b. Loop or thiazide diuretics
☐ Furosemide
☐ Hydrochlorothiazide
☐ _____
c. Potassium sparing diuretics
☐ Spironolactone
d. Iron therapy
☐ Ferrous sulphate
☐ Blood transfusion
☐ Ferrous gluconate
☐ _____
e. Beta-blockers
☐ Propranolol
☐ Atenolol
☐ Metoprolol
☐ _____
f. Calcium channel blocker
☐ Amlodipine
☐ Nifedipine
g. Antidiabetics
☐ Insulin
☐ Metformin
☐ Glibenclamide/daonil</td>
<td>h. Electrolytes replacement
☐ KCL
☐ Nacl salt
☐ Calcium gluconate
☐ _____
i. IV fluid
☐ Normal saline
☐ LR
☐ DNS
☐ 40 % glucose
☐ _____
j. Lipid lowering agent
☐ Atorvastatin
☐ Simvastatin
☐ Lovastatin
k. Antiplatelets
☐ Aspirin
☐ Clopidogrel
l. Anticoagulants
☐ Heparin
☐ Enoxaparin
☐ Warfarin
m. Miscellaneous medications
☐ Antibiotics
☐ Anti-pain
☐ Anti-ulcer
☐ Maintenance fluid
☐ None is given
☐ Others_____</td>
<td>☐ ACEI/ARB
☐ Diuretics
☐ Iron therapy
☐ lipid lowering agents
☐ Antidiabetics
☐ Anticoagulant
☐ antiplatelet
☐ CCB
☐ B-blocker
☐ Antibiotics
☐ No medication given
☐ Other_____
_____
Other management and support
☐ Salt free diet
☐ Sugar diet free
☐ In hospital rehabilitation therapy(bedside physiotherapy)
☐ Other_____</td>
</tr>
</table>

iv. Patient's Medication Adherence: A Morisky Medication Adherence Scales (MMAS-8)

No.	Morisky 8-Item Medication Adherence Questionnaire	Answer
1	Do you sometimes forget to take your medicine?	☐ Yes ☐ No
2	People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?	☐ Yes ☐ No
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	☐ Yes ☐ No
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	☐ Yes ☐ No
5	Did you take all your medicines yesterday?	☐ Yes ☐ No
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	☐ Yes ☐ No
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	☐ Yes ☐ No
8	How often do you have difficulty remembering to take all your medicine?	☐ Never/rarely ☐ Once in a while ☐ Sometimes ☐ Usually ☐ All the time
Total Correct sum		_____/8

Notice: Never/rarely = 0; Once in a while/ Sometimes/Usually/All the time = 1 and Yes =1 and No = 0

v. Laboratory investigations and other clinical examinations

Vital signs	BP (mmHg)	Pulse (beat/min)	RR (breath/min)	Temp (^{o}c)	
CBC	WBC	RBC	HGB	HCT	
	MCV	MCH	MCHC	PLT	
	RDW-SD	RDW-CV	NEUT	LYMPH	MONO
RFT	Serum Cr	BUN	BUN/srCr	eGFR (CG)	eGFR (MDRD)
LFT	AST/SGOT	ALT/SGPT	Alk Phos	Tot protein	Albumin
	Tot bilirubin	Dir. bilirubin	Indir.bilirubin		
Lipid Profile	TC	LDL-C	HDL-C	Non HDL-C	TG
Urinalysis	Blood	Glucose	Protein	Ketone	nitrates

	RBC	WBC	Cell	Urine output	bacteria
Electrolytes	Na+	K+	Cl-	Ca	PH

vi. Outcomes of the patient

In hospital mortality ☐ Yes ☐ No If yes, Evidence/source of death report:_____ **Date of death:_____**	**Discharge status** ☐ Alive ☐ Death **Date of discharge:_____**	**Outcome of the patient during discharge if alive** ☐ Improved ☐ Referred ☐ Self-discharge/left on follow up ☐ Complicated/ worsened ☐ Need dialysis/RRT	If patient alive at day 30,living situation is at: ☐ Home ☐ Community Facility ☐ In Hospital ☐ Other _____
Within 30 day mortality ☐ Yes ☐ No **Date of death:_____**	If died number of days of survival after admission_____ _____ If died number of days of survival after discharge_____ _____	**Possible reason of death**	**Length of hospital stay (days)**:_____ From _____ to _____
Laboratory and/or imaging during discharge _____			

Annex 4: Amharic Version of Informed Consent

የአማርኛ የመረጃ መስጫና የስምምነት ቅፅ

ስሜ እስክንድር አሚን እባላለው፣በጅማ ዩኒቨርሲቲ የሁለተኛ ድግሪ የክሊንካል ፋርማሲ ተማሪ ስሆን በአሁኑ ግዜ ለድህረ-ምረቃ ጽሁፍ የምሆን ጥናት ከ ኩላሊት ሕመም (CKD) የሕክምና ውጤት ጋር ተያይዘ ያሉትን ችግሮችን እና ስለ ህይወትሆ ያለበት ሁኔታ፣ስለ ጤንነትህ/ሽና ሌሎች የህይወት ዘርፎች ላይ ምርምርን እያደረኩ ስለሆነ ከእርሶ ጋር እንዳደርግ እንድሁም ከካርዶ መረጃን እንድወስድ እነድፈቀድልኝ በትህትና እጠይቆታለው። በዝህ ምርምር ውስጥ በመሳተፎ የምደርስቦት ጉዳት ወይም ባለመሳተፍዎ በፈት ከምያገኙ የህክምና አገልግሎት የሚቀርቦት የለም። እርሰዎ የስጡን መረጃ ሁሉም በምስጢር ይያዛል። ኣንድም የግሌዎ መረጃ አይጻፍም። በተጨማሪም በዚህ ምርምር ውስጥ መሳታፍዎ ሙሉ በሙሉ በፍላጎትዎ ላይ የተመሰረተ ነው። ስለምርምሩም ሆነ ስለምትጠየቁት ነገር ያልገባዎት ነገር ካለ በማንኛውም ግዜ ዋናውን ተመራማሪ መጠየው ይችላሉ።

የዋናው ተመራማሪ መረጃ፤ እስክንድረ አሚን

ስልክ ቁጥር፡ 09 10 68 66 40

E-mail፡ **eskeamin4@gmail.com**

Annex 5: Oromic Version of Informed Consent

Odeeffaannoo /ragaa dhunfaa hirmattotaa

Ani inniin qorannoo kanaaf filatame, odeeffanno fi kaayyo qorannoo kanaa dhagahuun hubadheen jira. Akkasumaas, waan narra eegamuus addan baafadheen jira. Dabalataaniis, odeeffannoo waa'ee kiyyaa kaannen akka maqaa kiyya fi deebiin ani kennu akka nama sadaffaaf hin kennamne hubaddheen jira. Kanaaf, qorannoo kanarratti hirmachuuf fadhii qabaachuu kiyya mallattoo kiyyaaniin ibsa.

Mallatto hirmaataa_____ Guyyaa_____

Maqaa odeeffanno sassaabaa_____ Mallattoo _____ Guyyaa_____

Annex 6: Amharic Version of Adherence Measurement Tool

Morisky 8-Item Medication Adherence Questionnaire

questions	መልስ	
1.እንድ አንድ ግዜ መድሃንትህን/ሽን መውሰድ ትረሳለክ/ሽ?	አዎ	አይደለም
2.ባለፉት 2 ሳምንታት ውስጥ መድሃንትህን/ሽን ሳትወስድ/ጂ የቅረህበት ቀን አለ?	አዎ	አይደለም
3.መድሃንትህን ስትወስድ ህመም ስለተሰማህ ሃኪም ሳታማክር ያቆምከበት ግዜ አለ?	አዎ	አይደለም
4.ጉዞ ስኖረክ ወይም ቤት ለቀህ ስትሄድ መድሃንትህን ይዘህ መሄድ አንድ አንድ ግዜ ትረሳለክ?	አዎ	አይደለም
5.ትናንት ሁሉንም መድሃንትህን ወስደካል ወይ?	አዎ	አይደለም
6.ህመምክ ስሻልክ መድሃንትህን መውሰድ አንድ አንድ ግዜ ታቆማለክ?	አዎ	አይደለም
7.ለተወሰኑ ሰዎች መድሃንታቸውን ሁልግዚ መውሰድ ላይመቻቸው ይችላል። አንተ ሁል ግዜ መድሃኒትህን መውሰድህ አሳስቦክ ያውቃል?	አዎ	አይደለም
8.መድሃንትህን መውሰድ ምንያህል ማስታወስ ያስችግራሃል?	ሀ. ፈፁሞ ለ. ከቡዙ ግዜ ኣንዴ ሐ. አንድ አንድ ግዜ መ. አብዛኛውን ግዜ ሠ. ሁል ግዜ	
Total score		

Annex 7: Oromic Version of Adherence Measurement Tool

Morisky 8-Item Medication Adherence Questionnaire

Gaaffilee		
1. **Yeroo tokko tokko qoricha HIV fudhachuu ni dagattaa?**	**Eyyee**	**Lakki**
2. **Torban lamaan darban keessatti, qoricha osoo hin fudhatin guyyaan hafte jiraa?**	**Eyyee**	**Lakki**
3. **Yeroo qoricha fudhattuu, dhukkuubni kee waan sif wayyeef ogeessa fayyaa osoo hin mariisisin yeroon dhaabde jiraa?**	**Eyyee**	**Lakki**
4. **karaa yeroo deemtu yookiin manaa yeroo baatu qoricha fudhachuu takka takka ni dagattaa?**	**Eyyee**	**Lakki**
5. **kaleessa qoricha kee hundumaa fudhateettaa?**	**Eyyee**	**Lakki**
6. **Dhukkuubni kee yeroo sitti wayyaa'u, qoricha kee fudhachuu takka takka ni dhaabda?**	**Eyyee**	**Lakki**
7. **Namoota tokko tokkoof, qoricha isaanii yeroo hunda fudhachuun isaanitti tolu dhiisu danda'a. Ati yeroo hunda qoricha kee fudhachuun si yaaddesse beekaa?**	**Eyyee**	**Lakki**
8**. Qoricha kee fudhachuuf yaaddahuun hagam si rakkisaa?**	**A. gonkuma** **B. darbee darbee** **C. yeroo tokko tokko** **D. Yeroo baay'ee** **E. Yeroo hundaa**	
Gatii walii galaa		

Research thesis final endorsement form to be filled before final submission to the school of pharmacy

Here with my signature, I declare that this thesis is done under my advisor ship and I have approved that this manual is the final thesis for submission to the school of pharmacy, SRP office of Jimma University.

Name_____ Signature _____

Here with my signature, I declare that this thesis has been examined by me and I have checked that the student has corrected the comment that I forwarded before final submission.

Name_____ Signature _____

Here with my signature, I declare that this thesis is done by me as a principal researcher and I assure that this manual is the final paper for submission to the school of pharmacy, SRP office of Jimma University.

Name_____ Signature _____