



ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE
DEPARTMENT OF EMERGENCY AND CRITICAL CARE
MEDICINE

**Pattern of acute kidney injury among COVID-19 patients
admitted to isolation and treatment center of SPHMMC, Addis
Ababa, Ethiopia: a retrospective study**

By: Chalachew Tadesse (MD, ECCM Resident)

Addis Ababa, Ethiopia

December, 2023 GC

ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

**DEPARTMENT OF EMERGENCY AND CRITICAL CARE
MEDICINE**

**Pattern of acute kidney injury among COVID-19 patients
admitted to isolation and treatment center of SPHMMC, Addis
Ababa, Ethiopia: a retrospective study**

By: Chalachew Tadesse (MD, ECCM Resident)

Advisors: Woldesenbet Waganew (MD, Assoc. Prof of ECCM)

Esubalew Gobignew (MD, Asst. Prof. of ECCM)

**A research paper to be submitted to the Department of ECCM of
St. Paul's Hospital Millennium Medical College for partial
fulfilment of speciality certificate in ECCM**

Addis Ababa, Ethiopia

December, 2023 GC

Abstract

Background: Despite the fact that the coronavirus disease-2019 (COVID-19) typically presents with respiratory symptoms, multi-organ manifestations including the kidney has been documented. However, literature regarding the magnitude and pattern kidney insults following COVID-19 is rather scattered and scarce in developing countries such as Ethiopia.

Objective: To assess the magnitude and pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of St. Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021.

Methods: A facility-based, retrospective study was conducted at SPHMMC. Systematic random sampling technique was applied to select 248 COVID-19-infected patients who were admitted from June 1, 2020 to May 30, 2021 to isolation and treatment center of SPHMMC. Data were entered to Microsoft Excel spreadsheet (version 2016) and analyzed using SPSS version 26. Descriptive analysis was used for statistical analysis, and multivariable logistic regression analysis was used to determine associations between dependent and independent variables. A p-value <0.05 was considered significant. Texts, tables and figures were used to present the results.

Results: In total, 243 patients were included in this study, with a response rate of 98%. Males (150;61.7%) predominated, and patients' median (interquartile range) age was 55 (40–65) years. AKI was diagnosed in 60 (24.7%; 95%CI: 19–30%) of the patients. Stages 1, 2, and 3 AKI accounted for 25%, 33.3% and 41.7%, respectively. Disease severity and exposure to nephrotoxic medications contributed to the development of AKI. Patients with severe COVID-19 [AOR(95%CI) = 3.62(1.02,12.89)], critical COVID-19 [AOR(95%CI) = 7.10(1.78,28.27)], exposure to nephrotoxins [AOR(95%CI) = 3.23(1.34,7.77)] were more likely to develop AKI.

Conclusion: Acute kidney injury is a common and serious complication among hospitalized COVID-19 positive patients, particularly among those with severe disease and exposure to nephrotoxic medications. Thus, it is imperative to prevent kidney injury in such vulnerable cohort of patients.

Keywords: Magnitude, Pattern, Acute kidney injury, COVID-19

Acronyms/Abbreviations

AaBET	Addis Ababa Burn, Emergency and Trauma Center
AKI	Acute Kidney Injury
AKIN	Acute Kidney Injury Network
eGFR	Estimated Glomerular Filtration Rate
ECCM	Emergency and Critical Care Medicine
GC	Gregorian Calendar
ICU	Intensive Care Unit
KDIGO	Kidney Disease: Improving Global Outcomes
MD	Medical Doctor
PI	Principal Investigator
RRT	Renal Replacement Therapy
SARS	Severe Acute Respiratory Syndrome
SPHMMC	Saint Paul's Hospital Millennium Medical College
WHO	World Health Organization

Acknowledgements

First, I would like to thank Department of Emergency and Critical Care Medicine of SPHMMC for providing me this opportunity of going through such a research experience. Next, my gratitude goes to my advisors, Dr. Woldesenbet Waganew (MD, Assoc. Prof of ECCM) and Dr. Esubalew Gobignew (MD, Asst. Prof. of ECCM), who gave me a great deal of their time and skill in guiding me to develop a thesis work of such kind. Finally, I want to acknowledge the dedication of the data collectors.

Table of Contents

Abstract	III
Acronyms/Abbreviations	IV
Acknowledgements.....	V
1. Introduction	1
1.1 Background	1
1.2 Statement of the problem	2
1.3 Significance of this study	2
2. Literature review.....	4
2.1 Overview of AKI.....	4
2.2 Incidence and pattern of AKI among COVID-19 patients	5
2.3 Factors affecting the incidence of AKI among COVID-19 patients	6
2.4 Conceptual framework.....	9
3. Objective of study	10
3.1 General objective.....	10
3.2 Specific objectives.....	10
4. Methods and Materials	11
4.1 Study area.....	11
4.2 Study design	11
4.3 Study period	11
4.4 Source population	11
4.5 Study population.....	12
4.6 Eligibility criteria.....	12
4.6.1 Inclusion criteria	12
4.6.2 Exclusion criteria	12
4.7 Sample size determination and sampling technique.....	12
4.8 Data collection tools and procedures	13
4.9 Study variables	13

4.9.1 Dependent variables	13
4.9.2 Independent variables.....	13
4.10 Operational definitions.....	14
4.11 Data processing and analysis.....	14
4.12 Data quality management.....	14
4.13 Ethical consideration.....	15
4.14 Dissemination of the study findings	15
5. Results	16
5.1 Socio-demographic characteristics of patients.....	16
5.2 Clinical profile of patients.....	16
5.3 Biochemical, complication and management related data of the patients.....	17
5.4 Factors associated with development of AKI	19
6. Discussion.....	22
7. Strength and Limitations	24
7.1 Strength	24
7.2 Limitations	24
8. Conclusion and Recommendation	25
8.1 Conclusion.....	25
8.2 Recommendation.....	25
References	26
Annex	1
Annex I.....	1
Annex II	2
Assurance of Investigator.....	5

List of tables

Table 1. Socio-demographic characteristics of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021 16

Table 2. Clinical characteristics of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021 17

Table 3. Biochemical, complication and management related data of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021 19

Table 4. Factors associated with AKI among adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia .. 21

List of figures

Figure 1. Conceptual framework for factors affecting development of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021. 9

Figure 2. Magnitude and pattern of acute kidney injury among adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021 18

1. Introduction

1.1 Background

Since its outbreak in Wuhan city, China in December 2019, the COVID-19 pandemic has continued to impose serious, multidimensional problems in human lives including remarkable unfavorable consequences for healthcare and economy (1). As of 6 April 2023, there had been about 762.2 million confirmed cases of COVID-19 and nearly 6.9 million deaths directly attributable to COVID-19 worldwide. Similarly, the viral infection has impacted and claimed the lives of many people in the sub-Saharan region as well. For instance, Ethiopia reported more than 500,633 confirmed cases with 7,573 deaths till 6 April 2023 (2).

Predominantly affecting the respiratory system, the clinical manifestation of this novel viral infection appears to be varied. Clinically, it involves extra-pulmonary features such as cardiac, hematological, digestive, nervous and renal systems, and it ranges from asymptomatic infection, mild upper respiratory tract illness, to severe viral pneumonia with respiratory failure and death (1,3,4). A sizeable number of studies documented that the kidney is a vulnerable organ in COVID-19 patients with evidence of acute kidney injury (AKI) occurring in up to 37.5% of fatal cases of COVID-19 (1).

Acute kidney injury (AKI), a sudden reduction in kidney function, has been noted to occur at all stages of COVID-19. In general, AKI is characterized by an acute decrease in renal function that can be multifactorial in its origin and is associated with complex pathophysiological mechanisms (5,6). Multiple pathophysiologic mechanisms have been suggested in COVID-19 cases, and they include intrinsic renal pathology such as thrombotic vascular processes, viral mediated tubular cell injury, and glomerulonephritis have been reported, as well as AKI resulting from extrinsic factors such as fluid depletion, multi-organ failure, and rhabdomyolysis (7,8). As an important poor prognosticating factor, AKI typically occurs among patients progressing to the most severe stage of illness involving extra-pulmonary systemic hyper-inflammation (9).

Different risk factors have been identified that predispose COVID-19 patients to development of AKI. Studies in the UK and USA observed that male sex, black ethnicity, baseline $eGFR < 60$ ml/min/1.73m², hypertension, and in-patient diuretic usage were contributing factors for development of AKI (10,11). The incidence of AKI is generally varied across different settings as a result of different factors including the clinical context and the

definitions used. Despite the recognition of AKI as a common complication of COVID-19 in the literatures, there remains lack of epidemiological data regarding its incidence and patterns in developing countries Ethiopian context that would help in optimizing measures and design mitigation strategies. Thus, the purpose of this study is to assess the magnitude of AKI in Ethiopian COVID-19 patients as well as the clinical patterns of AKI in COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia.

1.2 Statement of the problem

Although preliminary evidence indicated that the frequency of kidney disease in the COVID-19 population was negligible, a recent systematic review of the scientific literature with a meta-analysis of clinical studies indicated that the incidence of AKI in patients with COVID-19 during their hospital stay was common (around 15%), and the frequency of AKI among patients with severe COVID-19 was much more common (around 50%) (12).

In several literatures, AKI has been described as a frequent COVID-19 complication that significantly worsen the prognosis in critically ill patients (13–16). The overall mortality rate of COVID-19 was as high as 37.5% in certain sub-Saharan regions, with most deaths occurred during the first 24 hours of admission (17). As in many settings, the development of AKI is associated with an increased risk of mortality. The incidence of AKI in hospital-admitted COVID-19 patients was 25.3%, and mortality rate was remarkably higher in those group of patients (75.9% versus 24.1%) (18). Again, an Egyptian study found that AKI in COVID-19 patients is associated with a high mortality rate in ICU-COVID-19 patients (19).

In Ethiopia, although patients with severe forms of COVID-19 have been usually admitted to the ICU with associated unacceptably high mortality rate (20), published literature from the country on the magnitude, pattern and associated factors for AKI incidence is rather negligible. Early identification and timely management of AKI, particularly in high-risk patients, and post-AKI care for survivors of an AKI episode is likely to improve the worse short-term outcomes (4,16). However, such lack of evidence might have challenged the strategies that would help prevent the incidence and lessen the burden of AKI that would potentially lead to a higher death toll. Thus, this study is designed to bridge this knowledge gap.

1.3 Significance of this study

This study is hoped to be useful in adding to knowledge body regarding to assess the magnitude of AKI in COVID-19 patients as well as the clinical patterns of AKI in COVID-19

patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia. The finding of the study will be insightful to key stakeholders such as local policy makers, hospital society, health care providers and others by refocusing their policies and strategies at reducing the burden and impact of AKI, through better prevention, improved access to care, and promotion of clinical research to improve treatment standards. Thus, the study is believed to create in improved awareness among health-care providers and proactive prevention and management of AKI. Additionally, it is also expected that the findings will shed some light on potential action points for further quality improvement programs and integration of the existing intensive care protocols with the standard management guidelines. Finally, it also will be an additional source of information and an inspiration for further research undertakings in similar settings.

2. Literature review

2.1 Overview of AKI

Numerous literatures define acute kidney injury in different ways (21). The KDIGO 2012 defines acute kidney injury (AKI) based on the following criteria: (i) an increase in serum creatinine (SCr) by ≥ 0.3 mg/dl within 48 hours, or (ii) an increase in serum creatinine to ≥ 1.5 times baseline within the prior 7 days, and (iii) Urine volume < 0.5 mL/kg/h for 6 hours (22). On the other hand, the risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure (RIFLE) criteria defines AKI as an increase in serum creatinine to ≥ 1.5 or a decrease in estimated glomerular filtration rate (GFR) of more than 25% while the Acute Kidney Injury Network (AKIN) defines AKI as an increase in serum creatinine ≥ 0.3 mg/dl or increase $\geq 150\%$ to 200% (1.5- to 2-fold) from baseline within 48 hours (21–23).

Based on AKIN criteria, patients having an increase in serum creatinine ≥ 1.5 of the baseline or decrease in GFR $\geq 25\%$ are classified as stage 1. Alternatively, urine output < 0.5 mL/kg per hour for 6 hours is also feature of stage 1. Similarly, those having an increase in serum creatinine ≥ 2.0 of the baseline or decrease in GFR $\geq 50\%$ constitute stage 2. Stage 2 can also be defined by a urine output < 0.5 mL/kg per hour for 12 hours. And those having an increase in serum creatinine ≥ 3.0 of the baseline or SCr ≥ 4.0 mg/dL (354 $\mu\text{mol/L}$) or a decrease in GFR $\geq 75\%$ or those requiring RRT fall into stage 3. Or else, stage 3 can also be defined by a urine output < 0.3 mL/kg per hour for 24 hours or anuria for 12 hours (21).

Acute kidney injury (AKI) is a common and serious complication in critically ill patients. AKI is a clinical syndrome with multiple etiologies. In COVID-19 infected patients, it may arise from a constellation of factors such as hypotension, sepsis, rhabdomyolysis, multi-organ failure, use of nephrotoxic medications as well as direct infection in some cases (24). It is a common complication in hospitalized patients, and is associated with several both short- and long-term adverse outcomes (4). In fact, the association of AKI with short-term adverse outcomes is well recognized, and causes major patient and public health burden in terms of complications, need for renal replacement therapy, increased length of hospital stays, hospital readmission, and costs of treatment. Moreover, AKI-related complications are associated with an increased risk of in-hospital mortality, especially in severe AKI (25).

2.2 Incidence and pattern of AKI among COVID-19 patients

Globally, AKI was observed to frequently complicate the course of COVID-19 hospitalizations and is associated with increased severity of illness, prolonged duration of hospitalization, and poor prognosis (26). In a retrospective analysis of 536 COVID-19 cases across several hospitals in Hong Kong, Chu et al. reported acute renal impairment in 6.7% of admitted patients occurring at a mean duration of 20 days. Half of those with acute renal impairment had oliguria. Also, dipstick proteinuria was found in 84.6% of the 26 patients that developed acute renal failure though heavy proteinuria was uncommon (27).

In a large English study that included 1248 inpatients, 487 (39%) experienced AKI (51% stage 1, 13% stage 2, and 36% stage 3). The weekly AKI incidence rate gradually increased to peak at week 5 (3.12 cases/100 patient-days), before reducing to its nadir (0.83 cases/100 patient-days) at the end the study period (week 10) (28). On the other hand, a retrospective American study that includes the first 370 patients consecutively hospitalized with confirmed COVID-19 illness at a 242-bed teaching hospital reported AKI in 179 (54.7%) patients. Specifically, 69 (21.1%) had stage 1, 42 (12.8%) had stage 2, and 68 (20.8%) had stage 3 AKI. In 137 of 179 (76.5%) patients, the overall mortality rate was 40.7% (29). Also, Luther et al. conducted a prospective observational study of 57 patients admitted to intensive care. The author found that most (89%) of patients developed AKI, and 51% had KDIGO stage 2, and 23% had stage 3 AKI (30).

In the retrospective Mexican study carried out by Casas-Aparicio and colleagues, 99 patients with COVID-19 infection were studied, and 58.6% (n=58) developed AKI (31). Moreover, in an observational prospective study that included 41 Spanish COVID-19 cases with AKI, AKI etiology was prerenal in 61%, acute tubular necrosis in the context of sepsis in 24.4%, glomerular in 7.3% and tubular toxicity in 7.3% of the cases. The study reported proteinuria in 88.9% and hematuria in 79.4% of patients. Further, 48.8% of patients required renal replacement therapy (RRT) (32). In Sweden, the majority (n = 51, 89%) of patients developed AKI, and 27 (47%) patients had

predominantly oliguric AKI

In Italy, Alfano et al. reviewed the health medical records of 307 consecutive patients with COVID-19 hospitalized at the University Hospital of Modena. In this study, AKI was diagnosed in 69 out of 307 (22.4%) COVID-19 patients. Stages 1, 2, or 3 AKI accounted for 57.9%, 24.6% and 17.3%, respectively (33). Likewise, another study Oo et al. in Brunei

Darussalam reported that 109 (11.7%) out of the 930 COVID-19 patients had AKI, with KDIGO Stage 1 (67.9%), 2 (13.8%), and 3 (18.3%) (34).

Likewise, in July 2020, El-Sayed et al. analyzed the data of 734 COVID-19 cases admitted to the Ahmad Maher Teaching Hospital in Cairo, Egypt. The study noted that AKI was more common in hospitalized mild COVID-19 patients than in home-isolated and ICU COVID-19 patients (15.0% versus 10.8% and 14.2%, respectively). The overall occurrence rate of AKI was significantly higher in COVID-19 patients (14%). Hemodialysis, on the other hand, was required in 76% of the extreme ICU COVID-19 patients who developed AKI (22/29). The mortality rate in COVID-19 patients was tripled from 4.8% in those without AKI to 15.4% in those having concomitant AKI (19).

Recently, the incidence and mortality rates were reported to be very high in sub-Saharan African (SSA) countries compared to developed countries, with a very different pattern from that of more developed countries (35). In line with this, Diana and colleagues recorded a high incidence (33.9%) of AKI, which occurred in 374 out of the total 1102 COVID-19 infected patients admitted to the two hospital of South Africa. Among these AKI patients, 91 (24.3%) patients required intensive care, and 32 (8.6%) received kidney replacement therapy (35). In Somalia, a retrospective analysis of 102 COVID-19 patients presented to a tertiary teaching hospital in Mogadishu during the second wave of COVID-19 was done. The prevalence of acute kidney injury was 12.7% (36).

Likewise, in Ethiopia, Goffe et al. carried out a hospital-based retrospective cross-sectional study design admitted COVID-19 patients at two treatment centers of Addis Ababa by reviewing data from September 2020 to September 2021. The authors reviewed a total of 402 patient charts, and they reported that proportion of patients with acute kidney injury was remarkably high, standing at 18.9% (37).

2.3 Factors affecting the incidence of AKI among COVID-19 patients

A number of factors have been identified to contribute to incidence of AKI. Among the factors which has shown to be significantly associated with acute renal impairment in SARS epidemic were age, sex, and presence of acute respiratory distress syndrome, diabetes and heart failure (38). The incidence of acute renal impairment was shown to be higher among the elderly and in the presence of co-morbidities such as diabetes, heart failure, respiratory failure, acute respiratory distress syndrome (ARDS) and multiple organ system failure. SARS patients who subsequently developed acute renal failure (ARF) also had lower plasma sodium

and albumin with elevated alanine aminotransferase and plasma LDH on admission compared with those without ARF (27).

As in the case of SARS, older individuals are at a higher independent risk for the development of AKI in COVID-19. Other factors found to be associated with AKI in COVID-19 patients include male gender, multiple pre-existing comorbidities including hypertension, diabetes and cerebrovascular disease, greater severity of illness, increased infection indicators, lymphopenia, elevated D-dimer and impaired heart and liver functions (39). Oo et al. reported that age, male gender, gastrointestinal symptoms, antibiotics, and nephrotoxins exposure were significantly associated with AKI (34).

In the case of English patients, Jewell et al. reported that pre-existing renal impairment, and inpatient diuretic were independently associated with a higher risk for AKI. In addition, AKI was a strong predictor of 30-day mortality with an increasing risk across AKI stages. One third of AKI3 survivors (30.7%), had newly established renal impairment at 3 to 6 months (28). Alfano et al. also observed that COVID-19-associated AKI was independently associated with in-hospital death compared to non-AKI patients (33).

In the retrospective Mexican study carried out by Casas-Aparicio et al., AKI was regarded as an important risk factor for mortality along with obesity and requirement of vasoactive drugs on admission. Further, it was observed that in-hospital mortality was significantly higher in patients with AKI stage 3 (79.3%) and AKI stage 2 (68.7%) compared with those with AKI stage 1 (22). Moreover, the previous Spanish study observed that patients who developed AKI during hospital stay presented with higher C-reactive protein, Lactate dehydrogenase-LDH and d-dimer values, more severe pulmonary damage, more frequent intensive care unit-ICU admission, treatment with lopinavir/ritonavir and biological drugs and RRT requirement (32).

In other African settings, older age, pre-existing hypertension and biochemical evidence of severe disease, including high ferritin, lactate dehydrogenase, d-dimer and C-reactive protein, were significantly higher in the patients with AKI versus those without (35). Bashir et al. documented a significant association between acute kidney injury, CRP and ferritin among patients in Somalia (36). In the case of Ethiopia, it was documented that factors such as age of 35 years or younger, female gender, and isolation type ICU were significantly associated with acute kidney injury (37).

Therefore, from review of the related literature, it was learned that COVID-19 pneumonia presents as a systemic disease involving multiple systems. Further, it was observed that acute kidney injury is a common complication in hospitalized COVID-19 patients with varying magnitude across settings and a marker for poor patient outcomes. It was documented that factors associated with AKI in coronavirus infected patients may include elderly age, male sex, presence of comorbidities as well as pre-existing chronic kidney disease and end stage renal disease. However, it was indicated that there exists a knowledge gap in sub-Saharan region, Ethiopia included, as most of the studies are concentrated in the industrial countries.

2.4 Conceptual framework

This is the conceptual framework developed specifically for this study by the principal investigator through reviewing related literature such as the study done by El-Sayed and colleagues (19) in which this study aimed to assess. The framework tries to figure out associated factors that affect the development of AKI in COVID-19 patients, and is believed to support the study entitled '*Pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia*'

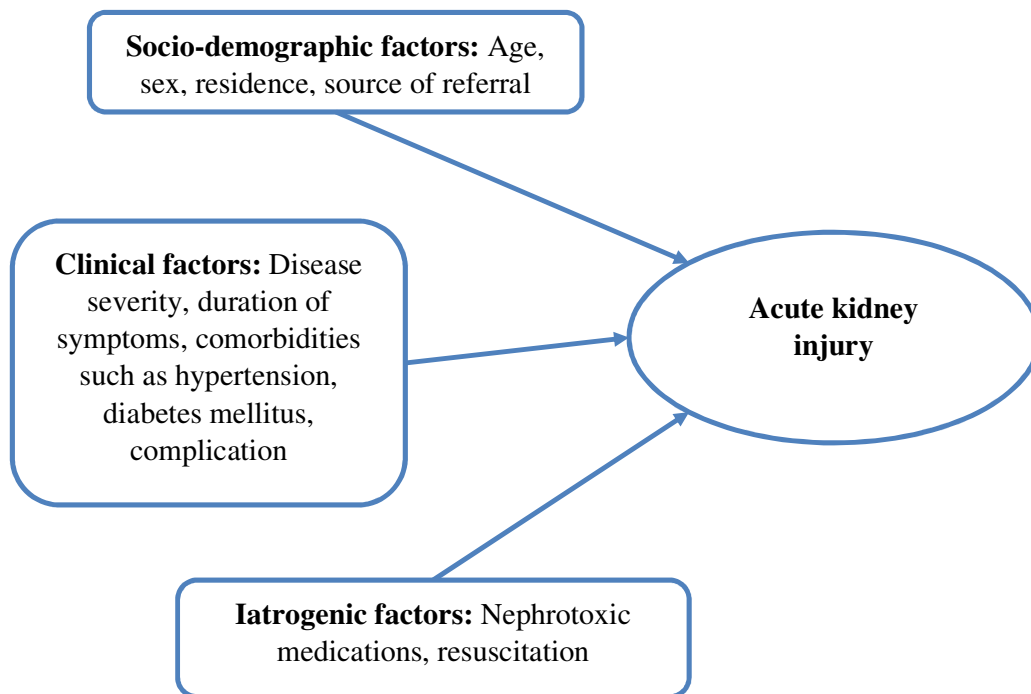


Figure 1. Conceptual framework for factors affecting development of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021.

3. Objective of study

3.1 General objective

- To assess the magnitude and pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia, from June 1, 2020 to May 30, 2021

3.2 Specific objectives

- To explore the magnitude of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia, from June 1, 2020 to May 30, 2021
- To assess the pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia, from June 1, 2020 to May 30, 2021
- To assess the outcome of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia, from June 1, 2020 to May 30, 2021
- To identify factors associated with the development of AKI among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia, from June 1, 2020 to May 30, 2021

4. Methods and Materials

4.1 Study area

The study was conducted at St. Paul's Hospital Millennium Medical College (SPHMMC), one of the largest government hospitals located in Addis Ababa, the capital city of Ethiopia. The college has more than 2800 clinical, academic and administrative and supporting staffs that provide medical specialty service to patients who are referred from all over the country. Built in 1969, the hospital serves about 200,000 patients annually on average and a catchment population of more than 5 million people from different parts of the country. On top of this, this referral hospital is a teaching center for both undergraduate and postgraduate health science students. It delivers clinical service in a variety of activities including COVID-19 patients. The hospital has more than 700 beds dedicated to inpatient service.

Since June 8, 2020, the hospital was officially designated as the national center for the management of COVID-19-infected patients in the country. It was repurposed to have different compartments on the already-existing building, including an intensive care unit (ICU) and Semi-ICU for treatment of patients at different levels of illnesses after being triaged as per the WHO criteria. The isolation and treatment center, where severe and critical cases of COVID-19 were admitted, has 10 beds with mechanical ventilator and dialysis machine with additional 13 beds at the adult ICU. It was dedicated for isolating and treating COVID-19 cases, with high turnover of patients. The care of ICU patients is given by a multidisciplinary team consisting nurses, residents, laboratory technologists, pharmacists, internists, anesthesiologists, pulmonologists, emergency and critical care specialists and other supporting staff.

4.2 Study design

A facility-based, retrospective study was employed.

4.3 Study period

The study period was from June 1, 2020 to May 30, 2021.

4.4 Source population

All adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC

4.5 Study population

All adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC during the study period selected via systematic random sampling technique and who fulfill the eligibility criteria

4.6 Eligibility criteria

4.6.1 Inclusion criteria

- Patients aging 15 years or more
- Patients with at least two records of renal function tests

4.6.2 Exclusion criteria

- Patients with incomplete or lost medical charts
- Those with pre-existing progressive kidney pathology

4.7 Sample size determination and sampling technique

Taking the population proportion of COVID-19 patients reported to have AKI to be 18.9% taken from the previous study done in previous Ethiopian report (37),

$$n = \frac{z^2 p(1-p)}{e^2}$$

n = the required sample size

p = proportion of COVID-19 patients reported to have AKI – 18.9%

$Z_{\alpha/2}$ = the critical value at 95% confidence level = 1.96

e = precision (margin of error) = 5%

Accordingly,

$$n = \frac{(1.96)^2 * 0.189(1 - 0.189)}{0.05^2}$$

$$n = \frac{(1.96)^2 * 0.189(0.811)}{0.05^2}$$

$$n = 236$$

Hence, adding 5% of the calculated sample size for contingency that might happen due lost charts or incomplete reports, the final sample size became 248. Therefore, as the total number

of COVID-19 patients admitted to the isolation and treatment center during the specified study period is estimated to be 547, systematic random sampling technique was employed to recruit study patients after selecting the first patient with a lottery method, and taking k as $2 \approx 547/248$.

4.8 Data collection tools and procedures

Data were collected from patients' medical records using structured data collection checklist. The data collection format includes questions divided into three parts (background information, clinical variables, and laboratory parameters). Data were gathered from logbook records of isolation and treatment patient registry over one-year period (from June 1, 2020 to May 30, 2021), and the charts of the selected ones were traced, retrieved and reviewed. Two professional general practitioners were recruited and brief training on data collection procedure was delivered by the principal investigator.

4.9 Study variables

4.9.1 Dependent variables

- Development of acute kidney injury
- Pattern of acute kidney injury
- Outcome of acute kidney injury

4.9.2 Independent variables

- Age
- Sex
- Residence
- Source of referral
- Severity of the illness
- Duration of illness
- Nephrotoxic medications
- History of kidney disease
- Comorbidity
- Need for a mechanical ventilator

- Presence of hospital acquired illness

4.10 Operational definitions

- **Acute kidney injury:** refers to an increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26.5 $\mu\text{mol/l}$) within 48 hours; or an increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or a urine volume <0.5 ml/kg/h for 6 hours
- **Baseline serum creatinine:** represents the first documented serum creatinine on admission or prehospital record of creatinine within seven days, whichever available
- **Hospitalized COVID-19 patient:** includes all patients who had COVID-19 pneumonia diagnosed by a positive PCR of a nasopharyngeal sample for SARS-CoV-2 and/or a typical chest computed tomography with requirement for supplementary oxygen and admitted to the hospital.

4.11 Data processing and analysis

Data entering, coding and cleaning were performed using Microsoft Excel spreadsheet (version 2016) and statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 26. Frequency and cross tabulation were used to check for missed value and variables. The demographic and clinical characteristics of patients were computed using descriptive statistics such as mean, percentage, frequencies, and standard deviation. Logistic regression was used to determine associations between independent and dependent variable (that is, development of AKI). Those variables with p value of ≤ 0.2 in binary logistic regression were exported to multiple logistic regression. Finally, the study findings were presented using texts, tables and figures.

4.12 Data quality management

An English version, pretested checklist was used to collect data. Pretesting was done 5% of the total sample size, after which feedback was sought from data collectors to modify and finalize the data collection tool. Brief training for the data collectors (two health professionals) about the process of data collection was given before the process of data collection. Close supervision was maintained during data collection and filled checklists were double-checked daily for consistency and completeness by data collectors and principal investigator before analysis.

4.13 Ethical consideration

Ethical clearance was obtained from Institutional Review Board (IRB) of Saint Paul's Millennium Medical College. Permission letter was submitted to the medical record unit from the Department of ECCM & Research Directorate to retrieve and review the charts. Following this, introduction and familiarization of the data collectors with the team unit was secured. The collected data were kept anonymous and confidential.

4.14 Dissemination of the study findings

The findings of this study will be submitted to the Department of ECCM of SPHMMC as a partial fulfillment of specialty certificate in ECCM. The outcome of this study will be presented at annual ECCM conference. Furthermore, as the results are assumed to be inputs for the health policy makers, efforts will be exerted to notify the Federal Ministry of Health (FMoH) on the key findings of the present study. Finally, the manuscript will be submitted to a reputable scientific journal for possible publication.

5. Results

5.1 Socio-demographic characteristics of patients

This study included data derived from a total of 243 adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, with a response rate of 98%. Among the studied patients, males (150;61.7%) predominated, with a male-to-female ratio of 1.61:1. Patients' age ranged from 17 to 100 with a median (interquartile range) of 55 (40–65) years, respectively. Of these, approximately half (112;46.1%) aged between 35 and 60 years by the time of the study. Most (182;74.9%) of the studied patients were residents of Addis Ababa. Half (121;49.8%) of the patients were transferred from other unit of the study facility (Table 1).

Table 1. Socio-demographic characteristics of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021

Variable	Frequency	Percent (%)
Sex		
Male	150	61.7
Female	93	38.3
Age group		
<35 years	43	17.7
35–60 years	112	46.1
>60 years	88	36.2
Residence		
Addis Ababa	182	74.9
Out of Addis Ababa	61	25.1
Source of referral		
Intra-facility	121	49.8
Health center	50	20.6
Public hospital	46	18.9
Private hospital	24	9.9
Self-referred	2	0.8

5.2 Clinical profile of patients

With respect to clinical profile of the studied patients, close to half (107;44%) had hypertension. Following this, diabetes mellitus (97;39.9%) and cardiac disease (28;11.5%) were the most frequently documented coexisting medical conditions. Cough (188;77.4%), shortness of breath (150;61.7%) and fatigue (116;47.7%) were the three most commonly reported clinical symptoms among the studied patients. Overall, the median duration of

symptoms at presentation was 6 days with an interquartile range of 4 to 7. Most (189;77.8%) presented within the first week after onset of symptoms (Table 2).

Majority (106;43.6%) of the patients were diagnosed to have severe COVID-19 disease based on WHO classification while a little more than one-third (86;35.4%) had a critical severity of the disease. Besides, half (120;49.4%) of the patients were exposed to nephrotoxins such as vancomycin during their stay at the hospital (Table 2).

Table 2. Clinical characteristics of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021

Variable	Frequency	Percent (%)
Comorbidity		
Hypertension	107	44.0
Diabetes mellitus	97	39.9
Cardiac disease	28	11.5
HIV/AIDS	13	5.3
Symptoms		
Cough	188	77.4
Shortness of breath	150	61.7
Fatigue	116	47.7
Fever	89	36.6
Myalgia	45	18.5
Sore throat	9	3.7
Abdominal pain	4	1.6
Duration of symptoms in days (median + IQR)	6	4–7
Disease duration		
≤7 days	189	77.8
>7 days	54	22.2
Disease severity		
Mild	86	35.4
Severe	106	43.6
Critical	51	21.0
Exposure to nephrotoxic medication		
No	123	50.6
Yes	120	49.4

5.3 Biochemical, complication and management related data of the patients

The median (IQR) of prothrombin time (PT) was 15.1 (13.5–17) seconds while that of partial thromboplastin time (PTT) being 26 (21.8–30.04) seconds. More than half (130;53.5%) of the total study population had medical complication during their hospital stay, with electrolyte

imbalance (102;42%), sepsis (51;21%) and bedsores (6;2.5%) being the most common ones (Table 3).

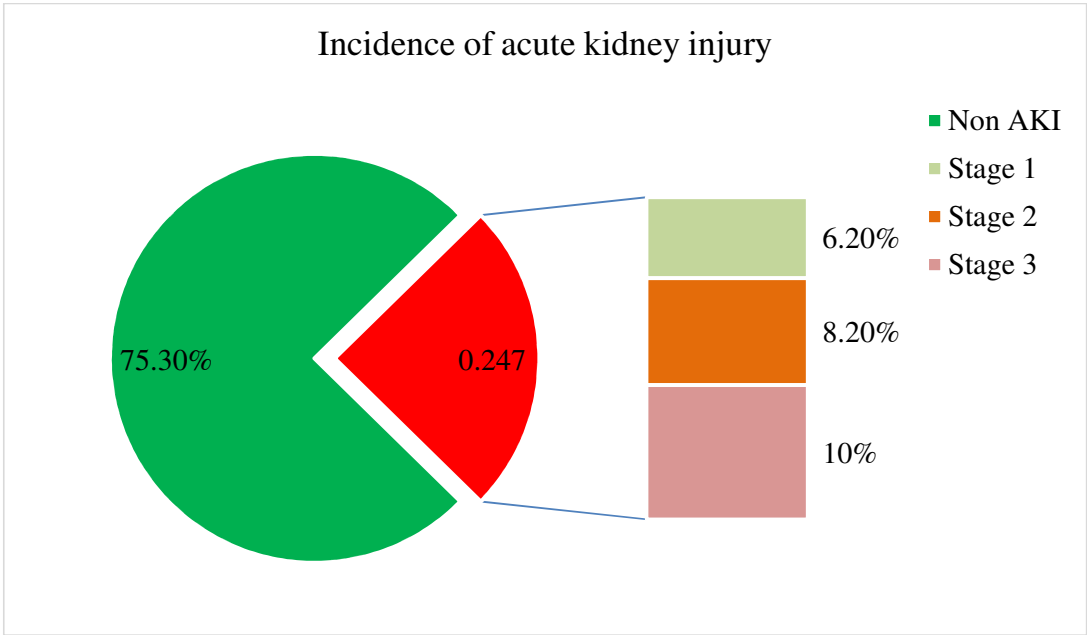


Figure 2. Magnitude and pattern of acute kidney injury among adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021

In this study, the incidence of AKI among hospitalized COVID-19 patients was 24.7% (95%CI: 19–30%). Of these, 25 (41.7%) developed stage 3 AKI and 20 (33.3%) had stage 2 AKI at its peak (Figure 2). About two-thirds (38;63.3%) of these AKI persisted for more than a week time. Renal replacement therapy was required for thirteen (21.7%) of the cases, but was done for only four of the patients. Finally, one-fourth (63;25.9%) of all patients died while 179 (73.7%) of the patients were discharged alive (Table 3).

Table 3. Biochemical, complication and management related data of adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia from June 1, 2020 to May 30, 2021

Variable	Frequency	Percent (%)
PT in seconds (median + IQR) (n=125)	15.1	13.5–17.0
PTT in seconds (median + IQR) (n=104)	26.0	21.8–30.04
INR (median + IQR) (n=118)	1.16	1.00–1.32
In-hospital complication		
No	113	46.5
Yes	130	53.5
Type of complication		
Electrolyte imbalance	102	42.0
Sepsis	51	21.0
Bedsore	6	2.5
Diabetic ketoacidosis	5	2.1
Delirium	4	1.6
Venous thromboembolism	3	1.2
Course of AKI (n=60)		
Resolved in 48 hours	2	3.3
Resolved in 48 hours to 7 days	20	33.3
Persisted to > 7 days	38	63.3
Hemodialysis status (n=60)		
Not required	47	78.3
Required, but not done	9	15.0
Done	4	6.7
Patient outcome		
Survived	179	73.7
Died	63	25.9
Referred	1	0.4

PT: Prothrombin time; PTT: Partial thromboplastin time

5.4 Factors associated with development of AKI

In this study, nineteen independent variables, namely age group, sex, place of residence, source of referral, history of diabetes mellitus, history of hypertension, history of cardiac disease, history of HIV/AIDS, duration of illness, nephrotoxic medication status, history of cough, shortness of breath, fatigue, fever, myalgia, sore throat, abdominal pain, WHO disease severity and sepsis were considered in the bi-variable regression analysis. In order to identify factors associated with development of AKI, variables that showed p value of ≤ 0.25 in the binary logistic regression were retained in the multiple regression model to compute adjusted odds ratio with corresponding 95% confidence intervals.

Following this, only seven factors, namely age group, history of hypertension, shortness of breath, myalgia, nephrotoxic medication status, WHO disease severity and sepsis were found to be candidates, and hence they were exported to further multiple logistic regression to control for possible confounders. Enter method was applied to enter variables in the multivariable analysis. Consequently, the only two factors that showed statistically significant association with development of AKI were disease severity and exposure to nephrotoxic medications (Table 4).

More specifically, this study showed that, when compared to patients with mild disease severity, those with severe and critical diseases were more likely develop AKI, with AOR of 3.62(95%CI 1.02,12.89) and 7.10(95%CI:1.78,28.27), respectively. Furthermore, patients who were exposed to nephrotoxic medications during their hospital stay had statistically significant higher odds of developing AKI in comparison to those who had no such iatrogenic exposure [AOR(95%CI) = 3.23(1.34,7.77)] (Table 4).

Table 4. Factors associated with AKI among adult patients with confirmed COVID-19 infection admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia

Variable	AKI		COR (95%CI)	AOR (95%CI)	P value
	Yes (%)	No (%)			
Age group					
<35 years	5	38	1	1	-
35–60 years	20	92	1.65(0.58,4.72)	1.41(0.43,4.61)	0.573
>60 years	35	53	5.02(1.80,14.00)	3.06(0.93,10.11)	0.066
History of Hypertension					
No	26	110	1	1	-
Yes	34	73	1.97(1.09,3.56)	1.16(0.56,2.38)	0.687
Shortness of breath					
No	17	76	0.56(0.30,1.05)	1.27(0.58,2.79)	0.549
Yes	43	107	1	1	-
Myalgia					
No	53	145	1.98(0.84,4.71)	1.58(0.59,4.25)	0.362
Yes	7	38	1	1	-
Disease severity					
Mild	4	82	1	1	-
Severe	31	75	8.47(2.86,25.14)	3.62(1.02,12.89)	0.047
Critical	25	26	19.71(6.28,61.88)	7.10(1.78,28.27)	0.005
Exposure to nephrotoxic medication					
No	10	113		1	-
Yes	50	70	8.07(3.85,16.94)	3.23(1.34,7.77)	0.009
Sepsis					
No	39	153	1	1	-
Yes	21	30	2.75(1.42,5.31)	1.40(0.66,2.94)	0.379

Only variables with p value <0.25 in multiple logistic regression are shown here

1: Reference category

6. Discussion

This study aimed to assess the magnitude and pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia. The results demonstrated that one-quarter (24.7%) of the patients developed AKI during their course of hospital stay, with majority (41.7%) having stage 3 AKI. Further, it was revealed that factors such as disease severity and exposure to nephrotoxic medications were associated with development of AKI among hospitalized COVID-19 patients.

The results demonstrated that one-quarter (24.7%) of the patients developed AKI during the course of their hospital stay, with the majority having stage 3. This was consistent with the study conducted in Tehran, Iran where 24.8% of patients were observed to develop of AKI (40). A comparable finding was also reported by Italian authors, who observed that AKI was diagnosed in 22.4% COVID-19 patients (33).

On the other hand, the present finding was relatively higher than the report of Goffe et al., who found that one-fifth (18.9%) of patients developed acute kidney injury (37). The finding of this study was also higher than a study conducted in Mogadishu, Somalia where the corresponding proportion of patients who developed AKI was low (12.7%) (36). Likewise, the current finding was comparatively higher than that of the study done in Brunei, where the incidence of AKI was 11.7% (34). The present finding was different from that of Hirsch et al., who found that more than one-third (36.6%) developed AKI, with the most common peak stage being stage 1 (10). Also, the current finding was much lower than what was obtained in Sweden, where majority (89%) of COVID-19 patients developed AKI and (51%) of patients had KDIGO stage 2 (30).

The geographical dissimilarities in the rates of AKI can potentially be explained by the differences in the study population, the criteria used to define AKI, admission criteria (as a result of hospital admission protocols applied to healthcare systems), the quality of hospital care and ethnic predisposition to kidney involvement. For instance, out of the patients studied in Somalia, only 10.8% had diabetes mellitus, and only 8.8% hypertension (36) while in the present study, a higher proportion (39.9%) had diabetes mellitus and 44% had hypertension.

Furthermore, this study showed severity of COVID-19 was positively associated with in-hospital incidence of AKI among patients. This was in agreement with previous reports such as Fabrizi et al. and Chan et al., who similar findings among Italian and American

populations, respectively as well as the report of Enikeev et al. (12,41,42). Several factors contribute to the development of AKI in patients with severe COVID-19, including systemic hemodynamic instability, endothelial injury, microvascular thrombi, local inflammation, and immune cell infiltration that would be more pronounced among these patients. Additionally, cytokine storm and damage-associated molecular patterns (DAMPs) secretion from severely injured tissues, such as the lung, may contribute to cell death of renal cells such as podocytes and proximal tubular cells (43). Again, critically ill patients with COVID-19 may be at increased risk of AKI due to hypoperfusion of kidneys as a result of circulatory collapse secondary to hypovolemia, sepsis or cardiogenic shock from underlying cardiovascular disease (44).

Finally, it was also demonstrated that exposure to nephrotoxic medications such as vancomycin is an important factor contributing to the development of AKI among hospitalized COVID-19 patients. This is supported by the findings independently obtained in Brunei, Turkey and Columbia, where exposure to nephrotoxins were significant predictors of AKI among COVID-19 positive patients (34,45,46). Nephrotoxic drugs can increase the incidence of acute kidney injury (AKI) among hospitalized patients through various mechanisms. Exposure to nephrotoxic drugs can lead to impaired glomerular filtration, tubular cell toxicity, interstitial nephritis, and crystal nephropathy, ultimately causing AKI (47).

7. Strength and Limitations

7.1 Strength

- ✓ A very high chart retrieval rate was obtained, with a chart retrieval rate of 98%.
- ✓ The fact that the study was a retrospective chart review in its nature and no patient was contacted physically, there was no concern of COVID-19 transmission during the process of data collection.

7.2 Limitations

- Some potentially important variables that can affect the incidence of AKI among patients with COVID-19 were not consistently available for all patients, and as a consequence, they were not included in the final model. These include body mass index, C-reactive protein, D-dimer, qSOFA score, troponin, and procalcitonin.
- Finally, the study was conducted at a single-center, and thus, the findings should be cautiously generalized to other settings, where varying clinico-demographic characteristics are anticipated.

8. Conclusion and Recommendation

8.1 Conclusion

This study showed that AKI is a common complication among hospitalized COVID-19 positive patients. Its incidence is influenced by certain factors such as disease severity and exposure to nephrotoxic medications among hospitalized COVID-19 patients.

8.2 Recommendation

Based on the results of this study, the following recommendations can be forwarded.

For health care professionals,

In order to reduce the incidence of in-hospital AKI, health care professions should deliver prompt management with strict monitoring to hospitalized COVID-19 patients, with particular attention to those with severe disease and exposure to nephrotoxic medications.

For local health policy makers,

Local policy makers and other concerned stakeholders should devise mechanisms such as customized protocols to enhance the quality of care and reduce incidence of in-hospital AKI and further potentially preventable complications among patients with novel virus infections and for future viral outbreaks or pandemics.

For researchers,

Stronger and multicenter studies should be considered to validate the findings obtained in this study, and they should include more variables such as body mass index, C-reactive protein, D-dimer, qSOFA score, troponin, and procalcitonin.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* [Internet]. 2020 Feb;395(10223):497–506. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673620301835>
2. World Health Organization (WHO). WHO Coronavirus (COVID-19) Dashboard _ WHO Coronavirus (COVID-19) Dashboard With Vaccination Data [Internet]. Available from: <https://covid19.who.int/>
3. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *Int J Surg* [Internet]. 2020 Apr;76(January):71–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1743919120301977>
4. Raina R, Mahajan ZA, Vasistha P, Chakraborty R, Mukunda K, Tibrewal A, et al. Incidence and Outcomes of Acute Kidney Injury in COVID-19: A Systematic Review. *Blood Purif*. 2021;2.
5. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, et al. World incidence of AKI: A meta-analysis. *Clin J Am Soc Nephrol*. 2013;8(9):1482–93.
6. Ribeiro HS, Vieira EA. Brief Communication | Comunicação Breve Epidemiological profile of acute kidney injury in critically ill patients admitted to intensive care units : A Prospective. 2020;580–5.
7. Selby NM, Forni LG, Laing CM, Horne KL, Evans RDR, Lucas BJ, et al. Covid-19 and acute kidney injury in hospital: Summary of NICE guidelines. *BMJ* [Internet]. 2020;369(May):1–5. Available from: <http://dx.doi.org/doi:10.1136/bmj.m1963>
8. Peleg Y, Kudose S, D'Agati V, Siddall E, Ahmad S, Nickolas T, et al. Acute Kidney Injury Due to Collapsing Glomerulopathy Following COVID-19 Infection. *Kidney Int Reports* [Internet]. 2020;5(6):940–5. Available from: <https://doi.org/10.1016/j.ekir.2020.04.017>
9. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical–therapeutic staging proposal. *J Hear Lung Transplant*. 2020;39(5):405–7.
10. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int* [Internet]. 2020 Jul;98(1):209–18. Available from:

- <https://linkinghub.elsevier.com/retrieve/pii/S0085253820305329>
11. Mohamed MMB, Lukitsch I, Torres-Ortiz AE, Walker JB, Varghese V, Hernandez-Arroyo CF, et al. Acute Kidney Injury Associated with Coronavirus Disease 2019 in Urban New Orleans. *Kidney360*. 2020;1(7):614–22.
 12. Fabrizi F, Alfieri CM, Cerutti R, Lunghi G, Messa P. COVID-19 and Acute Kidney Injury: A Systematic Review and Meta-Analysis. *Pathogens* [Internet]. 2020 Dec 15;9(12):1052. Available from: <https://www.frontiersin.org/articles/10.3389/fmed.2022.705908/full>
 13. Martinez-Rojas MA, Vega-Vega O, Bobadilla XNA. Is the kidney a target of SARS-CoV-2? *Am J Physiol - Ren Physiol*. 2020;318(6):F1454–62.
 14. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* [Internet]. 2020 May;97(5):829–38. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0085253820302556>
 15. Kant S, Menez SP, Hanouneh M, Fine DM, Crews DC, Brennan DC, et al. The COVID-19 nephrology compendium: AKI, CKD, ESKD and transplantation. *BMC Nephrol*. 2020;21(1):1–13.
 16. Robbins-Juarez SY, Qian L, King KL, Stevens JS, Husain SA, Radhakrishnan J, et al. Outcomes for Patients With COVID-19 and Acute Kidney Injury: A Systematic Review and Meta-Analysis. *Kidney Int Reports* [Internet]. 2020;5(8):1149–60. Available from: <https://doi.org/10.1016/j.ekir.2020.06.013>
 17. Omar SM, Musa IR, Salah SE, Elnur MM, Al-Wutayd O, Adam I. High mortality rate in adult covid-19 inpatients in Eastern Sudan: A retrospective study. *J Multidiscip Healthc*. 2020;13:1887–93.
 18. Oweis AO, Zeyad HN, Alshelleh SA, Alzoubi KH. Acute Kidney Injury Among Patients with Multi-Drug Resistant Infection: A Study from Jordan. *J Multidiscip Healthc*. 2022;15(February):2759–66.
 19. El-Sayed EE, Allayeh AK, Salem AA, Omar SM, Zaghlol SM, Abd-Elmaguid HM, et al. Incidence of acute kidney injury among COVID-19 patients in Egypt. *Ren Replace Ther*. 2021;7(1):1–7.
 20. Kaso AW, Agero G, Hurissa Z, Kaso T, Ewune HA, Hareru HE, et al. Survival analysis of COVID-19 patients in Ethiopia: A hospital-based study. *PLoS One* [Internet]. 2022;17(5 May):1–11. Available from: <http://dx.doi.org/10.1371/journal.pone.0268280>

21. Lin C-Y. Acute kidney injury classification: AKIN and RIFLE criteria in critical patients. *World J Crit Care Med.* 2012;1(2):40.
22. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron - Clin Pract.* 2012;120(4):179–84.
23. Mehta RL, Kellum JA, Shah S V, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network : report of an initiative to improve outcomes in acute kidney injury. 2007;11(2):1–8.
24. Egbi OG, Adejumo OA, Akinbodewa AA. Coronavirus infection and kidney disease: A review of current and emerging evidence. *Pan Afr Med J.* 2020;37(149):1–15.
25. Libório AB, Leite TT, De Oliveira Neves FM, Teles F, De Melo Bezerra CT. AKI complications in critically ill patients: Association with mortality rates and RRT. *Clin J Am Soc Nephrol.* 2015;10(1):21–8.
26. Sabaghian T, Kharazmi AB, Ansari A, Omid F, Kazemi SN, Hajikhani B, et al. COVID-19 and Acute Kidney Injury: A Systematic Review. *Front Med.* 2022;9(April):1–9.
27. Chu KH, Tsang WK, Tang CS, Lam MF, Lai FM, To KF, et al. Acute renal impairment in coronavirus-associated severe acute respiratory syndrome. *Kidney Int.* 2005;67(2):698–705.
28. Jewell PD, Bramham K, Galloway J, Post F, Norton S, Teo J, et al. COVID-19-related acute kidney injury; incidence, risk factors and outcomes in a large UK cohort. *BMC Nephrol [Internet].* 2021;22(1):1–11. Available from: <https://doi.org/10.1186/s12882-021-02557-x>
29. Nimkar A, Naaraayan A, Hasan A, Pant S, Durdevic M, Suarez CN, et al. Incidence and Risk Factors for Acute Kidney Injury and Its Effect on Mortality in Patients Hospitalized From COVID-19. *Mayo Clin Proc Innov Qual Outcomes [Internet].* 2020;4(6):687–95. Available from: <https://doi.org/10.1016/j.mayocpiqo.2020.07.003>
30. Luther T, Bülow-Anderberg S, Larsson A, Rubertsson S, Lipcsey M, Frithiof R, et al. COVID-19 patients in intensive care develop predominantly oliguric acute kidney injury. *Acta Anaesthesiol Scand.* 2021;65(3):364–72.
31. Casas-Aparicio GA, León-Rodríguez I, La Barrera CA De, González-Navarro M, Peralta-Prado AB, Luna-Villalobos Y, et al. Acute kidney injury in patients with severe COVID-19 in Mexico. *PLoS One.* 2021;16(2 February):1–16.
32. Tarragón B, Valdenebro M, Serrano ML, Maroto A, Llópez-Carratalá MR, Ramos A, et al. Acute kidney failure in patients admitted due to COVID-19. *Nefrologia.*

2021;41(1):34–40.

33. Alfano G, Ferrari A, Fontana F, Mori G, Magistroni R, Meschiari M, et al. Incidence, risk factors and outcome of acute kidney injury (AKI) in patients with COVID-19. *Clin Exp Nephrol* [Internet]. 2021;25(11):1203–14. Available from: <https://doi.org/10.1007/s10157-021-02092-x>
34. Oo AP, Riaduzzaman MN, Alsaman MI, Rubel AR, Pisharam J, Khalil MAM, et al. Factors Predictive of Development of Acute Kidney Injury in Patients With COVID-19 in Brunei Darussalam. *Cureus*. 2023;15(4):0–10.
35. Kahindo CK, Mukuku O, Wembonyama SO, Tsongo ZK. Prevalence and Factors Associated with Acute Kidney Injury in Sub-Saharan African Adults: A Review of the Current Literature. *Int J Nephrol*. 2022;2022.
36. Bashir AM, Mukhtar MS, Cetinkaya O, Fiidow OA, Mohamed YG. Prevalence of Acute Kidney Injury in Covid-19 Patients-Retrospective Single-Center Study. *Infect Drug Resist*. 2022;15(March):1555–60.
37. Goffe TK, Alemu ZA, Derese TN. Acute Kidney Injury Among Admitted COVID-19 Patients in Addis Ababa , Ethiopia. 2023;(March):83–92.
38. Huang J-W, Chen K-Y, Tsai H-B, Wu V-C, Yang Y-F, Wu M-S, et al. Acute renal failure in patients with severe acute respiratory syndrome. *J Formos Med Assoc* [Internet]. 2005 Dec 22;104(12):891–6. Available from: <https://journals.lww.com/01515467-201607000-00014>
39. Xiao G, Hu H, Wu F, Sha T, Zeng Z, Huang Q, et al. Acute kidney injury in patients hospitalized with COVID-19 in Wuhan, China: a single-center retrospective observational study. *Nan Fang Yi Ke Da Xue Xue Bao*. 2021;41(2):157–63.
40. Mansour A, Sajjadi-Jazi SM, Kasaeian A, Khosravi B, Sorouri M, Azizi F, et al. Clinical characteristics and outcomes of diabetics hospitalized for covid-19 infection: A single-centered, retrospective, observational study. *EXCLI J*. 2020;19:1533–43.
41. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, et al. AKI in hospitalized patients with COVID-19. *J Am Soc Nephrol*. 2021;32(1):151–60.
42. Enikeev D, Taratkin M, Efetov S, Shlomina A, Boldyreva M, Galkina I, et al. Acute kidney injury in COVID-19: Are kidneys the target or just collateral damage? A comprehensive assessment of viral RNA and AKI rate in patients with COVID-19. *Curr Opin Urol*. 2021;31(4):363–8.
43. Chávez-Valencia V, Orizaga-de-la-Cruz C, Lagunas-Rangel FA. Acute Kidney Injury in COVID-19 Patients: Pathogenesis, Clinical Characteristics, Therapy, and Mortality.

- Diseases. 2022;10(3):53.
44. See YP, Young BE, Ang LW, Ooi XY, Chan CP, Looi WL, et al. Risk Factors for Development of Acute Kidney Injury in COVID-19 Patients: A Retrospective Observational Cohort Study. *Nephron*. 2021;145(3):256–64.
 45. Özen H, Aslan AD, Balaban B, Perk O, Uçmak H, Özcan S, et al. Acute kidney injury in critically ill children with COVID-19 and MIS-C. *Pediatr Nephrol* [Internet]. 2023;38(10):3475–82. Available from: <https://doi.org/10.1007/s00467-023-05987-x>
 46. Contreras-Villamizar K, Barbosa O, Muñoz AC, Suárez JS, González CA, Vargas DC, et al. Risk factors associated with acute kidney injury in a cohort of hospitalized patients with COVID-19. *BMC Nephrol* [Internet]. 2023;24(1):1–7. Available from: <https://doi.org/10.1186/s12882-023-03172-8>
 47. Kwiatkowska E, Domański L, Dziedziejko V, Kajdy A, Stefańska K, Kwiatkowski S. The mechanism of drug nephrotoxicity and the methods for preventing kidney damage. *Int J Mol Sci*. 2021;22(11).

Annex

Annex I

Information sheet to medical director of the hospital

St. Paul's Hospital Millennium Medical College

This sheet will be read for medical director of the hospital before collecting any information from the registries.

Greetings. My name is Dr. Chalachew Tadesse and I am a postgraduate student in Emergency and Critical Care Medicine at SPHMM

This governmental hospital was selected to conduct the proposed study "Pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia: a retrospective study" as it has been one of the largest government isolation and treatment center in the country with well-functioning ICU, and it represents patients from various parts of the country.

I am humbly requesting your esteemed office to give me permission to conduct the stated study in this hospital. Please read the following information for further understanding:

What the study is about: The purpose of this study is to assess the pattern of acute kidney injury among COVID-19 patients admitted to isolation and treatment center of SPHMMC, Addis Ababa, Ethiopia. The study is designed to be retrospective study on patients with laboratory-confirmed COVID-19 infection admitted to ICU.

What I will ask you to do: If you agree to facilitate the undertaking of this study; I will be using a checklist to collect necessary data from the medical records of patients. The checklist will include questions about socio-demographic and clinical data of laboratory-confirmed COVID-19 infection admitted to ICU. I would very much appreciate your cooperation in this study.

Risks and benefits: The result of the study is believed to help responsible body to advance ICU care and optimize care for high-risk COVID-19 patients.

Confidentiality: All information gathered from the log book and patient medical record will be kept confidential. Any of patients' personal information will not be registered. The records of this study will be kept private. In any sort of public report, any information that will be making it possible to identify the patient will not be included. Research records will be kept in a locked file; only the researcher will have access to the records.

Contact Address of the Principal Investigator

Name: Chalachew Tadesse

Annex II

English version Questionnaire

St. Paul's Hospital Millennium Medical College

Department of Emergency and Critical Care Medicine

Section 1: Demographic data			
S.N.	Question item	Possible answer	
101	Age in years		
102	Sex	1. Male ☐	2. Female ☐
103	Residence	1. Addis Ababa 2. Out of Addis Ababa (specify _____)	
104	Source of referral	1. Inpatient (intra-facility transfer) 2. Government hospital 3. Health center 4. Private clinic 5. Self-referred	
105	Pre-existing comorbid condition (more than 1 answer possible)	1. Diabetes mellitus 4. Cardiac disease 2. Hypertension 5. None 3. HIV/AIDS 6. Other _____	
106	Weight in KG		
107	Height in CM		
Section 2: Clinical data of the patient			
201	Fever	Yes ☐	No ☐
202	Cough	Yes ☐	No ☐
203	Dyspnea	Yes ☐	No ☐
204	Sore throat	Yes ☐	No ☐
205	Diarrhea	Yes ☐	No ☐
206	Fatigue	Yes ☐	No ☐
207	Abdominal pain	Yes ☐	No ☐
208	Myalgia	Yes ☐	No ☐
209	Disease severity according to WHO criteria at initial presentation	Mild ☐ Severe ☐ Critical ☐	
210	Duration of illness in days		

211	Nephrotoxic medications taken	No ☐ Yes ☐
212	If the patient was taking a nephrotoxic drug, specify	Vancomycin ☐ Ibuprofen ☐ Aminoglycoside antibiotics ☐ Indomethacin ☐ Other (specify _____)
213	Development of AKI	No ☐ Yes ☐
214	Stage of AKI	Stage 1 ☐ Stage 2 ☐ Stage 3 ☐
Section 3: Laboratory and outcome parameters		
301	Baseline serum creatinine, mg/dL	_____
302	Coagulation profile	PT _____ PTT _____ INR _____
303	In-hospital complication	Sepsis ☐
		Bedsore ☐
		DVT ☐
		PE ☐
		Electrolyte imbalance ☐
		Others (please specify) _____
304	Course of AKI	Resolved in 48 hours ☐ Resolved in 48 hours to 7 days ☐ Persisted to > 7 days ☐
305	Hemodialysis done	Not required ☐ Required, but not done ☐ Done ☐
306	If hemodialysis was done, how many times	_____
307	Patient outcome on discharge	Survived: ☐

		Death: ☐ Referred: ☐ Others (specify): ☐
--	--	---

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: _____

Name of Advisors

Name of Advisors: _____

Signature: _____

Date: _____

Name of co-advisors: _____

Signature: _____

Date: _____