

Incidence and Predictors of Acute Kidney Injury Among Critically Ill Adult Patients Admitted at Mbarara Regional Referral Hospital

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Background: Severely ill patients are vulnerable to developing Acute Kidney Injury (AKI), with variable incidence, but limited data from LMICs. We evaluated the incidence, predictors, treatment, and outcomes of AKI among very ill adult patients at a public tertiary hospital in southwestern Uganda.

Methods: This prospective cohort study categorized patients who had a NEWS-2 above 5 as critically ill. We used the “Kidney Disease Improving Global Outcomes (KDIGO)” definition of AKI as a 0.3 mg/dl increase in serum creatinine within 48 hours. Participants were followed up until day 7 of admission, death or discharge, whichever occurred first. STATA version 13 was used for data analysis. Predictors of AKI were determined by logistic regression.

Results: Of 161 critically ill patients, the median age was 48 years (IQR: 31–65). The incidence of AKI was 70 (95% CI 55–90) per 1000 person days of observation. About, 39.1% (127) drugs used during hospitalization were deemed potentially nephrotoxic, and 60% (96) of participants were exposed to at least one nephrotoxic drug. Penicillins and loop diuretics were the most commonly used nephrotoxic drugs. Predictors of AKI included: previous hospitalization in the last 3 months (aOR 2.56, 95% CI: 1.08–6.06, P=0.032), admission to the surgical ward (aOR 4.32, 95% CI: 1.22–15.24, P=0.023), elevated baseline creatinine (>1.2 mg/dl) (aOR 2.44, 95% CI: 1.13–5.27, P=0.023) and elevated baseline WBC count (>12 × 10⁹/μL) (aOR 2.57, 95% CI: 1.21–5.46, P=0.014). Most AKI patients were managed conservatively; 25% of patients with stage 3 received hemodialysis, and 25% of those with incident AKI died in the hospital.

Conclusion: We found a high prevalence of AKI among critically ill patients (70 per 1000 person days). Previous hospitalization in the past 3 months, high baseline creatinine, high baseline WBC count and admission to the surgical ward were independently associated with AKI.

Keywords: critically ill patients, acute kidney injury, predictors, Uganda, nephrotoxic drugs

Introduction

Acute Kidney Injury (AKI) is a rapidly progressive decline in glomerular filtration rate (GFR) indicated by a rise in serum creatinine (SCr) of 0.3mg/dl or more within 48 hours or to 1.5 times the baseline in 7 days and/or reduction in urine output (UOP) to less than 0.5 mL/kg/hour for at least 6 hours.¹ Globally, AKI affects approximately 13.3 million people, causing 1.7 million deaths each year.² AKI is not only a very common condition, but also a predictor of

morbidity, and can cause chronic kidney disease (CKD) or progress to kidney failure, which further complicate patient management and worsen prognosis.³ However, AKI may be reversible if detected early enough.⁴ Critically ill patients are more likely to develop AKI. AKI in critically ill adults arises from hemodynamic, inflammatory, and nephrotoxic factors. Ischemic injury due to reduced renal perfusion is a common pathway, particularly in conditions like sepsis and shock. The resulting hypoxia and oxidative stress can cause direct tubular damage and apoptosis.⁵ Inflammatory cytokines and mediators released during systemic infections and critical illnesses contribute to endothelial dysfunction, increased vascular permeability, and further renal injury.³

Moreover, the administration of nephrotoxic agents, either as part of therapeutic regimens or inadvertently, exacerbates renal injury. Drugs such as aminoglycosides, contrast agents used in diagnostic imaging, and certain chemotherapeutic agents have well-documented nephrotoxic effects.⁶ The cumulative impact of these factors leads to the clinical manifestation of AKI.

Generally, AKI affects about 10–15% of in-hospital patients, and more than 60% of patients admitted in ICUs.^{7–9} Severe AKI occurs in about 4–5% of critically ill patients^{9–11} due to resistant volume overload, uncontrollable electrolyte disorders, uremic complications, and drug toxicity. The exact mechanism of how AKI influences the clinical outcomes in severely ill patients remains unclear. However, it's thought that it induces multi-system inflammatory responses.¹² Variations in reported incidences across studies on AKI among critically ill patients are attributed to differences in the study population, geographical area of study, patient baseline characteristics, length of observation period, and the criteria used to determine AKI.^{13–18} Patients who develop AKI have an 8.8 times higher risk of developing CKD, posing far greater long-term health and cost consequences.^{7,19–21} Early recognition and management of AKI can prevent its major complications.^{22,23} Because critically ill patients may develop multi-organ dysfunction, the development of AKI in this population may have an impact on the outcome. Despite the overwhelming morbidity caused by AKI in critically ill patients, data on the incidence and predictors of AKI in this patient population in Uganda is limited. Bagasha et al (2015) studied the prevalence of AKI among adult patients with sepsis on the medical ward of a national referral hospital in Uganda and found a prevalence of 16.3% and in-hospital mortality of 21%.²⁴ Similarly, Kimweri et al (2021) studied the incidence and risk predictors of AKI among HIV-positive patients with sepsis at Mbarara Regional Referral Hospital. In their study, the incidence of AKI in 48 hours was 19.2%.²⁵ However, the incidence and predictors of AKI among other critically ill patient populations in Uganda have not been studied. This study intended to assess the incidence and independent predictors of AKI among critically ill patients at Mbarara Regional Referral Hospital (MRRH) in southwestern Uganda. The study also aimed to describe the management of AKI and evaluate the treatment outcomes among patients with incident AKI. The study, ultimately, aimed to guide health workers and policy makers to innovate and implement strategies towards mitigating the burden of AKI and reducing the associated complications in critically ill patients.

Methods

Study Setting

The site of the study was Mbarara Regional Referral Hospital (MRRH) in Mbarara city of southwestern Uganda. This is a tertiary 600-bed health facility serving a population of at least 4 million people from Mbarara and neighboring districts, including those from the Masaka Health Region and neighboring countries in the south western area. It is also the teaching hospital for Mbarara University of Science and Technology, Mayanja Memorial Training Institute and Bishop Stuart University.

The major specialized services provided are Emergency medicine (surgical and medical), Community Health, Internal Medicine, Obstetrics & Gynaecology, Paediatrics, and Surgery. The hospital's emergency ward accommodates both medical and surgical patients. Patients will typically be admitted to the emergency ward for stabilization before they are transferred to the general medical and surgical wards for continued care. The hospital also has an 8-bed capacity ICU which serves critically ill patients. It also has 2 nephrologists and can provide hemodialysis to patients who require the intervention.

Study Design

This was a prospective cohort study among critically ill in-patients between 1st February and 30th May 2024.

Study Population

All critically ill adult patients who provided informed consent by themselves or through their next of kin were recruited into the study. The critically ill patients who were diagnosed with AKI at admission, or were dialysis-dependent, got discharged, or died within the first 48 hours of admission were excluded. Eligible participants were recruited consecutively over the study period without predefined sample size calculation, as recruitment was based on availability of critically ill patients within the study timeframe. Post-hoc power analysis was done to assess the sufficiency of the sample size to answer the study objectives.

Data Collection and Procedure

The team of research assistants who collected data were taken through a one-week's training on the study protocol and tools such as the National Early Warning Score 2 (NEWS-2). They also completed the Responsible Conduct of Research (RCR) and Ethics in Research training, to enhance safety of the participants and integrity of data.

We used the “National Early Warning Score 2 (NEWS-2)” to assess and determine the degree of illness of a patient thus prompting critical care intervention.²⁶ A patient with a NEWS score of 5 or more was considered to be critically ill and requiring prompt emergency assessment. Critical illness in this study was defined as a potentially reversible life-threatening condition in which there is a decline in the function of vital organs, and death is imminent in case of absence of appropriate care.²⁷ Accordingly, critically ill patients were screened and consecutively enrolled from the intensive care unit (ICU), resuscitation bays at the medical emergency and surgical emergency wards as well as the adult general medical and surgical wards. Upon admission, patients were assessed using the “National Early Warning Score 2 (NEWS-2)”.

After obtaining informed consent, the relevant data including socio-demographic characteristics, medical history, admission vitals, NEWS 2 score, baseline serum creatinine (SCr), blood urea nitrogen and serum electrolytes, complete blood count, random blood sugar, AKI management, exposure to nephrotoxic drugs, current drug and alcohol use were collected using a structured data abstraction form. Follow-up serum creatinine measurements were done after 48 hours to assess for incident AKI. Blood samples were tested at the Mbarara Regional Referral Hospital laboratory which does routine external quality assurance.

The “Kidney Disease Improving Global Outcomes (KDIGO)” AKI definition as “an increase in serum creatinine by greater or equal to 0.3mg/dl within 48 hours”²² was used for this study. Whenever CKD was suspected, the diagnosis was made using evidence from past records when available, history including the duration of symptoms, urinalysis and hematological indices, and the use of kidney ultrasound to determine the kidney sizes. The ultimate decision was made in consultation with the nephrologist.

Participants were followed until discharge, death or day 7 from enrolment, whichever would come first.

Data Statistical Analysis

Data cleaning was done using Epi-Info, after which data was imported into STATA version 13 for analysis. Numeric variables were summarized using means or medians with their respective measures of dispersion according to their distribution. Categorical variables were summarized using frequencies and percentages. The Fisher exact test or χ^2 test was used to compare the participants baseline characteristics. The incidence of AKI was computed by dividing the number of participants who incurred AKI by the total number of study participants. The total person-days was computed as a sum of the days each of the participants stayed in the hospital. We computed the incidence rate by dividing the total number of participants who developed AKI by the total person-days, then multiplied the quotient by 1000. Univariate and multivariate logistic regression analysis was used to identify the independent predictors of AKI. A p-value ≤ 0.05 was considered statistically significant.

Ethical Considerations

This study was carried out in compliance with the Declaration of Helsinki. The MUST Research and Ethics Committee approved the study [Reference No: MUST-2023-1235] and site clearance was given by the hospital administration. The patient, or caretaker for those who were too sick, gave written informed consent before enrollment of any participant.

Results

Over 4 months, 420 patients were screened. Out of these, 220 were excluded because they were not critically ill. Out of 200 eligible patients, 28 were admitted to the ICU while 172 were admitted to both the surgical and medical/emergency wards. Overall, 161 participants who satisfied the eligibility criteria were involved in the final analysis. This data is shown in the study flow diagram in [Figure 1](#).

Baseline Characteristics of the Study Participants

The study sample comprised 161 participants, of whom the majority were male (59.6%), without a statistically significant difference in gender distribution between those who developed AKI and those who did not (64.6% vs 35.4%, $P=0.432$). The overall median age was 48 years (IQR: 31–65). The highest number of participants (52.8%) were admitted in the general medical or medical emergency wards, and only 11.2% of participants were admitted in the ICU.

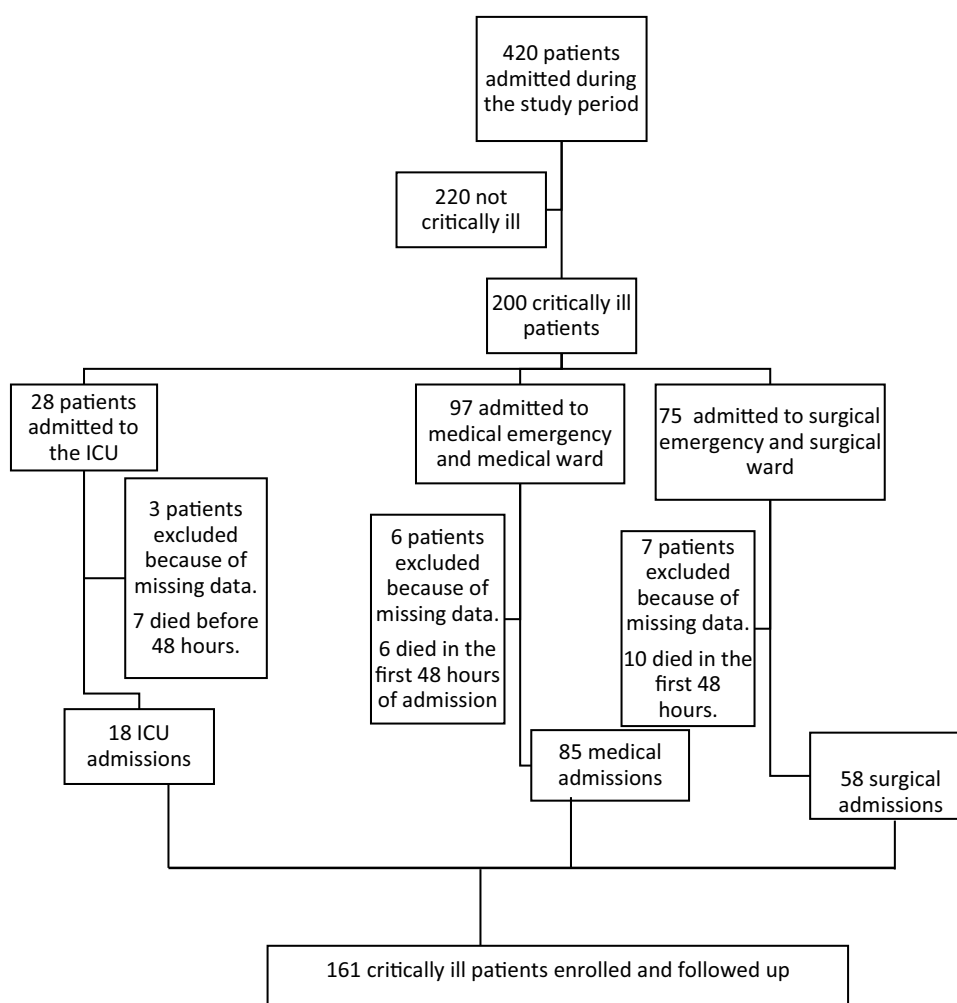


Figure 1 Study flow diagram showing the enrolment of patients.

Table 1 Baseline Characteristics of Study Participants

Characteristic	Overall N=161	AKI (N=100)	No AKI (N=61)	p-value
Males, n (%)	96 (59.6)	62 (64.6)	34 (35.4)	0.432
Age, median (IQR) -years	48 (31–65)	49 (34.5–65)	46 (29–65)	0.406
Level of education, n (%)				0.214
• No education	35 (21.7)	20 (57.1)	15 (42.8)	
• Primary	83 (51.6)	54 (65.1)	29 (34.9)	
• Secondary	38 (23.6)	21 (55.3)	17 (44.7)	
• Tertiary	5 (3.1)	5 (100)	0 (0)	
Current alcohol use, n(%)	58 (36.0)	34 (58.6)	24 (41.4)	0.493
Current tobacco use, n(%)	35 (21.7)	18 (51.4)	17 (48.6)	0.141
Length of hospital stay median (IQR) -	6 (4–10)	6 (4–10)	7 (5–9.5)	0.307
Herbal medicine use within the past 4 weeks, n(%)	7 (4.4)	2 (28.6)	5 (71.4)	0.061
Admission ward, n (%)				0.295
• ICU	18 (11.2)	9 (50.0)	9 (50.0)	
• Medical/medical emergency	85 (52.8)	51 (60.0)	34 (40.0)	
• Surgical/surgical emergency	58 (36.0)	40 (69.0)	18 (31.0)	
Trauma patient	30 (18.6)	19 (66.3)	11 (36.7)	0.878
Previous hospitalization, n (%)	46 (28.6)	35 (76.1)	11 (23.9)	0.021

Abbreviations: ICU, Intensive care unit; IQR, Interquartile range; n, number; %, percent.

There was a statistically significant increase in AKI incidence among participants who had been recently hospitalized within the past 3 months. About, 76.1% of the participants who developed AKI had reported a history of previous hospitalization compared to 23.9% of those without AKI ($P=0.021$). This data is elaborated in [Table 1](#).

Clinical Characteristics of Study Participants

Among the notable co-morbidities, hypertension was the most prevalent, affecting 26.1% of participants overall. However, the prevalence of comorbidities between the participants who incurred AKI and those who did not was comparable. The overall mean NEWS-2 (National Early Warning Score 2) was 11.9 (SD: 2.4), suggesting a high risk of clinical deterioration among participants. However, the comparative analysis did not show a statistically significant difference in the NEWS 2 scores of the “AKI” and “No AKI” groups ($P = 0.102$).

Among the laboratory parameters, the median WBC count was significantly higher in AKI patients ($12.7 \times 10^9/L$) compared to non-AKI patients ($10.1 \times 10^9/L$) ($P=0.006$). The median creatinine level at 0 hours was also significantly higher in AKI patients (1.0 mg/dl) compared to non-AKI patients (0.9 mg/dl) ($P=0.028$). This data is summarized in [Table 2](#).

Incidence of Acute Kidney Injury Among Critically Ill Patients

Among all the 161 participants who were followed up for a median duration of 6 days (IQR: 4–10), the incidence rate of AKI was 70 (95% CI 55–90) per 1000 person days of observation ([Table 3](#)). Out of the 100 participants who developed AKI, 84% (84/100) had stage 1 AKI, while those with stage 2 were 8/100 (8%) and stage 3 were 8/100 (8%).

Medications Used Among Critically Ill Patients Admitted at Mbarara Regional Referral Hospital

Out of 161 study participants, about 96 (60%) were exposed to at least one (mean, 0.8) potentially nephrotoxic drug during hospitalization ([Figure 2](#)). A total of 127 (39.1%) drugs used by the study participants during hospitalization were deemed potentially nephrotoxic. Penicillins, Angiotensin receptor blockers (ARBs), loop diuretics, proton pump

Table 2 Clinical Characteristics of the Study Participants (N=161)

Characteristic	Overall (N=161)	AKI (N=100)	No AKI (N=61)	p-value
Comorbidities, n (%)				
HIV	22 (13.7)	14 (63.6)	8 (36.4)	0.874
Diabetes Mellitus	22 (13.7)	17 (77.3)	5 (27.7)	0.115
Hypertension	42 (26.1)	27 (64.3)	15 (35.7)	0.736
Vital signs				
Temp. (°C), mean (SD)	37.4 (1.3)	37.4 (1.5)	37.3 (1.1)	0.485
SBP (mmHg), mean (SD)	118.7 (31.9)	120.5 (33.6)	115.8 (28.9)	0.372
MAP (mmHg), mean (SD)	87.7 (24.3)	89.1 (25.6)	85.5 (21.9)	0.364
O ₂ sat (%), median (IQR)	92 (88–96)	92 (87.5–96)	92 (88–97)	0.566
PR (bpm), mean (SD)	113.4 (25.4)	112.5 (27.1)	115 (22.5)	0.543
GCS, mean (SD)	9.5 (2.9)	9.3 (2.7)	9.6 (3.1)	0.523
NEWS 2 score, mean (SD)	11.9 (2.4)	12.1 (2.6)	11.5 (2.0)	0.102
Laboratory parameters				
Creatinine (0 hours) (mg/dl), median (IQR)	0.9 (0.7–1.1)	1.0 (0.8–1.1)	0.9 (0.7–1.1)	0.028
RBS (mmol/l), median (IQR)	5.2 (3.8–8.3)	5.1 (3.8–8.5)	5.2 (4.2–7.8)	0.901
WBC count ($\times 10^9/L$), median (IQR)	10.9 (8.4–15.8)	12.7 (9.0–17.0)	10.1 (6.7–13.3)	0.006
Hb (g/dl), median (IQR)	12.1 (9.9–14.2)	12.2 (10.2–14.6)	12 (9.3–13.8)	0.253

Abbreviations: HIV, Human Immunodeficiency Virus; °C, degrees Celsius; IQR, Inter-quartile range; SD, Standard Deviation; mmol, millimoles; Hb, Hemoglobin; mg/dl, milligrams per deciliter; bpm, beats per minute; g/dl, grams per deciliter; WBC, White Blood Cell, %-percent.

Table 3 Incidence of Acute Kidney Injury Among Critically Ill Adults

Parameter	Frequency
Total number of AKI incidents	100
Total person-days	862
AKIs/person-days $\times 1000$	70
AKIs/admission	62.1

inhibitors, Angiotensin converting enzyme inhibitors (ACEIs), and Tenofovir Disoproxil Fumarate, and Phenytoin being the most commonly used. See [Figures 3](#) and [Box 1](#).

Predictors of AKI Among Critically Ill Patients

Patients who developed AKI had higher odds of having been previously hospitalized within the last 3 months, with a significant association observed in both univariable (cOR 2.44, 95% CI: 1.13–5.29, $P=0.023$) and multivariable analyses (aOR 2.56, 95% CI: 1.08–6.06, $P=0.032$). Admission to the surgical ward was another significant predictor of AKI (aOR 4.32, 95% CI: 1.22–15.24, $P=0.023$). Further, elevated serum creatinine at 0 hours (≥ 1.2 mg/dl) significantly increased the odds of developing AKI (aOR 2.44, 95% CI: 1.13–5.27, $P=0.023$). Similarly, a baseline WBC count $\geq 12 \times 10^9/L$ was a significant independent predictor of AKI (aOR 2.57, 95% CI: 1.21–5.46, $P=0.014$) ([Table 4](#)).

Management and Outcomes of Incident AKI Among Critically Ill Adult Patients

Out of 100 participants who developed AKI, only 2% ($n=2$) underwent hemodialysis. The rest of the patients were managed conservatively. The mortality rate among the patients who developed AKI was 25% (25/100) compared to

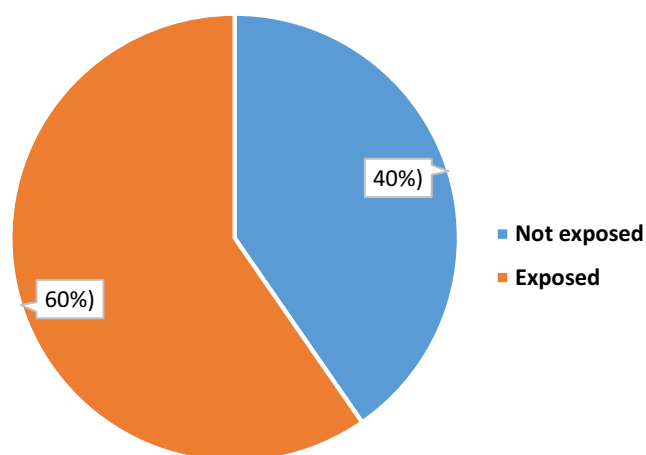


Figure 2 Prevalence of potentially nephrotoxic drug exposure among study participants.

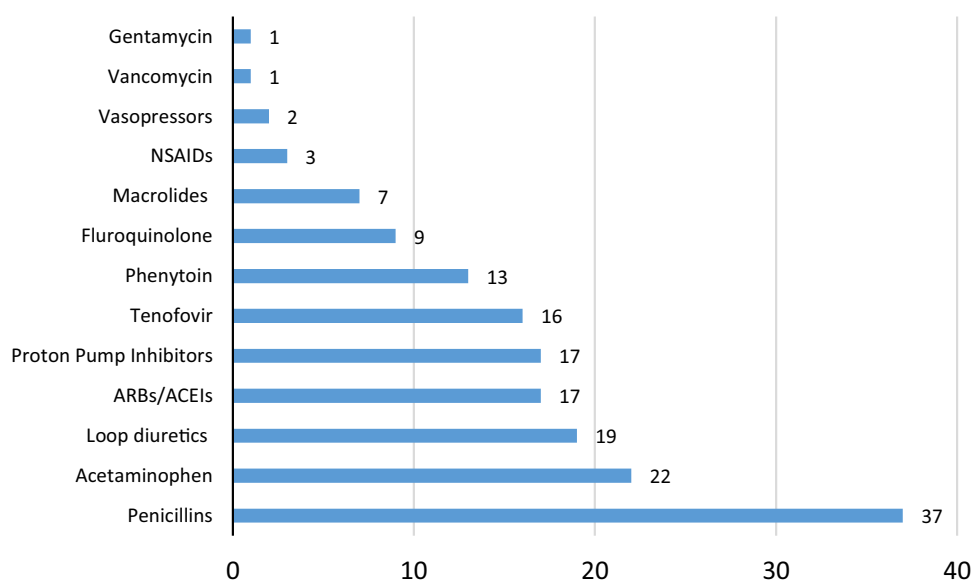


Figure 3 Commonest drugs used by study participants.

13.1% (8/61) among the non-AKI group. Of the patients who survived, 19% (n=14) had complications secondary to the underlying illnesses. The commonest complication was hemiplegia (n=12). Long-term effects of AKI could not be assessed during the follow-up period of 7 days. Despite not having shown statistical significance in multivariable

Box 1 Other Medications Used by Critically Ill Patients During Hospitalization

Lamivudine/Dolutegravir (16), Morphine (1), Methyl dopa (1), Ceftriaxone (123), Nifedipine (13), Ceftriaxone/Sulbactam (7), Carvedilol (2), Spironolactone (7), Insulin Mixtard (8), Diazepam (3), Thiamine (1), Tramadol (1), Atorvastatin (4), Bisoprolol (1), Epinephrine (1), Levodopa/Carbidopa (1), Propranolol (1), Apixaban (3), Amlodipine (2), Rifampicin (1), Isoniazid (1)

Table 4 Predictors of Incident AKI Among Critically Ill Adults

	Univariable		Multivariable	
	cOR, 95% CI	P value	aOR, 95% CI	p value
Age				
• <45 years	Ref			
• ≥45 years	1.13 (0.59–2.14)	0.703		
Gender				
• Male	Ref			
• Female	1.29 (0.67–2.47)	0.432		
Current Tobacco use				
• No	Ref		Ref.	0.248
• Yes	0.56 (0.26–1.21)	0.143	0.56 (0.21–1.49)	
Current Alcohol use				
• No	Ref			
• Yes	0.79 (0.41–1.54)	0.494		
Admission ward				
• ICU	Ref		Ref.	
• Medical ward	1.51 (0.54–4.16)	0.436	2.71 (0.82–8.98)	0.104
• Surgical ward	2.22 (0.75–6.53)	0.147	4.32 (1.22–15.24)	0.023
Previous hospitalization				
• No	Ref		Ref.	
• Yes	2.44 (1.13–5.29)	0.023	2.56 (1.08–6.06)	0.032
NEWS - 2 score				
• <11	Ref			
• >11	1.31 (0.67–2.55)	0.415		
Oxygen saturation				
• ≥90%	Ref			
• <90%	0.99 (0.96–1.04)	0.966		
Systolic BP, mmHg				
• 90–139	Ref			
• <90	0.98 (0.42–2.28)	0.966		
• ≥140	1.34 (0.62–2.98)	0.443		
MAP, mmHg				
• ≥70	Ref			
• <70	1.03 (0.47–2.29)	0.935		
• >100	1.39 (0.65–2.99)	0.397		
Creatinine at 0 hour				
• <1.2 mg/dl	Ref		Ref.	
• ≥1.2 mg/dl	2.69 (1.36–5.33)	0.004	2.44 (1.13–5.27)	0.023
Baseline WBC count				
• <12 × 10 ⁹ /μL	Ref		Ref.	
• ≥12 × 10 ⁹ /μL	2.16 (1.12–4.17)	0.021	2.57 (1.21–5.46)	0.014
IV fluids in 24 hours				
• <2000 mL	Ref			
• >2000 mL	1.28 (0.66–2.45)	0.463		

(Continued)

Table 4 (Continued).

	Univariable		Multivariable	
	cOR, 95% CI	P value	aOR, 95% CI	p value
Use of herbal medication • No • Yes	Ref 0.23 (0.43 –1.22)	0.084	Ref. 0.14 (0.15–1.46)	0.102
Trauma patient • No • Yes	Ref 1.06 (0.46–2.42)	0.87		
HIV • No • Yes	Ref 1.07 (0.42–2.74)	0.874		
Diabetes mellitus • No • Yes	Ref 2.29 (0.80–6.58)	0.122	Ref 1.56 (0.48–5.13)	0.462
Hypertension • No • Yes	Ref 1.13 (0.55–2.36)	0.736		

Note: Statistically significant.

Abbreviations: cOR, crude Odds Ratio; aOR, adjusted Odds Ratio; HIV, Human Immunodeficiency Virus; IQR, Inter-quartile range; μ L, microliter; mg/dl, milligrams per deciliter; IV, Intravenous; mL, milliliter.

analysis, the patients who developed AKI had up to 2.2 more odds of dying than the ones who did not (OR 2.20, 95% CI: 0.92–5.27, $P=0.074$). The median overall time of hospitalization was 6 days (IQR: 4–10) with no significant difference between those who had AKI (6 days, IQR: 4–10) and those without AKI (7 days, IQR: 5–9.5) ($P=0.307$).

Discussion

Incidence of Acute Kidney Injury

We found an overall incidence rate of AKI of 70 (95% CI 55–90) per 1000 person days of observation among critically ill adult patients. This high incidence indicates the susceptibility of critically ill patients to AKI. Patients in low- and middle-income countries have a higher incidence of AKI than those in high-income countries. For example, Ashine et al conducted a retrospective follow-up study in Central Ethiopia, which revealed an incidence rate of AKI of 30.1 per 1000 person-days of observation.²⁸ We found the incidence rate of AKI in our population to be twice as high as that reported by that study. Conversely, a study by Susantitaphong et al (2013) in the United States reported incidence rates of AKI between 5% and 7% in critically ill patients. This is due to differences in patient demographics, healthcare practices, and underlying comorbidities.²⁹ Furthermore, majority of the patients had stage 1 AKI. Therefore, optimum patient care may be achieved by early recognition of AKI and initiating timely interventions which may prevent further kidney damage.³⁰

Predictors of Incident AKI Among Critically Ill Adult Patients

Previous hospitalization in the last 3 months was a strong predictor of AKI. This finding aligns with previous studies that showed a history of hospitalization to increase the risk of AKI, likely due to pre-existing comorbidities and exposure to nephrotoxic agents during previous hospital stays.³¹

The odds of developing AKI also significantly increased among patients admitted to the surgical ward. This could be resulting from postoperative complications and exposure to nephrotoxic medications among these patients. Hobson et al

(2015) showed that patients with surgical conditions are at a risk for AKI due to fluid shifts and blood loss.³² This highlights the importance of monitoring and correcting fluid imbalances among surgical patients.

Patients with higher creatinine levels at admission also had higher odds of developing AKI. Coca et al (2009) had similar findings in their research which established baseline renal function as a critical determinant of AKI.³³ Patients with underlying renal impairment are likely to be more vulnerable to further insults during critical illness.

Having higher baseline white blood cell (WBC) count also significantly increased the odds of developing AKI. A raised WBC may reflect an underlying inflammatory state or infection contributing to AKI. Inflammatory processes contribute to the pathogenesis of AKI, and elevated WBC counts have been revealed to be a risk factor in previous studies as well.³⁴

Potentially Nephrotoxic Medications Use

In our study, more than half (60%) of study participants were exposed to potentially nephrotoxic medications during hospitalization. Avoidance or dose-adjustment of potentially nephrotoxic drugs is recommended in the acute care settings. However, lack of clear evidence for choice of equally effective but less nephrotoxic alternative drugs leads to inevitable use of nephrotoxic drugs like proton pump inhibitors, loop diuretics, NSAIDs, and some beta-lactam antibiotics like piperacillin/tazobactam. The high prevalence of nephrotoxic drug use and the diverse mechanisms of renal injury caused by these drugs might explain the high incidence of AKI in critically ill patients in resource-limited settings.

Management and Outcomes of Patients with Incident AKI

Only 2% of the patients who developed incident AKI were managed with hemodialysis. This is because hemodialysis bills at our hospital are met by the patients and their families, most of whom have no health insurance and therefore, cannot afford the service. On the contrary, higher rates of specialized treatments like hemodialysis are seen in high-income countries. This difference can be explained by the readily available resources and the different thresholds for initiating dialysis.²

Death occurred in 25% (25/100) of those who developed AKI compared to 13.1% (8/61) in the No-AKI group. Similarly, studies by Bellomo et al (2017) and Coca et al (2015) have shown high mortality rates among patients with AKI. The pooled mortality rate due to AKI in a meta-analysis by Susantitaphong, P. et al (2013) was 23.9%.^{29,35,36}

We found no difference in length of hospital stay between the AKI and No-AKI groups. However, other studies have demonstrated longer durations of hospital stay among patients with AKI. This has been attributed to the development of complications and the need for closer monitoring and management among these patients.^{29,37}

Limitations

Only one study site was used for this study, limiting the generalizability of the findings. We only measured serum creatinine at 2 time points; at admission and 48 hours later. This limited our follow-up of patients for the onset of AKI beyond 48 hours of admission. Serum creatinine takes time to increase, therefore, using its levels to detect AKI might lead to missing the detection in some cases. The short duration of follow-up for a maximum of 7 days did not allow for assessment of reduction in urine output during the study period and the long-term effects of AKI. Additionally, we did not assess the dosage and duration of exposure to individual nephrotoxic drugs. This limited our assessment of the causative relationship between nephrotoxic drug exposure and AKI incidence. Subsequent studies should focus on addressing these limitations to provide more insight into this topic.

Conclusions

There is a high incidence of AKI among critically ill patients. We found an incidence rate of 70 (95% CI 55–90) per 1000 person days of observation in this study.

A history of previous hospitalization within the past 3 months, having a baseline serum creatinine above 1.2 mg/dl, a white blood cell counts above $12 \times 10^9/L$, and being admitted to the surgical ward were independently associated with incident AKI.

The majority of the patients with incident AKI received conservative management while only 2% underwent hemodialysis. A quarter of the participants with incident AKI died in hospital.

Recommendations

These findings highlight the importance of considering previous hospitalization, surgical admission, elevated baseline creatinine, and WBC counts as key predictors of AKI in critically ill patients. Prioritization of critically ill patients according to the number of these risk factors and subsequent closer monitoring might serve in the prevention, early diagnosis, and timely management of AKI, thus mitigating the burden of AKI in this vulnerable population.

We also recommend interventions at all levels to make RRT, particularly hemodialysis, more accessible and affordable in centers that manage critically ill patients to provide higher standard care and improve patient outcomes, especially among those with stage 3 AKI. For instance, one priority should be setting up a dialysis center at every regional referral hospital, training and employing dialysis nurses and equipping these centers with reagents and maintenance to minimize out-of-pocket expenditure for RRT services.

Furthermore, we recommend the implementation of standardized protocols for the management of AKI, and multi-disciplinary care to optimize clinical outcomes and reduce mortality rates.

Further research on this topic should focus on studying the long-term effects of AKI in critically ill patients both during and after admission.

Abbreviations

AKI, Acute Kidney Injury; BMI, Body Mass Index; BP, Blood Pressure; CBC, Complete Blood Count; CKD, Chronic Kidney Disease; DM, Diabetes Mellitus; eGFR, Estimated Glomerular Filtration Rate; GCS, Glasgow Coma Score; GFR, Glomerular Filtration Rate; HIV, Human Immunodeficiency Virus; HT, Hypertension; ICU, Intensive Care Unit; KDIGO, Kidney Disease Improving Global Outcome; MAP, Mean Arterial Pressure; MRRH, Mbarara Regional Referral Hospital; MUST, Mbarara University of Science and Technology; RLS, Resource Limited Setting; RR, Respiratory Rate; RRT, Renal Replacement Therapy; SCr, Serum Creatinine; SSA, Sub-Saharan Africa; TDF, Tenofovir Disoproxil Fumarate; UOP, Urine Output; WHO, World Health Organization.

Data Sharing Statement

The complete datasets for this study will be availed by the corresponding author on request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no competing interests for this work.

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