

Incidence and Risk Factors of Acute Kidney Injury in ICU Patients of Omdurman Teaching Hospital

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Abstract

Background: Acute kidney injury (AKI) is a common complication in critically ill patients and it is commonly associated with high mortality and morbidity with adverse short and long term outcome. **Objectives:** The main objective of this study was to determine the incidence of acute kidney injury in ICU patients in Omdurman teaching hospital, and to assess the risk factors associated with the development of acute kidney injury in a critically ill patient. We also intended to find out the impact of acute kidney injury on ICU outcomes. **Methods:** In this descriptive prospective, cohort hospital-based study, 211 patients were studied and followed up during admission in ICU from November 2019 until July 2020 in Omdurman teaching hospital. **Results:** 61 patients of the total 211 patients developed renal impairment during their stay in ICU. 64% (39 patients) were males and 36% (22 patients) were female, mean age was 41 ± 5 , renal impairment developed after a mean of 5 days of admission and the most common cause was decreased level of consciousness and severe hypotension, sepsis accounting for 40% of the admission. The outcome in ICU showed that the mortality rate was high up to 41% in patients who developed acute kidney injury, Sepsis accounted for over 96% (24 patients) who have passed away. **Conclusions:** Development of AKI in ICU is an important risk factor for poor outcomes in critically setting. Prevention is the best method for avoiding AKI, with the early identification and recognition of high-risk patients.

Keywords

Acute Kidney Injury, ICU, Risk Factors, Outcome, Frequency

1. Introduction

AKI is a common complication in patients admitted to the intensive care unit

(ICU) and is commonly associated with adverse outcomes, increasing the length of ICU stay, increasing short and long term mortality, and contributing to developing chronic kidney disease (CKD).

The identification and studying of the risk factors associated with the development of acute kidney injury will help in providing and establishing preventive measure that could improve survival in those patients. As recognition of those high-risk patients will allow developing steps and guidelines help in prevention, diagnosis and treatment of AKI.

Although acute kidney injury is preventable and treatable in most cases, it carries a high mortality rate in a critical care setting, especially in developing countries. This research was focused on the frequency, risk factors, and outcome.

2. Literature Review, Rationale & Objectives

2.1. Literature Review

Over the past decades, there was an increased incidence of acute kidney injury, and given the adverse outcomes especially in the long term, AKI is now a growing concern for health care worldwide.

Acute kidney injury is a challenging medical complication with hospital costs exceeded only by those for acute myocardial infarction and stroke. This condition is a sudden decline in kidney function during hours to days originating in either the community or hospital setting [1]. Mortality rates progress proportionally with the severity of the decrease in kidney function [2]. Acute renal injury defined as 1) Increase in serum creatinine by 0.3 mg/dL or more within 48 hours or 2) Increase in serum creatinine to 1.5 times baseline or more within the last 7 days or 3) Urine output less than 0.5 mL/kg/h for 6 hours using Kidney Disease Improving Global Outcomes (KDIGO) [3].

In the hospital setting, patients with AKI have lengths of stay 2.4 times longer than patients who do not have AKI Hospital mortality rates are as high as 60% in ICU patients and 80% in patients requiring renal replacement therapy (RRT).

2.2. Risk Factors

The potential risk factors include sex, race, reference creatinine, estimated glomerular filtration rate (eGFR) derived from the reference creatinine.

Elderly patients are at risk of AKI due to decreased renal reserve and altered kidney function inhibiting kidney function recovery following acute injury. The incidence of AKI has increased steadily in recent years, and this increase is associated strongly with advancing age in the population because epidemiologic data indicate that AKI is much more common in the elderly. In the ageing population, there is heightened susceptibility to drug toxicity, partially owing to altered drug pharmacokinetics and pharmacodynamics. Furthermore, the elderly consume twice as many medications overall, including nephrotoxic agents, compared with younger patients [3].

Severe sepsis is one of the leading causes of acute kidney injury (AKI). Pa-

tients with sepsis-associated AKI demonstrate high-hospital mortality. During the past decades, the incidence of severe sepsis has increased. A study reported a 75% increase in ICU treated severe sepsis from 1993 to 2001 in France [4]. Of patients with sepsis in the ICU, 31% - 61% have AKI [5].

Overall, the prevalence of AKI in the setting of MI is 16%. Patients with AKI had a substantially higher risk of mortality than those without AKI. Patients with AKI are at a substantially higher risk of in-hospital major bleeding events, despite lower rates of invasive strategies [6].

Studies have recently shown that up to 40% of the population has CKD, and this confers up to the 8-fold increased risk of mortality among affected patients [7]

Diabetes is the most frequent cause of end-stage renal disease in our society. Acute kidney injury remains a clinical and prognostic problem of fundamental importance since incidences have been increased in recent years, while mortality has not substantially been improved [8]. Approximately 40% of all patients requiring dialysis therapy on a regular basis suffer from diabetes mellitus as the respective cause [9].

Diabetic kidney disease, commonly termed diabetic nephropathy (DN) is the most common cause of the end-stage renal disease (ESRD) worldwide. The characteristic histopathology of DN includes glomerular basement membrane (GBM) thickening, mesangial expansion, nodular glomerular sclerosis, and tubulointerstitial fibrosis. Diabetes is associated with many metabolic derangements, such as reactive oxygen species (ROS) overproduction, hypoxic state, mitochondrial dysfunction, and inflammation [10].

Multiple studies have shown that diabetes alone is an independent risk for acute kidney injury [11] [12]. The incidence of AKI was found to be higher in diabetic patients undergoing surgery [13]. Renal insults resulting in tissue injury, including acute tubular injury, may affect kidney function and the rate of chronic functional impairment in diabetic patients since the subsequent maladaptive recovery fails to fully reverse the insults.

Aminoglycosides are potent bactericidal antibiotics that are highly effective against gram-negative bacterial infections. They have increasingly been used as gram-negative organisms have become progressively more resistant to beta-lactam antibiotics and fluoroquinolones.

They were recently found to be prescribed in 12.1% of the cases in which an antibiotic was necessary for the ICU [14].

The most important adverse effects of aminoglycosides are nephrotoxicity, ototoxicity, and, more rarely, neuromuscular blockade. Renal injury can occur in a substantial number of patients receiving an aminoglycoside, and whether it occurs depends on the patient's clinical condition and interactions with other nephrotoxic drugs [15] [16] Aminoglycoside-associated kidney injury may manifest as a decrease in the glomerular filtration rate, enzymatic, aminoaciduria, glycosuria, hypomagnesemia, hypocalcemia, and hypokalemia. Fanconi-like and

Bartter-like syndromes, as well as impaired renal concentrating mechanisms, have also been described [15].

Several risk factors for aminoglycoside-associated nephrotoxicity have been identified, including the presence of comorbidities, volume depletion, liver dysfunction, sepsis, renal dysfunction, hypokalemia, hypomagnesemia, advanced age, prolonged therapy, the type of aminoglycoside, the frequency of aminoglycoside dosing, an elevated serum aminoglycoside concentration, the timing of aminoglycoside administration, the simultaneous consumption of other medications, and interactions with other nephrotoxic drugs [17].

2.3. Rationale

According to our knowledge, and local data available we found there were no study has been conducted in our region that investigating the incidence and risk factors of developing renal injury as the problem among ICU patients so, for this reason, we intended to carry out this study as it will add a huge knowledge and advances in management and control of this disease.

3. Objectives

3.1. Main Objective

The main objective of this study was to determine the incidence of acute kidney injury in ICU patients in Omdurman teaching hospital.

3.2. Specific Objectives

- 1) To determine the incidence of acute kidney injury in ICU patients.
- 2) To assess the risk factors associated with the development of acute kidney injury in critically ill patients.
- 4) To find out the impact of acute kidney injury on ICU outcomes.

3.3. The Research Problem

Some patients admitted to ICU with no history of kidney disease developed acute kidney injury and required urgent intervention which significantly affects the outcome and course of treatments for those patients.

4. Methods

4.1. Study Area

The study was conducted from November 2019 until July 2020 in Omdurman teaching hospital, ICU department.

Omdurman teaching hospital is a tertiary hospital work at the level of major medical and surgical specialities. The ICU department consists of major room accommodate Eight ICU beds for general medicine and surgical patients and small room specialized for septic patients. The staff of ICU consists of three intensivists, two medicine specialist and 21 ICU residents.

4.2. Study Design

It was a prospective, cohort hospital-based study.

4.3. Study Population

Adult Patients admitted to the ICU department for more than 24 hours with normal renal profile.

4.4. Exclusion Criteria

Patient with the previous history of renal impairment or admitted with a condition known to cause kidney injuries such as poisoning or drugs overdose.

4.5. Data Collection Techniques

Secondary Data was collected using a checklist and datasheet to collect data from files and medical records. The data collected by trained volunteer following local ICU protocols of infection controls, this data sheet was containing demographic data and history of the illness. Demographic data as age sex resident occupation chronic disease, ICU cause of admission, ICU Score simplified acute physiology score and lab investigation result has been recorded for every patient since day 1 of ICU admission, all the patients assessed in a regular interval after 48. The risk factors included in the analysis were significant predictors of AKI in previous studies [18] and [19].

4.6. Sampling Technique

The sample was total coverage of all the patients' eligible for the study.

4.7. Ethical Consideration

The proposal of the study has been presented to the ethical Clearance committee of the Khartoum ministry of health and approved. Hospital directors and participants informed about the purposes and objectives of the study and voluntary consent obtained. The privacy of the patient has been strictly maintained all through the study no information shared with others or used in different research.

4.8. Data Analysis

Statistical analyses were performed with SPSS Statistics (version 25.0, SPSS Inc., Chicago, IL, USA). Continuous variables were given as means and standard deviation provided. Categorical variables were summarized by percentages. Chi-square tests have been used for categorical variables, t-tests for normally distributed variables and Mann-Whitney tests for non-parametric variables for between-group comparisons. A $P < 0.05$ was considered significant.

5. Result

5.1. General Patient Characteristics

Table 1 shows the demographic and clinical characteristics of the ICU patient's

Table 1. Demographic and clinical characteristics of ICU patient's population.

Variables	All cases, N 211
Gender (M/F), n	123/88
Age , years, Mean (SD)	45 (10)
Height cm , Mean (SD)	171 (5)
Weight kg , Mean (SD)	76 (5)
Comorbidities	
Diabetes, n (%)	47 (22%)
Hypertension, n (%)	32 (14%)
Respiratory disease, n (%)	15 (7%)
GIT disease, n (%)	7 (3%)
Cardiac disease	2 (22%)
CNS disease	2 (22%)
Total days spent in ICU	
Mean, n (SD)	9 (5)
Minimum	2
maximum	45
Causes of Admission to ICU, n (%)	
Brain Hemorrhage	35 (17%)
DKA	29 (29%)
Post-Operative	19 (9%)
Septic Shock	18 (8%)
GBS	17 (8%)
Stroke	16 (8%)
Meningoencephalitis	13 (6.2%)
Pulmonary Embolism	11 (5%)
Cerebral Malaria	9 (4%)
Road Traffic	8 (4%)
The outcome in ICU admission	
Improvement	146 (69%)
passed away	65 (31%)

M/F = male/female; SD = Standard Deviation, GIT = gastrointestinal tract, CNS = central nervous system, DKA = diabetic ketoacidosis. GBS Gillian bare syndrome. Values are n (%) unless otherwise specified.

population. During the study period, 211 patients were included. 58% male (123 Patients), and 42% female (88 patients) minimum age was 18 and the maximum was 95 with a mean age of 45 ± 10 years. Weight and height were documented with mean 76 ± 5 and 171 ± 5 respectively.

Comorbidities also we included in this study. 22% (47 patients) were diabetics, 14% (32 patients) were hypertensive, 7% (15 patients) reported a respiratory condition mostly asthma and COPD, 4% (7 patients) had a gastrointestinal condition mostly heartburn, irritable bowel syndrome and one patient had peptic ulcer, only 2 patients had epilepsy and 2 patient had previous ischemic heart disease.

The mean of Total days spent in ICU was 9 ± 2 days in this study minimal stays as short as 2 days and maximum stay as long as 45 days. the most common Causes of Admission to ICU was decreased level of consciousness and reported

in 33.6% (71 patients) followed by observation in 29% (61) and severe acidosis in 15% (31 patients) and severe hypoxia in 12% (26 patients) and severe hypotension in 6% (12 patients) and lastly post-cardiac arrest in 5% (10 patients).

The outcome in ICU admission showed that 69% (146 patients) showed signs of improvement after admission and discharged from ICU while 31% (65 patients) passed away.

The most common diagnosis is brain hemorrhage irrespective of the cause is 17% (35 patients) then Diabetic Keto Acidosis (DKA) in 14% (29 patients) then post-operative observation in 9% (19 patients) septic shock in 8% (18 patients) and Guillain-Barre syndrome (GBS) 8% (17 patients) stroke 8% (16 patients) Meningoencephalitis 6.2% (13 patients) and pulmonary embolism 5% (11 patients) cerebral malaria 4% (9 patients) road traffic in 4% (8 patients).

The overall ICU mortality was 31%, for patients with renal impairment it was 41% which was greater than the 23% mortality of those patients with normal renal function.

5.2. Renal Impairments

61 patients (29%) involved in the study developed renal impairment during their stay in ICU. 39 (64%) patients were males and 22 (36%) were female. mean age was 41 ± 5 with maximum age was 79 and the minimum was 21, mean weight and height was 76 kg and 175 cm respectively.

Total days spent in ICU was ranging from a minimum as 3 days and maximum as long as 20 days with a mean of 10 days while renal impairment developed after mean of 5 days after admission with a maximum of 9 days and a minimum of 3 days (**Table 2**).

Table 2. Demographic and clinical characteristics of ICU patient's population who developed acute kidney injury.

Variables	All cases, N 61
Gender (M/F), n	39/22
Age, years, Mean (SD)	41 (5)
Height cm, Mean (SD)	175 (5)
Weight kg, Mean (SD)	76 (5)
Comorbidities	
Diabetes, n (%)	19 (31%)
Hypertension, n (%)	9 (14%)
Respiratory disease, n (%)	4 (7%)
GIT disease, n (%)	3 (5%)
Cardiac disease	3 (5%)
CNS disease	1 (2%)
Total days spent in ICU	
Mean, n (SD)	10 (5)
Minimum	3
maximum	20

Continued

Causes of Admission to ICU, n (%)	
brain haemorrhage	9 (15%)
DKA	15 (25%)
post-operative	7 (11%)
septic shock	25 (40%)
road traffic	5 (9%)
The outcome in ICU admission	
Improvement	29 (48%)
passed away	25 (41%)
discharged with deficit	7 (11%)

Cause of admission to ICU (**Figure 1**) showed the most common cause was decreased level of consciousness 36% (22 patients), severe hypotension 20% (12 patients) followed by severe acidosis 18% (11 patients), 16% (10 patients) admitted for observation of vitals and 7% (4 patients) with severe hypoxia and only 3% (2 patients) admitted after had cardiac arrest irrespective of the cause.

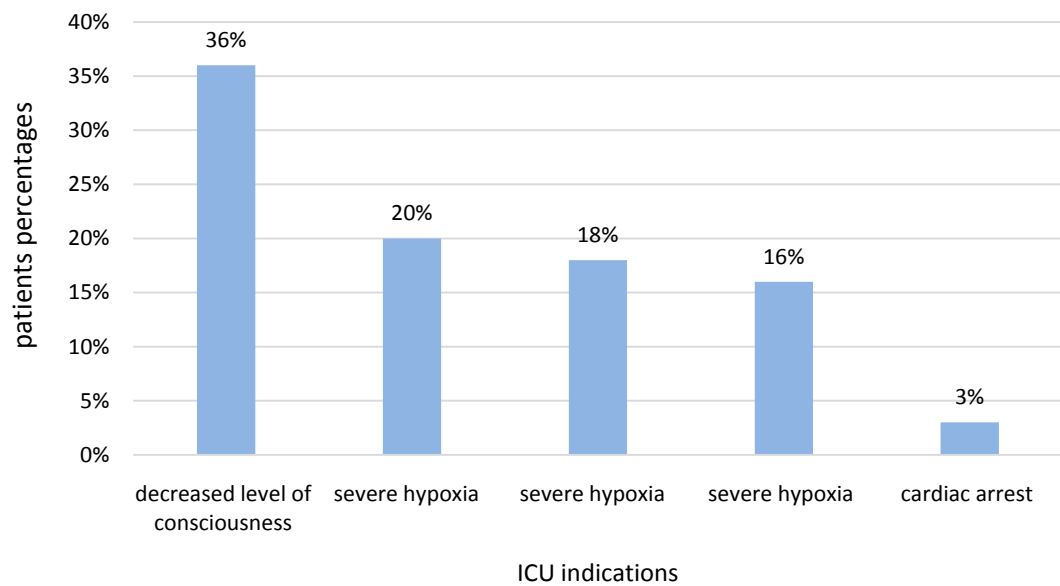


Figure 1. Showed percentage of the most common indication for admission to ICU in patients who developed AKI.

The most common diagnosis admitting the patient to ICU was sepsis accounting for 40% (25 patients), followed by diabetic ketoacidosis 25% (15 patients), post-operative recovery 15% (9 patients), and brain haemorrhage accounting for 11% (7 patients) and least road traffic accident was 9% (5 patients) (**Figure 2**).

45% (28 patients) developed renal impairment while receiving inotropes in ICU. 44% (27 patients) received a mechanical ventilator Statistical Analysis showed significant differences between the patients developed renal impairment and who revived inotropes and mechanical ventilators (0.005) and (0.007) re-

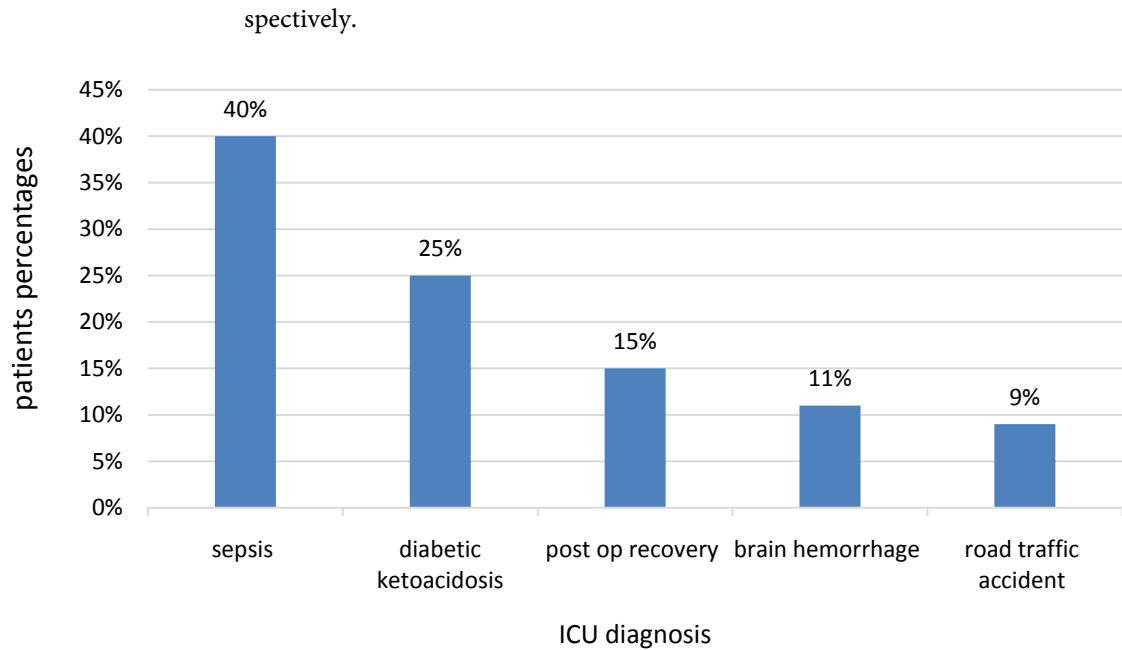


Figure 2. Showed percentage of the most common diagnosis in patients who developed AKI in ICU.

Sepsis and hypovolemia were the most frequent reported etiologies for AKI. Accounting for 51 patients other causes include nephrotoxic drugs (including gentamycin, vancomycin, and contrast dye) causes 6 patients and 4 patients due to rhabdomyolysis after a road traffic accident.

Renal replacement therapy

Of the 61 causes of AKI, 38 patients had received renal replacement therapy (RRT) either hemodialysis or peritoneal dialysis with a 45% Mortality, while 23 patients were managing conservatively with a 36% Mortality (**Table 3**). The majority of RRT procedures were emergency dialysis through a temporary catheter for 2 hours duration.

Table 3. Shows percentages of patients received renal replacement therapy and who managed conservatively in relationship with mortality percentages.

	N (%)	MORTALITY
Renal Replacement Therapy	38 (62%)	45%
Conservative treatment	23 (38%)	36%

Outcome

The outcome in ICU showed 48% (29 patients) recovered from renal impairment, 41% (25 patients) has the past way and 11% (7 patients) discharged with long term renal replacement therapy afterwards (**Figure 3**). Statistical Analysis showed significant differences between the outcome and total days spent in ICU (0.003). Sepsis accounts for over 96% (24 patients) who have passed away (p 0.004).

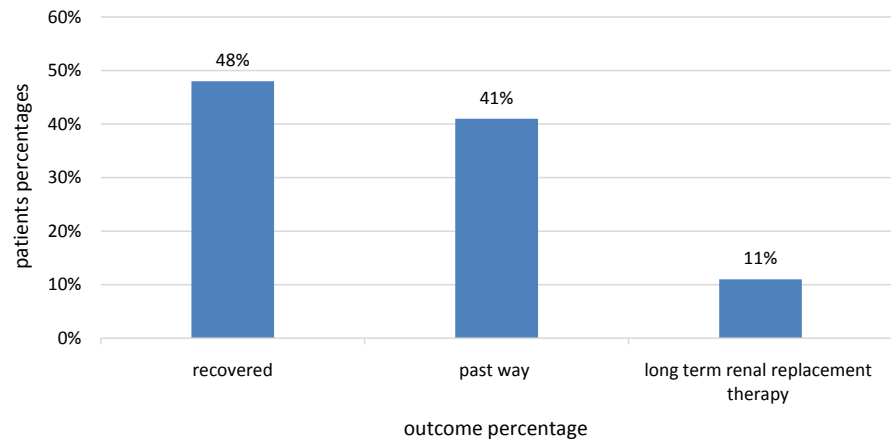


Figure 3. Showed patients percentages of the outcome in patients who developed AKI in ICU.

6. Discussion

The aim of this study was not only to determine how frequent renal impairments, is But also to assess and identify the risk factors associated with the development of AKI in those critically ill patients and to find out the impact of developing acute kidney injury on the general ICU outcomes. Early recognition of those high-risk patients provides an opportunity to develop strategies for prevention, diagnosis and early therapeutic intervention.

In this study, we observed 211 selected patient for the study and found that almost 29% of those patients had developed acute kidney injury, with a mean age of 41 ± 5 with a mortality up to 41%.

Literature reviews [20] reported in a large multi-centre study that the incidence of AKI was 39.3% and mortality was 33.7% which is lower than our estimation probably due to advanced caregiver to the patients compared to our care the patients received in our ICU. Another study [21], Estimates of AKI prevalence range from <1% to 66% and explained These variations be population differences and the use of AKI classification criteria.

In our study, some factors were observed associated with a greater likelihood of developing acute kidney injury. One of these factors is the length of stay in ICU, the result supports our theory that the longer patient stays increase like-hood of developing acute kidney injury. Our result was significant ($p = 0.003$). We thought this is might be due to increasing the risk espouse to the patient in ICU that the longer patient stays in ICU the longer chance to be exposed to infection and sepsis, nephrotoxic drugs, or stress. this is also observed in a study [22] as reported in Patients who developed AKI had higher APACHE II score and longer ICU stays ($P < 0.001$), and higher mortality rates ($P < 0.001$), our result also support the Chinese study [23] A retrospective study across China found AKI was associated with longer length of stay and higher daily costs [23].

The use of invasive mechanical ventilator and inotropes were associated with

increased incidence and mortality in this study. This association might also reflect the severity of illness in a subset of our patients having other organ system failure leading to mortality. 44% of patients with AKI have been used an invasive mechanical ventilator and the result showed a significant impact on the outcome ($p = 0.007$) this was also observed in the study [3] which reported that Invasive mechanical ventilation is associated with a threefold increase in odds of acute kidney injury in critically ill patients also AKI appears to develop more often in patients with invasive Mechanical Ventilators than in those with Non-Invasive Ventilations (NIV). Another study [24] correlate the same finding and reported 21% of the patients subsequently developed AKI, but without significant difference between ventilation strategies [25].

Our study reported a 45% of the patients developed AKI have received inotropes which was a significant result ($p = 0.005$), and Norepinephrine is the most commonly used vasopressor in our patients along with dopamine and epinephrine. This observation can be explained by the fact that the pathophysiology of hypotension and its effect on kidney perfusion will significantly produce a reduction in renal perfusion and overwhelm autoregulation and precipitate an acute fall in Glomerular filtration rate (**GFR**). These mechanisms have been described in [26].

In our study, we found sepsis is the most common diagnosis required the patient to be admitted to ICU. In around 40% of the patients, we observed that sepsis is the leading cause and responsible for almost 84% of the mortality causes of sepsis observed in the present study due to pneumonia, urosepsis and Meningoencephalitis. Many studies have demonstrated the association between sepsis and mortality. In a study [27] Incidence reported Sepsis was considered the cause of acute kidney injury in (47.5%) of the patients and it was associated with greater aberrations in hemodynamics and laboratory parameters, greater severity of illness, and a higher need for mechanical ventilation and vasoactive therapy. A retrospective study across China including 146,148 patients found AKI in 47.1% of sepsis cases [23]. Another study reported AKI is common even among patients without severe sepsis or shock 34% of non-severe community-acquired pneumonia developed AKI [28]. Literature reviews [4] reported that a 75% increase in the intensive care unit (ICU)-treated severe sepsis from 1993 to 2001 in France.

In this study, the association of comorbidities, *i.e.* hypertension, diabetes, heart disease, the respiratory condition was not statistically significant. Although diabetes and number of comorbidities were found to be related to mortality in AKI patients in the previous studies [29] have shown that diabetes alone is an independent risk for acute kidney injury (AKI) and Diabetes significantly increases the overall morbidity and mortality, particularly by elevating the cardiovascular risk. e incidence of AKI was found to be higher in diabetic patients undergoing.

Nephrotoxic medication is the second cause of AKI in our study after sepsis

accounting for 10% of our patients, these drugs include gentamycin, vancomycin and contrast dye. The most important adverse effects of aminoglycosides are nephrotoxicity, ototoxicity, and, rarely, neuromuscular blockade. Renal injury can occur in a substantial number of patients receiving an aminoglycoside, and whether it occurs depends on the patient's clinical condition and interactions with other nephrotoxic drugs. A study [30] reported nephrotoxic drugs to contribute to AKI in 19% - 25% of cases in the ICU. And [31] reported AKI was observed in 609 patients (61%) these numbers are different from our estimation probably these studies are focused on nephron toxic medication as the main study problem with a large number of patients and advanced diagnostic modalities.

In the current study, there was a significant relationship between initiation of renal replacement therapy and the outcome, we observed 45% mortality of patients received RRT comparing to 36% in patients managed conservatively.

We acknowledge that our study has several limitations. First, the relatively small number of patients studied in this research may not representative of other Centers in the same region, Secondly this study conducted in a single centre which may limit the statistical power where a small number of patients were included. Thirdly the decision to initiate renal replacement therapy was purely clinical and judgmental.

7. Conclusions

The high frequency and mortality of AKI in ICU patients cause a significant health challenge. Further studies should be required to adopt and formulate therapeutic strategies to prevent the occurrence of AKI in ICU patients and reduce mortality.

This study states that the development of AKI in ICU is an important risk factor for poor outcomes in the critical care setting. Prevention is the best method for avoiding AKI, with the early identification and recognition of high-risk patients.

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I wish to express my sincere gratitude to our ICU staff for their support throughout the study, and also wish to express my sincere gratitude to the patients and their families who made this work possible.

Declaration

I declare that this work to be original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere.

Ethical Approve

I declare this work has been approved by the authorized ethical committee in the ministry of health, the Republic of Sudan and by the scientific committee in

Omdurman teaching hospital.

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I declare this work to be self-funding by the authors, no financial support could have influenced the result of this work.

Authors Contribution and Consents

All the work in this research done by the authors listed. AS carried out the discussion and conclusion. NE carried out the data collecting and result. Both AS and NE contribute to the introduction, literature review, methodology and manuscript format. I confirm this manuscript has been revised and approved for submission by all the named authors.

Availability of Data

Data is available.

Consent for Publication

Not applicable.

Conflicts of Interest

I declare I have no conflicts of interest to disclose.

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Abbreviations

AKI acute kidney injury

ICU intensive care unit