



ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

FACTORS ASSOCIATED WITH OUTCOME OF RENAL REPLACEMENT THERAPY INITIATION AMONG PATIENTS WITH ACUTE KIDNEY INJURY ADMITTED TO INTENSIVE CARE UNITS AT REFERRAL HOSPITALS IN ADDIS ABABA, ETHIOPIA

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A thesis to be submitted to the department of internal medicine and school of public health, SPHMMC, in partial fulfillment for the requirements of specialty certificate in internal medicine.

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THERAPY INITIATION AMONG PATIENTS WITH ACUTE KIDNEY INJURY
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ADDIS ABABA, ETHIOPIA

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Abstract

Background: Acute kidney injury (AKI) is common among patients admitted to the intensive care unit (ICU). It is an independent risk factor for morbidity and mortality. There is uncertainty regarding the optimal time to initiate renal replacement therapy (RRT) in critically ill patients with acute kidney injury (AKI).

Objective: To assess the clinical profile and factors associated with outcome of renal replacement therapy in patients with acute kidney injury admitted to the intensive care unit at St. Paul's Hospital Millennium Medical College (SPHMMC) and Zewditu Memorial Hospital (ZMH).

Methods: A hospital based retrospective clinical records review was conducted among 140 critically ill AKI patients who underwent hemodialysis at SPHMMC and ZMH from January 1 2021 to December 31 2022. Records of the study population were assessed for completeness before data entry and the entered data was checked by investigator for incompleteness and/or inconsistency. Data was entered and analyzed with SPSS version 29. Binary and multivariable logistic regression analysis were employed to identify independent predictors of outcome of initiated renal replacement therapy. Statistical significance was declared at a P-value of < 0.05 .

Results: 140 patients required renal replacement therapy and the majority had sepsis 38(27.1%). The most common clinical factors associated with renal replacement therapy initiation were refractory fluid overload 55(38.6%), followed by uremic encephalopathy 54(37.9%). Renal replacement therapy was initiated at stage 3 of acute kidney injury in all of study participants. The composite outcome of death, dialysis dependence and diuretic dependence at intensive care unit (ICU) discharge was 81% and ICU mortality was 47.9%. Anuria (AOR=27.05, 95% CI: 8.06,90.73) and being on vasopressor (AOR=15.14 ,95% CI: 3.3,68.8) at the initiation of renal replacement therapy was associated with the outcome of ICU death.

Conclusion: The study population was young, predominantly female and with a relatively high burden of sepsis. The observed current threshold for renal replacement therapy was late (stage 3 acute kidney injury with classic/emergent indications). Patient with anuria and on vasopressor who were initiated on renal replacement therapy had high ICU death post renal replacement therapy.

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Acronyms and Abbreviations

AKI	Acute Kidney Injury
BUN	Blood Urea Nitrogen
CKD	Chronic Kidney Disease
ETB	Ethiopian Birr
ESRD	End stage renal disease
GN	Glomerulonephritis
ICU	Intensive Care Unit
KDIGO	Kidney Disease: Improving Global Outcomes
IHD	Intermittent Hemodialysis
MOF	Multi Organ Failure
MOH	Ministry of Health
RRT	Renal Replacement Therapy
SCr	Serum creatinine
TASH	Tikur Anbesa Specialized Hospital
SPHMMC	St Paul hospital millennium medical college
ZMH	Zewditu Memorial Hospital

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1.Introduction

1.1 Background of the study

Acute kidney injury (AKI), previously known as acute renal failure (ARF), is an acute decline in kidney function, leading to a rise in serum creatinine and/or a fall in urine output (1).

Acute kidney injury (AKI) is conventionally diagnosed utilizing the kidney disease: Improving Global Outcomes (KDIGO) criteria. Kidney Disease: Improving Global Outcomes (KDIGO) criteria defines AKI as an increase in serum creatinine by ≥ 0.3 mg/dL within 48 hours, or an increase in serum creatinine ≥ 1.5 times baseline, known to have occurred within the prior seven days or urine volume < 0.5 mL/kg/hour for at least six hours (2).

In May 2004, a new classification, the RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification, was proposed in order to define and stratify the severity of acute kidney injury (AKI). This system relies on changes in the serum creatinine (SCr) or glomerular filtration rates and/or urine output, and it has been largely demonstrated that the RIFLE criteria allows the identification of a significant proportion of AKI patients hospitalized in numerous settings, enables monitoring of AKI severity, and is a good predictor of patient outcome(3).

Using the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, AKI is staged as follows:

- Stage 1 – Increase in serum creatinine to 1.5 to 1.9 times baseline, or increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 micromol/L), or reduction in urine output to < 0.5 mL/kg/hour for 6 to 12 hours.

- Stage 2 – Increase in serum creatinine to 2.0 to 2.9 times baseline, or reduction in urine output to < 0.5 mL/kg/hour for ≥ 12 hours.

- Stage 3 – Increase in serum creatinine to 3.0 times baseline, or increase in serum creatinine to ≥ 4.0 mg/dL (≥ 353.6 micromol/L), or reduction in urine output to < 0.3 mL/kg/hour for ≥ 24 hours, or anuria for ≥ 12 hours, or the initiation of kidney replacement therapy, or, in patients < 18 years, decrease in estimated glomerular filtration rate (eGFR) to < 35 mL/min/1.73 m²(1).

Acute kidney injury occurs in patients with intercurrent illness, without symptoms or signs specific to the kidneys, and is diagnosed when kidney function tests are performed. Patients may present in many different ways (e.g., with sepsis, hypotension, decreased urine output, lower urinary tract symptoms, or oedema). We should suspect AKI when there is an acute rise in serum creatinine and/or a fall in urine output. More severe AKI can be complicated by hyperkalemia and acidemia along with uremic encephalopathy or pericarditis(2).

AKI is an increasingly common complication of critical illness, with some researches showing that as high as 1 in 5 adults and 1 in 3 children experiencing AKI per hospital admission. Whether occurring in the community or in the hospital, the clinical and public health importance of AKI is well established due to the association with high mortality and its separate independent effect on the risk of death and resource use(3).

The cause of acute kidney injury is often multi-factorial and complex in critically ill patients, but regardless of the underlying etiology, if the renal injury cannot be easily rectified, and if the patient's primary condition has a reasonable degree of reversibility, then renal replacement therapy should be considered(4).

The epidemiology of AKI in developing countries is unique in that certain causes, such as the infections, obstetric causes and nephrotoxins, which are largely obsolete in developed countries remain important causes. Regardless of cause, the management of AKI is mainly supportive, with dialysis being indicated when medical management fails to treat the complications. Hemodialysis is the most commonly used renal replacement therapy in Africa. However, poverty, maladministration of resources and lack of adequate funding for health in nearly all African countries has massively stunted the growth of hemodialysis as a modality of renal replacement therapy(5).

It is expensive to manage and associated with high-rate prolonged hospitalization and in-hospital mortality. The in-hospital mortality rate is reported at 24% and increases with the severity of the disease(6).

Management strategies continue to reflect supportive measures focusing on fluid delivery, diuretics, avoidance of nephrotoxic agents and RRT for the most severe cases(7).

Hemodialysis is a form of renal replacement therapy mostly used in both acute and chronic kidney failure to slow down the progression of the failure. It is the process of removing solutes from the body using a semi permeable artificial membrane when blood comes in contact with the same during extracorporeal circulation. It aims to maintain the fluid and electrolytes in normal homeostasis(8).

Untreated severe AKI in critically ill patients is associated with high mortality, and renal replacement therapies (RRTs) represent the cornerstone of the management of severe AKI(9).

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1.2 Statement of the Problem

Acute kidney injury affects up to half of medical intensive care unit patients and is associated with increased length of ICU stay, increased hospital stays, development of chronic kidney disease and increased short-term and long-term mortality. Renal replacement therapy (RRT) is applied to 10–15% of critically ill patients with AKI(10).

Mortality rates in critically ill patients with AKI is reported to be 50% and is associated with a six-fold increased risk of dying in the hospital(11).

Factors that might influence the decision of when to start RRT are the severity of the underlying disease ,the degree of dysfunction in other organs, the prevalent or expected solute burden (e.g.in tumor lysis syndrome), and the need for fluid input related to nutrition or drug therapy(1).

There is limited evidence to support the current practice of RRT in intensive care units. Various modes of RRT are complementary to each other with no definite benefits to mortality or renal function preservation(12). Therefore, assessment of RRT practice among AKI patients admitted at ICU at Saint Paul's Hospital Millennium Medical College (SPHMMC) and Zewditu Memorial Hospital (ZMH), Addis Ababa, Ethiopia, which are among the country's largest tertiary hospitals, will help identify its outcome too.

1.3 Significance of the study

Acute kidney injury (AKI) is common among patients admitted to the intensive care unit (ICU) It is an independent risk factor for morbidity and mortality.

Even though the decision regarding whether to start RRT, optimal timing for initiation, modality used, and frequency of RRT in acutely ill patients is an area of ongoing investigation and remains controversial, knowing the clinical factors associated with initiation of hemodialysis in critically ill AKI patients is very important.

There is a paucity of data on current practices of RRT within ICUs in Ethiopia. This study will add insight into the practice of initiating RRT in patients admitted to the ICU with AKI. This study will also be a valuable addition to the limited local information there is on the subject matter and will help to base recommendations on patient management.

2.Litrature Review

Estimates of AKI prevalence ranges from <1% to 66%. These variations can be explained by not only population differences but also inconsistent use of standardized AKI classification criteria. The etiology and incidence of AKI also differ between high- income and low to middle income countries. High income countries show a lower incidence of AKI than do low to middle income countries, where contaminated water and endemic diseases such as malaria contribute to a high burden of AKI. Outcomes of AKI are similar to or more severe than those of patients in high-income countries. In all resource settings, suboptimal early recognition and care of patients with AKI impede their recovery and lead to high mortality, which highlights unmet needs for improved detection and diagnosis of AKI and for efforts to improve care for these patients(13).

A prospective international multicenter study of AKI in the intensive care unit have shown that patients in emerging countries were more likely to have glomerulonephritis (GN) and acute interstitial nephritis, while those in developed countries had higher reported rates of prerenal AKI, sepsis and acute tubular necrosis. Residence in an emerging country was associated with more than a twofold increase in hospital mortality and a threefold lower rate of renal recovery in survivors(14).

The indications for renal replacement therapy are not absolute, and several renal and non-renal factors play a role when considering whether renal replacement therapy should be started. Notably, there are no universally accepted levels of urea, creatinine, potassium or pH at which to commence therapy(4).

Deciding when to initiate dialysis in a critically ill patient remains one of the most challenging questions in the management of critically ill patients. Although several approaches have been offered, there is considerable variation in when dialysis is offered in the ICU setting(15).Based on limited evidence, when considering the timing of initiating of RRT in MOF, individual patients physiological reserve based on age, cardiovascular risk factors, pulmonary comorbidities, baseline renal function, and the trend of inflammatory and renal injury markers should be assessed. A delayed strategy of waiting for 48–72hrs after progressing to AKI KDIGO 3 or until an absolute indication which arises may be applicable to most medical patients with septic shock(16–18).

Different modalities of RRT have been and are used in the treatment of AKI, including continuous RRT (CRRT), intermittent hemodialysis (IHD), sustained low-efficiency dialysis (SLED) and

peritoneal dialysis (PD). A worldwide survey showed that CRRT was the most prevalent initial modality for AKI patients (80.0%), followed by IHD (16.9%), and PD and SLED (3.2%)(9,19).

The study done at French hospitals on influence of initial renal replacement therapy modality on renal recovery at hospital discharge shows overall mortality of 56.1%, and overall renal recovery of 86.2%. intermittent hemodialysis as an initial modality was associated with lower renal recovery at hospital discharge among patients with acute kidney injury, although the difference seems somewhat clinically limited(20).

Four out of five recent RCTs failed to demonstrate a survival benefit of early RRT initiation, in patients without evident urgent indications(16,17,21–24). The recent AKIKI 2 trial compared ‘delayed’ with ‘very delayed’ initiation of RRT and demonstrated no difference in the number of RRT-free days between both groups(22). But 60-day mortality was higher in the ‘very delayed’ arm. Robust evidence for biomarker-guided RRT initiation is lacking(25). There was a significant association between mortality and the volume of urine production before RRT initiation. Mortality was highest for those patients with marked oligoanuria(26–28).

A prospective observational study performed in 6 intensive care units (ICUs) at 3 Canadian hospitals showed at RRT initiation, the majority of patients fulfilled RIFLE-Failure (76.9%), whereas fewer were classified as RIFLE-Injury (20.5%) or RIFLE-Risk (2.6%). Additional common factors included hypoxemia, with a $PaO_2/FiO_2 \leq 200$ (54.5%), oliguria (32.9%), and a $\%FO_{N10\%}$ (30.0%). In total, 28.6% of patients developed a worsening RIFLE category before start of RRT. On the contrary, RRT initiation in association with hyperkalemia, acidemia, anuria, or uremia was relatively uncommon(26). a greater absolute number of (nonrenal) failing organs at the time of RRT initiation is also associated with higher mortality(29–31).

There is a paucity of data on current practices within ICUs in Africa. A study done in south Africa showed 39.4% incidence of AKI in ICU. The study population was young, predominantly male and had post emergency surgery with a high burden of sepsis and HIV. The observed threshold for RRT was late (stage 3 AKI with classic/emergent indications)(32).

A hospital-based prospective observational study conducted on Clinical Profile and Short-Term Outcomes of Acute Kidney Injury in Patients Admitted to a Teaching Hospital in Ethiopia: showed a total of 11 (7%) patients needed renal replacement therapy. Of those patients who required renal

replacement therapy, 7 (4%) patients had preexisting CKD. The main indications of the need for renal replacement therapy were severe hyperkalemia (42%), uremic syndrome (29%), refractory edema (17%), and metabolic acidosis (12%). The overall in-hospital mortality rate was 6% (n=9). Some evidence of renal recovery was observed in 75% of patients at hospital discharge(33)

A study done at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia on 71 critically sick patients with AKI showed Nineteen (26.8%) had the indications for dialysis, of which 16 (84.2%) received conventional intermittent hemodialysis service. Fluid overload (n=7; 36.8%), metabolic acidosis (6; 31.6%) and uremic encephalopathy (n=6; 31.6%) were the most common indications for hemodialysis. AKI was most often caused by sepsis, complicated by fluid overload and metabolic acidosis, and associated with a 45.1 % all-cause mortality(34).

2.1 Proposed conceptual framework

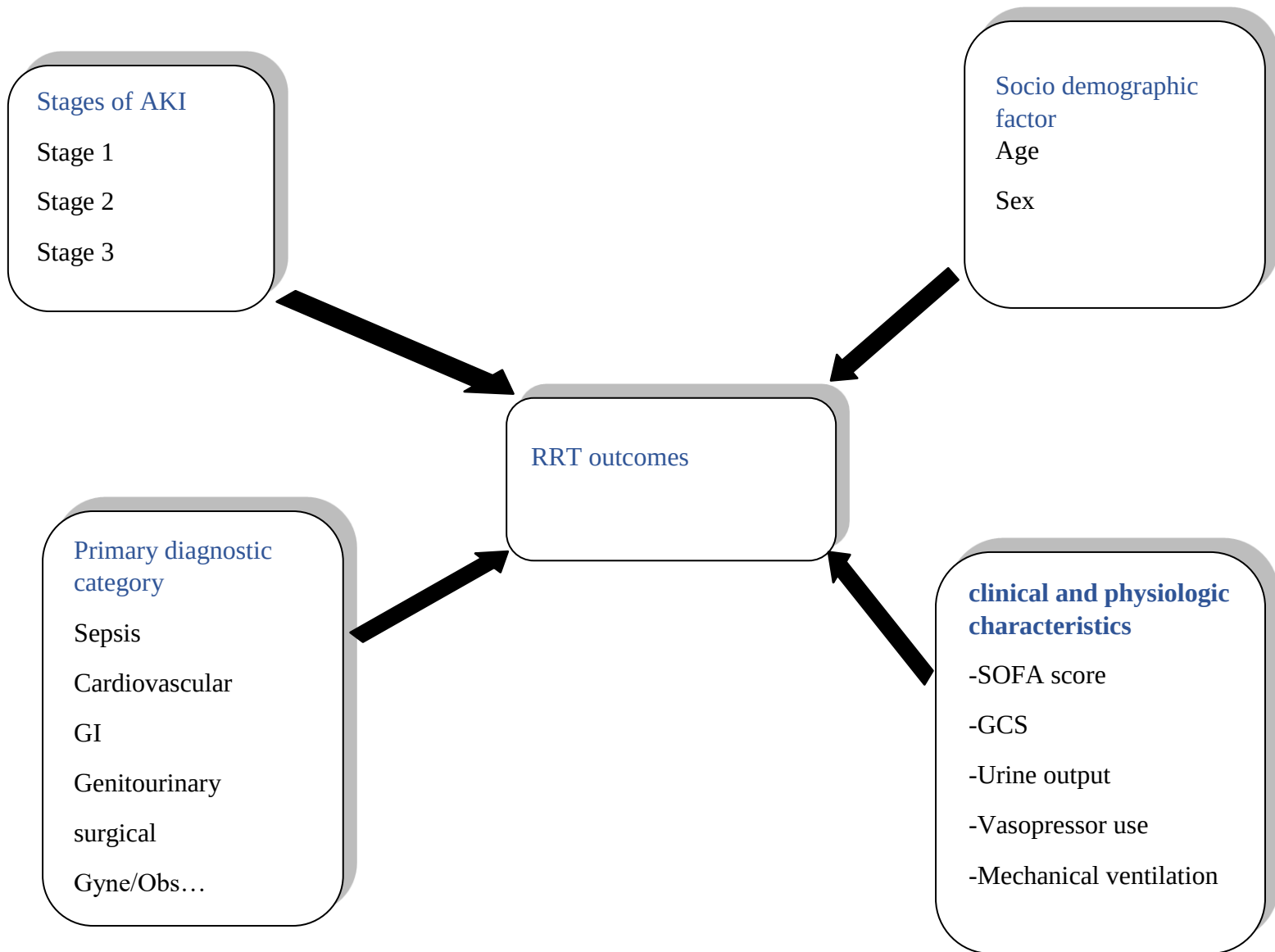


Figure 1. Schematic presentation of conceptual frame work on factors associated with outcome of RRT.

3. Objectives

3.1. General objective

To assess the clinical profile and factors associated with outcome of Renal Replacement Therapy initiation among patients with AKI admitted to ICU at referral hospitals in Addis Ababa.

3.2. Specific objectives

- To assess the clinical profiles associated with the initiation of Renal Replacement Therapy among AKI patients admitted to ICUs in referral hospitals of Addis Ababa.
- To find out factors associated with the outcome of Renal Replacement Therapy initiation among AKI patients admitted to ICUs at referral hospitals in the study areas.

4. Methods

4.1. Study Area

The study was conducted at St. Paul's Hospital Millennium Medical College and Zewditu Memorial Hospital Renal Replacement Therapy initiation centers in Addis Ababa, Ethiopia

St. Paul's Hospital Millennium Medical College is the second-largest governmental tertiary care hospital located in Gulele sub-city, Addis Ababa, Ethiopia. It is a medical center for a catchment area of more than 5 million people. It is a center of excellence in medical services for renal center providing a dialysis and also the first hospital in the country with renal transplantation center. The renal unit established in 2012, started dialysis service a year later limited to AKI and has the only transplant center in the country with the first transplant done in 2015. The renal unit has around 32 dialysis machines in the dialysis unit and the transplant center which provides dialysis to patients who are waiting their turn to receive a kidney transplant, with capability of dialyzing 30-40 patients daily.

Zewditu Memorial Hospital is located at the central part of Addis Ababa and it is one of referral hospitals in the city. It was built by the Seventh-day Adventist church and currently it is operated by the ministry of health. The hospital has many departments of specialties beneath it. The dialysis unit started service in 2009 E.C.

4.2. Study Design and Period

A hospital based retrospective clinical record review was conducted from January 1, 2021 to December 31, 2022.

4.3. Population of the study

4.3.1 General population

All AKI patients admitted to ICU who required renal replacement therapy. from January 1, 2021 to December 31, 2022. The medical record numbers of all patients admitted during the study period were identified from the ICU log book and the clinical records will be retrieved from the hospital chart record office.

4.3.2 Source population

All AKI patients admitted to SPHMMC and ZMH intensive care units who required renal replacement therapy.

4.3.3 Study population

All AKI patients admitted to SPHMMC and ZMH intensive care units who were initiated renal replacement therapy from January 1, 2021 to December 31, 2022 and those who fulfill the inclusion criteria.

4.4 Inclusion and exclusion criteria

4.4.1. Inclusion Criteria

All critically ill patients of age 14 and above with AKI and have been dialyzed at least once therapy from January 1, 2021 to December 31, 2022 were included.

4.4.2. Exclusion Criteria

- Patients receiving RRT for non-AKI indications (e.g., dialyzable toxin)
- RRT before ICU admission
- Patients receiving maintenance dialysis for end-stage kidney disease

4.5. Sampling Method

Sample size is calculated by using the single population proportion formula

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

n= required sample size

Z= confidence level at 95% (standard value of 1.96)

d= margin of error = 5%

P= Renal replacement therapy (RRT) is applied to 10–15% of critically ill patients with AKI(10).

So, when we substitute the values in the formula, it gives us a sample size of 139.

$$n = (1.96)^2 * 0.1 * 0.9 / (0.05)^2$$

$$n = 138.2976$$

The minimum required sample size was 139 patients. I recruited 140 participants who fulfil the inclusion criteria over a 2-year period (January 1, 2021 to December 31, 2022) was analyzed.

4.6. Variables of the study

- Dependent Variable
 - Outcomes of initiated RRT
- Independent Variables
 - Socio demographic factors: Age, sex
 - Clinical and physiologic characteristics at dialysis initiation
 - Stages of AKI
 - Primary diagnostic category

4.7. Operational definitions

Baseline serum creatinine: the first documented serum creatinine on admission.

Dialysis dependence: patient in need of dialysis at discharge from hospital.

Diuretic dependence: patient discharged with diuretic from hospital apart from other clinical indications like hypertension.

Renal replacement therapy: conventional intermittent hemodialysis [IHD] since other forms of dialysis are not available in our setup.

Recovered Renal Function: those patients who had eGFR of more than 60ml/min/1.73m², in no requirement of RRT and urine output of more than 1L/24hrs at ICU discharge.

Died: those patients who died in the ICU despite initiation of RRT

Survived: those patients with outcome of dialysis dependent, diuretic dependent or recovered renal function at ICU discharge.

4.8. Data Collection Procedure and Data Quality Management

Data was collected from April to June 2023. Data collection checklist prepared in English language, with components of, age and sex of the patient, indication for hemodialysis, prepared based on review of records prior to the study period and similar literature used for this study will

be used. Records of critically ill patients who have undergone hemodialysis from January 1, 2021 to December 31, 2022 will be taken for this study. A day long training was given to eight data collectors (Internal Medicine residents of SPHMMC) on the components of the checklist and how to fill the data into a computer. Records of the study population was assessed for completeness before data entry and the entered data will be checked by the investigator on a daily basis for any incompleteness and/or inconsistency.

4.9. Data Analysis

Data was analyzed using the Statistical Package of Social Sciences (SPSS) version 29.0 for Microsoft Windows. Means, standard deviations and percentages was calculated and cross-tabulation was used to compare different variables and subjected to Chi-square analysis to assess various relationships. Each variable was evaluated independently in a bivariate analysis and association was determined using cross tabulation and crude odds ratio (COR) with 95% CI. Multivariate analysis between dependent and independent variables were performed using binary logistic regression with a significance level of P-value < 0.05. The results were presented by the use of tables, and texts. Microsoft Excel 2021 was used to make tables.

4.10. Ethical Consideration

Ethical clearance was obtained from the Institutional Review Board of St. Paul's Hospital Millennium Medical College, and then permission was sought from the school administration through the academic provost of the school to carry out the study. Each patient's information were collected using a structured checklist. The collected information was only be used for this particular study and was kept confidential.

4.11. Dissemination of Results

The output of this study will be communicated to the Department of Internal Medicine and Public Health, St. Paul's Hospital Millennium Medical College in partial fulfillment of the requirement for a specialty certificate in Internal Medicine. It will also be submitted to the hospital's Nephrology unit. Attempts will be made to publish the information in peer-reviewed journals and make presentations in scientific conference.

5. Results

5.1 Baseline characteristics

A total of 140 patients with AKI fulfilling the criteria during the study period was initiated on RRT. The mean (SD) age of our participants was 41.15 (18.063) years, of which 57.9 were women and 10 were Gyne/Obs. Sepsis was the most common primary admission diagnosis (27.1%). Details of baseline demographics, admission characteristics, and premorbid kidney Function are shown in Table 1.

Table 1. Baseline demographic, clinical, and physiological characteristics at ICU admission

Characteristics	
Age (y), mean (SD)	41.15 (18.083)
Sex (female), n (%)	81(57.9)
Primary diagnostic category, n (%)	
Sepsis	38 (27.1)
Cardiovascular	24 (17.1)
Hepatic	3 (2.1)
Respiratory	18 (12.9)
Gastrointestinal	2 (1.4)
Genitourinary	25 (17.9)
Gyne/Obs	14 (10)
Surgical	7 (5)
Others (a)	9 (6.4)
Premorbid (baseline) kidney function	
SCr (mg/dl), median (IQR)	2 (3.70)
Urea (mg/dl), median (IQR)	63.45 (92.33)
eGFR (mL/min/1.73 cm ²), median (IQR)	34.42 (75.07)
ICU admission kidney function	
SCr (mg/dl), median (IQR)	6.71 (6.05)
Urea (mg/dl), median (IQR)	165 (119.98)
eGFR (mL/min/1.73 cm ²), median (IQR)	9.03(8.03)
AKI Stage at ICU admission, n (%)	
Stage 1	1 (0.7)
Stage 2	13 (9.3)
Stage 3	126 (90)

(a) Others includes primary neurological, endocrine and hematological diagnoses.

5.2. Clinical and physiologic characteristics at RRT initiation

A summary of clinical and physiological parameters at the time of RRT initiation are shown in Table 2. Patients had a median (IQR) SOFA score of 9 (4-21) and a median (IQR) of 3 (1-5) number of failing organs. The majority of patients were mechanically ventilated (60.0%) and 29.3% of patients required vasopressor therapy. The mean (SD) sodium and potassium were 132 (8.51) mmol/L and 4.8(1.28) mmol/L, respectively. Oliguria (<400 mL/24 hours) and anuria (<100 mL/24 hours) were present 45.71% and 54.29%, respectively.

Table 2. Details of clinical and physiological characteristics at the time of initiation of RRT

Parameters	
SOFA score, median (IQR)	9 (5)
Number of failing organs (a), median (IQR)	3 (1)
Vasopressor therapy, n (%)	41 (29.3)
Mechanical ventilation, n (%)	84 (60.0)
Glasgow Coma Scale, median (IQR)	14 (2)
Bilirubin (μmol/L), median (IQR)	0.89 (0.7)
Platelets (cells/10 ⁹), mean (SD)	239 (113)
Sodium (mmol/L), mean (SD)	132.325 (8.5173)
Potassium (mmol/L), mean (SD)	4.8 (1.28)
AKI stage at RRT initiation, n (%)	
Stage 1	0 (0)
Stage 2	0 (0)
Stage 3	140 (100)
Worsening of AKI stage before RRT initiation, n (%)	14 (16.3)
Urine output	
<400 mL/24 h, n (%)	64 (45.71)
<100 mL/24 h, n (%)	76 (54.29)

(a) Organ failure defined as SOFA score ≥ 2 points

5.3. Clinical outcomes

The ICU mortality and dialysis dependence were 47.9% and 13.6%, respectively (Table 3). Those patients who survived at ICU discharge with full recovery of renal function were 13.6%.

Table 3. Summary of characteristics of clinical outcomes

Outcome variable	frequency	percentage
Death in ICU	67	47.9
Dialysis dependence	19	13.6
Diuretic dependence	35	25.0
Recovered renal function	19	13.6

Those patients who were dialysis dependent at ICU discharge required a median of 18 dialysis sessions (table 4).

Table 4. Summary of total session of RRT at ICU discharge.

Outcome variable	median	IQR
Total session of RRT (d), median (IQR)		
Death in ICU	6	1-32
Dialysis dependence	18	4-47
Diuretic dependence	6	3-26
Recovered renal function	8	13-14

The prevalence and associated mortality outcome for traditional triggers for RRT initiation are shown in Table 5. At RRT initiation, all of patients fulfilled stage 3 (100%). Participants who were anuric (urine output <100ml/24hrs) at the time of RRT initiation had 88.06% ICU mortality.

Table 5. Summary of indications for initiation of RRT.

Variable	Frequency (%)	ICU mortality (%)
Stage of AKI at dialysis initiation		
Stage 3	140(100)	47.9
refractory fluid over load	54(38.6)	35.82
uremic encephalopathy	53(37.9)	49.25
refractory hyperkalemia	16(11.4)	2.99
metabolic acidosis	15(10.7)	11.94
uremic pericarditis	2(1.4)	0
Urine output		
<400 mL/24 h	64(45.71)	11.94
<100 mL/24 h	76(54.29)	88.06

5.4. Factors associated with outcome of RRT

Each variable was evaluated independently in a bivariate analysis and association was determined using cross tabulation and crude odds ratio (COR) with 95% CI. All variables associated with ICU death at a probability level of less than or equal to 0.25 on the bivariate analysis were entered into a multivariate binary logistic regression analysis to control for confounders.

As shown in Table 6, on bivariate analysis number of organ failure, vasopressor requirement, SOFA score, urine output, and mechanical ventilator requirement during initiation of RRT showed significant associations and on multivariate analysis except vasopressor requirement and anuria (urine output<100ml/24h hrs.) at the time of RRT initiation the rest of the above variables didn't show statically significant association.

Patients requiring vasopressor therapy during the initiation of RRT were 15 times more likely to die in the ICU than who were not on pressor [AOR=15.79 (95% CI: 3.3-68.8)]. Patients who were anuric during RRT initiation were 27 times more likely to die in the ICU than those who were not anuric [AOR=27.05 (95% CI: 8.06-90.73)] (Table 6).

Table 6. Multivariate Analysis of Factors associated with outcome of renal replacement therapy initiation among patients with acute kidney injury admitted to intensive care units at referral hospitals in Addis Ababa, Ethiopia, from January 1/2021 to December 31, 2022.

variables	outcome		COR (95% CI)	P-value	AOR (95% CI)	P-value
	Died	Survived				
Sofa score						
<9	14(20.9%)	44(60.3%)	1.0		1.0	
≥9	53(79.1%)	29(39.7%)	5.74(2.7-12.2)	<0.001	0.96(0.24-3.82)	0.95
Total organ failed						
<3	35(52.2%)	60(82.2%)	1.0		1.0	
≥3	32(48.8%)	13(17.8%)	4.22(1.95-9.09)*	<0.001	2.52(0.79-8.06)	0.11
On vasopressor						
Yes	36(53.7%)	5(6.8%)	15.79(5.65-44.1)*	<0.001	15.14(3.3-68.8)*	<0.001
No	31(46.3%)	68(93.2%)	1.0		1.0	
On MV						
Yes	53(63.1%)	31(36.9%)	5.13(2.42-10.85)*	<0.001	2.86(0.72-11.37)	0.13
No	14(25%)	42(75%)	1.0		1.0	
Urine output						
<100ml/24hr	59(77.6%)	17(22.4%)	24.29(9.7-60.7)*	<0.001	27.05(8.06-90.73)*	<0.001
<400ml/24hr	8(12.5%)	56(87.5)	1.0		1.0	

*Significant association, MV-Mechanical Ventilation COR -Crude Odds Ratio, AOR- Adjusted Odds Ratio

6. Discussion

The study assessed 140 critically ill patients with AKI who received RRT to describe factors associated with RRT initiation, to explore the association of clinical, physiological, and biochemical characteristics at the time of RRT initiation with important clinical outcomes including mortality and dialysis dependence.

In this study IHD modality of RRT have been used in the treatment of all participants. A worldwide survey showed that CRRT was the most prevalent initial modality for AKI patients (80.0%), followed by IHD (16.9%), and PD and SLED (3.2%)(9,19). This variation is because of the only available modality of RRT in the study area is IHD.

The median age of the study population was 41.1 years and 81(57.9%) are females. This is in contrast to the study populations in the AKIKI, IDEAL-ICU and ELAIN trials, where the median age of all groups was >60 years and 31% were females(23).

Overall. In this study, in-ICU mortality was 47.9%, and 13.6% of survivors remained dialysis-dependent at ICU discharge which is comparable with study done at Tikur Anbessa Specialized Hospital (TASH), which showed a 45.1 % all-cause mortality(34). This is because, in both studies it's found that critically ill patients with AKI who were initiated on RRT were complex and characterized by a high illness severity and multiorgan dysfunction.

Refractory fluid overload 38.6%, uremic encephalopathy 37.9% followed by refractory hyperkalemia 11.7%, were the most common indications for hemodialysis which is discordant with the above similar study that showed severe hyperkalemia (42%), uremic syndrome (29%), refractory edema (17%), and metabolic acidosis (12%) as the most common indications. cause mortality(34). Apart from refractory hyperkalemia other indications was consistent and sepsis was the common underlying cause in both studies.

All of patients fulfilled stage 3 AKI at the time RRT was initiated. This is consistent with earlier studies. In a study on the indications for and timing of hemodialysis in critically ill patients with acute kidney injury in Johannesburg, South Africa, Overall, 90% or more of the study participants underwent RRT after reaching KDIGO stage 3(32).

These observations indirectly imply the use of RRT may represent an important organ support modality in critically ill patients, not solely to replace selected aspects of kidney function but also

to aid in maintaining homeostasis in others. Importantly, I believe these data are the first to provide insight into the current standards of practice for RRT initiation in our context.

In addition to the evaluation of traditional indications for RRT initiation, we also examined whether additional thresholds of clinical, physiological, and laboratory factors had any important associations with mortality. We found that selected factors, in particular vasopressor requirement, acidosis and decreased urine output is associated with higher mortality. This is consistent with multiple studies that showed a significant association between mortality and the volume of urine production before RRT initiation. Mortality was highest for those patients with marked oliguria (<100 mL/24 hours). Oliguria has repeatedly been associated with higher mortality in AKI(26–28).

In my study, higher organ failure scores (SOFA score >9) at the time of RRT initiation is associated with higher mortality. Numerous other studies have reported that a higher burden of organ failure at RRT initiation portends a worse prognosis(29–31). This is not unexpected, as RRT may not be initiated for severe AKI per se but more commonly as part of a strategy of multiorgan and homeostatic support in critical illness.

This study confirms that RRT initiation in critically ill patients is a complex process and is conditional on numerous patient-specific factors. Although I have identified clinical parameters at the time of RRT initiation that are associated with worse clinical outcomes, my data suggests the immediate indications were “traditional” indications that commonly encountered in critically ill patients.

7.Limitation of the study

This was a retrospective study with a relatively small sample size done at 2 centers. The aforementioned can all lead to a non-representative sample of the general population. Since this study used a retrospective clinical record review it is not possible to find temporal relationship between cause and effect.

8. Conclusion

My study population is predominantly young as compared to the reviewed literatures, with the mean age being 41.1 years. The most common cause of ICU admission was sepsis in our case. The observed timing for RRT initiation was late (stage III AKI) with emergent & classical indications. The ICU mortality and dialysis dependence were 47.9% and 13.6%, respectively. Our study found anuria & the need for vasopressor support to be associated with poor outcomes.

9.Recommendation

For Ministry of Health (MOH)

MOH should increase the availability of RRT and other modalities apart from IHD.

For SPHMMC

-Conducting Further research looking at patients that were not dialyzed but potentially required it would offer greater insights.

-I recommend further study with a larger study population, prospective design incorporating patients who were started on RRT earlier for better comparison.

For SPHMMC ICU Team

Early recognition of sepsis and timely management could decrease the burden of sepsis associated AKI and associated dire outcome.

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Annexes

ANNEX I

Information Sheet

Research Title: FACTORS ASSOCIATED WITH OUTCOME OF RENAL REPLACEMENT THERAPY IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY AT TERTIARY CENTERS, ADDIS ABABA, ETHIOPIA

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Takele Menna (MPH, PHD.)

Sponsor St. Paul's Hospital Millennium Medical College

ANNEX II:

Data Collection Checklist

Date-----

Card number -----

1. Baseline characteristics

S. R	Question	Response category
101	Age (in years)	
102	Sex	1. Male 2. female
103	Primary diagnostic category	1. Sepsis 2. Cardiovascular 3. Hepatic 4. Respiratory 5. Gastrointestinal 6. Genitourinary 7. Surgical 8. Gyne/obs 9. Others
104	Premorbid (base line) kidney function	1. SCr 2. BUN 3. eGFR
105.	ICU admission kidney function	1. SCr 2. BUN 3. eGFR)-
106	Stage of AKI at ICU admission	1. Stage 1 2. Stage 2 3. Stage 3

2. Details of clinical and physiologic characteristics at dialysis initiation

S. N	Questions	Response
201.	SOFA score	
202	Number of failing organs	
203	GCS	
204	Bilirubin	
205	Platelet count	
206	Vasopressor therapy	1.Yes 2.No
207	Mechanical ventilation	1.Yes 2.No
208	Serum electrolyte	1.sodium _____ 2.potassium _____ 3.chloride _____
209	Urine output	1.>400/24hr 2.<100/24hr
3	Indication for dialysis	1.refractory fluid overload 2.refractory hyperkalemia

		3.uremic encephalopathy 4.uremic pericarditis 5.metabolic acidosis 6.others
4.	Total session of dialysis at ICU discharge/death	
5.	Outcome	1.Death in ICU 2.Dialysis dependence 3.Diuretic dependence 4.Recovered renal function

ANNEX III

Assurance of Investigator

I the undersigned resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident: _____

Signature: _____

Date: _____

Approval of Advisors

Name of Public Health Advisor: _____

Signature: _____

Date: _____

Name of Clinical Advisor: _____

Signature: _____

Date: _____