THE PREVALENCE AND SHORT-TERM OUTCOMES OF ACUTE KIDNEY INJURY IN PATIENTS HOSPITALIZED WITH COVID-19 INFECTION

By

OGANGA MAUREEN ALEXANDRIA

H58/34310/2019

Department of Clinical Medicine and Therapeutics

University of Nairobi

Dissertation submitted in partial fulfilment of the requirements for the Master of Medicine Degree (MMed) in Internal Medicine of the University of Nairobi.

DECLARATION

I, **Dr. Oganga Maureen Alexandria**, declare that this is my original work and that to the best of my knowledge it has not been presented before for a degree or any other academic award at this or any other university.

Signed: ..... Date: 31/07/23

MAUREEN ALEXANDRIA OGANGA

RESIDENT INTERNAL MEDICINE

DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

FACULTY OF HEALTH SCIENCES

UNIVERSITY OF NAIROBI

H58/34310/2019

This dissertation has been submitted with the approval of my supervisors:

Prof. S. O. McLigeyo, MBChB, MMed Internal Medicine, Consultant Physician and Nephrologist FISN, FRCP (Nephrology and Hypertension), Professor of Medicine, Department of Clinical Medicine and Therapeutics School of Medicine, College of Health Sciences, University of Nairobi.

Signed: ..... Date: 31/7/23.

Dr. A. S. Mohammed, MBChB, MMed Internal Medicine, Consultant Physician and lecturer, Department of Clinical Medicine and Therapeutics School of Medicine, College of Health Sciences, University of Nairobi.

Signed: ..... Date: 31/07/23.

Dr. B. M. Wambugu, MBChB, MMed Internal Medicine, FISN Consultant Physician and Nephrologist - Kenyatta National Hospital.

Signed: ..... Date: 31/7/2023

Dr. K. B. Soki, MBChB, MMed Internal Medicine, FISN (UK) Consultant Physician and Nephrologist- The Nairobi Hospital

Signed: ..... Date: 31/07/2023

Prof. E. O. Amayo

Chairman, Department of Clinical Medicine and Therapeutics- University of Nairobi

Signed..... Date.....3/08/2023

ACKNOWLEDGEMENT

I thank God for His grace and blessings during the course of my study.

I thank my supervisors for their encouragement, commitment and insightful comments throughout my study.

Much appreciation to my family and friends for their moral support.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS AND ACRONYMS

ACE-	Angiotensin Converting Enzyme
ACEI-	Angiotensin Converting Enzyme Inhibitor
AKI -	Acute Kidney Injury
ARBs -	Angiotensin II Receptor Blockers
ARDS-	Acute respiratory distress syndrome
BMI -	Body Mass Index
CABG-	Coronary Artery Bypass Grafting
COVID-19 -	Coronavirus Disease 2019
DM -	Diabetes Mellitus
eGFR -	Estimated Glomerular Filtration Rate
ESRD -	End-Stage Renal Disease
GFR -	Glomerular Filtration Rate
HIV-	Human Immunodeficiency Virus
ICU-	Intensive Care Unit
KDIGO -	Kidney Disease Improving Global Outcomes
KNH-	Kenyatta National Hospital
MI-	Myocardial Infarction
PCI-	Percutaneous Coronary Intervention
PCR-	Polymerase Chain Reaction
RRT-	Renal Replacement Therapy
SARS-CoV-2 -	Severe acute respiratory syndrome coronavirus 2
STATA-	Statistical software

TNH- The Nairobi Hospital

WHO- World Health Organization

ABSTRACT

Background:

Acute Kidney Injury is common among COVID-19 patients and is associated with adverse outcomes. This study aims to determine the prevalence and short-term outcomes of AKI among admitted COVID-19 patients, as this is not well documented in East Africa.

Methods:

Retrospective cohort study of patients hospitalized in a private facility in Nairobi between 1st January and 31st December 2021. We included all PCR positive COVID-19 patients ≥ 18 years with ≥ 2 creatinine levels. Patients with confirmed ESRD at admission or on chronic RRT before admission were excluded. AKI and its severity were defined using KDIGO, and short-term outcomes at discharge were in hospital death and renal recovery. Descriptive statistics were used to profile patient characteristics. Non-AKI and AKI groups compared using Mann- Whitney and Kruskal- Wallis test, and chi-square test for continuous and categorical variables respectively. Multivariable logistic regression used to test association of AKI with presence of selected risk factors. Prior to that, a bivariable logistic regression was fit for each of the predictor variables and only included in the multivariable logistic regression if the predictor variables had a p-value ≤ 0.20 with exception of age, sex and race as possible confounders. P<0.05 was considered statistically significant.

Results: Of the 365 eligible patients, majority were male (61.4%) aged ≥ 50 years. AKI developed in 74 (20.3%) patients with 52.7%, 18.9% and 28.4% in stages 1, 2 and 3 respectively. Of these 13.5% needed RRT, 32 (43.2%) were admitted to ICU, 18 (24%) were ventilated, 24.3% died and 75.7% were discharged. Of the AKI survivors, 42 (75%) achieved full renal recovery at discharge. AKI risk factors were older age (OR 1.046 p<0.001), male sex (OR 2.490 p 0.002), multiple comorbidities (OR 3.694 p 0.001), hypertension (OR 2.598 p 0.001), diabetes mellitus (OR 2.586 p<0.001) and pre-existing CKD (OR 10.550 p<0.001).

Conclusions: AKI in hospitalized COVID-19 patients is common. The prevalence is predominantly higher in critically ill patients and is associated with a higher chance of mortality. Majority of the patients have mild disease with most of them achieving full renal recovery at discharge.

CHAPTER ONE

1. INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first noted in China in December 2019 to cause an outbreak of viral pneumonia. Since then there have been several waves of the disease. WHO declared it a pandemic on 11th March 2020 (1). In Kenya, it was first diagnosed on 12th March 2020. The pandemic has tested the capacity of healthcare systems worldwide, especially in developing countries. Severe COVID-19 infection results in prolonged hospital admissions and adverse outcomes in critically ill patients (2,3).

COVID-19 mainly causes pneumonia with acute respiratory distress syndrome (ARDS) in some patients. The noted extra-pulmonary complications have been postulated to be due to the spread and replication of the causative virus or due to the host's immunological response (4). Some of the common complications of COVID-19 are ARDS, AKI, sepsis and coagulopathy amongst others (5).

AKI is a syndrome that refers to a sudden decline in renal function, this includes both kidney injury and impaired function. Kidney Disease Improving Global Outcomes (KDIGO) criteria have been used to define and stage AKI using the patient's serum creatinine (SCr) and urine output (UO) (6). AKI is common in hospitalized patients in low to middle-income income countries especially those who are critically ill. The syndrome occurs in around 20% of in-patients and can lead to increased morbidity and mortality. The aetiology of AKI is multifactorial and could lead to delayed diagnosis and treatment (7,8).

During the pandemic, there have been increased nephrology consults and hemodialysis requirements, especially in critically ill patients (9). AKI in patients with COVID-19 is a poor prognostic indicator that leads to the development or worsening of comorbid conditions and a heavy economic burden in the health sector. (10–14). Lower rates of AKI in COVID-19 (3-7%) previously reported in research from China, were mainly attributed to differences in study

characteristics and nephrology practices (15–17). Current research has approximated the rate at 25 to 35% of which around 10% end up requiring renal replacement therapy (RRT) (10,11,14,18–22). Higher rates of up to 75% have been reported in critically ill patients (10). Locally, data is limited to a small sample size of 40 critically ill patients reporting the rate at 24% (23).

Around 40% of admitted COVID-19 patients who developed AKI were in KDIGO stage 1 with approximately 30% in stage 3 (10–12). There is limited data in hospitalized COVID-19 patients who develop AKI.

COVID-19 associated AKI has led to the development or worsening of comorbidities, prolonged admissions, long-term complications like end stage renal disease (ESRD) requiring RRT and increased mortality (5,10,12,17,21). The mortality rate is around 20-40% in patients who develop AKI compared to 7-10% in those without AKI. Critically ill patients on hemodialysis have been reported to have a higher mortality rate of up to 50% (5,15,18,21). Local data reports the mortality rate at 50% of critically ill patients, however, there is no data on general patients.

Around 75% of admitted COVID-19 patients who develop AKI fully recover their renal function at discharge and do not require RRT. The rate of recovery has been associated with KDIGO severity stages of which stages 1 and 2 have been shown to have favourable outcomes without requiring RRT at discharge (12). Locally data on renal recovery has not been determined. Some of the reported risk factors for severe disease are: older age, male sex, comorbidities (diabetes mellitus, hypertension and heart failure) and AKI stage 3 (5,21).

1.2 LITERATURE REVIEW

1.2.1 COVID-19

SARS-CoV-2 is a ribonucleic acid virus that genetically clusters within Betacoronavirus. COVID-19 is highly transmissible and began as atypical pneumonia (24,25).

As of 15th February 2022, around 438 million cases and 5 million deaths have been reported globally. While in Kenya 322,945 cases and 5,638 deaths have been reported. Globally around half of the population (4 billion) have been fully vaccinated while in Kenya only 14% (7 million) have been fully vaccinated (26).

The virus is mainly transmitted via respiratory droplets from person to person. Once in the body, it binds to the Angiotensin Converting Enzyme 2 (ACE2) receptor then it's endocytosed and replicates (24). Severe symptoms occur when the virus involves the lower respiratory tract leading to cytokine storm and multiorgan dysfunction (27–29).

COVID-19 commonly occurs in patients aged 40 to 70 years. The most common presentations are cough, fever, dyspnea and malaise (15,16,30–34). Reported risk factors of COVID-19 are male sex, older age, obesity and comorbidities like hypertension, diabetes mellitus, and obesity amongst others (13,31,32,35,36). The complications have been mainly attributed to the cytokine storm and include ARDS, AKI, coagulopathy, and acute cardiac injury amongst others (4,5). In admitted COVID-19 patients worldwide the mortality rate has been reported at around 25 to 30%. In Africa a study by Nlandu et al reported the rate at 32% while in Kenya Ombajo et al reported it at 15% (3,5,32).

1.2.2 AKI

The 2012 KDIGO guidelines define AKI as SCr increase ≥ 1.5 above the known or presumed baseline in less than 7 days or SCr increase ≥ 26.5 micromole/L from the baseline within 48 hours or UO < 0.5 mL/kg/h for 6 hours. The AKI severity stages are: Stage 1 SCr 1.5 to 1.9 times above the baseline or 26.5 micromole/L or more or UO < 0.5ml/kg/hour for six to twelve hours. Stage 2 SCr 2 to 2.9 times above the baseline or UO less than 0.5ml/kg/hour for twelve hours or more. Stage 3 SCr 3 times above the baseline or ≥ 354 micromole/L or need for RRT or eGFR <35ml/min/1.73m2 in patients <18 years or anuria for twelve hours or more (6).

AKI is a public health concern especially in developing countries because of the disease burden, late presentation of patients to hospital and inadequate health-care resources. The prevalence of AKI in non-COVID-19 illnesses ranges between 5-11% and has been mainly attributed to infectious diseases (malaria, HIV, diarrhea amongst others), nephrotoxic agents, obstetric and surgical complications. Higher rates of up to 50% have been reported in critically ill patients which are associated with adverse outcomes (37).

Locally the prevalence of AKI in hospitalized patients is around 8.1% at admission with the most common cause being pre-renal AKI. Increasing severity has been linked with poor outcomes (8). Therefore, early diagnosis and management are recommended to help reduce adverse outcomes and health care costs (7,38).

AKI commonly occurs in admitted patients. Its development is related to complications like chronic kidney disease, electrolyte imbalances, cardiovascular issues; and increased mortality especially in patients with comorbidities. Prolonged AKI leads to the accumulation of waste and renally excreted drugs, electrolyte imbalance and induction of systemic inflammation.

1.2.3 COVID-19 ASSOCIATED AKI

AKI in hospitalized COVID-19 patients is a poor prognostic indicator. Earlier research from China reported low rates (around 3 to 7%) of AKI, these were mainly attributed to differences in nephrology practices and study characteristics (15–17). Most of the recent research has reported AKI to occur in approximately 20 to 40% of hospitalized COVID-19 patients, of which 10-20% end up requiring RRT (5,10,12,17,23,39).

A large United States study by Hirsch et al reviewed 5,499 medical records from 13 hospitals in New York reported the rate of AKI in admitted COVID-19 patients at around 36% with 14% requiring RRT (10). A systematic review and meta-analysis in South Africa by Silver et al reported the pooled prevalence of AKI and RRT in COVID-19 in-patients at 28% and 9% respectively (19). Pitre et al reported higher rates of COVID-19 associated AKI (53.9%), in this study they had community-acquired than hospital acquired AKI (18). A study by Nlandu et al in Democratic Republic of Congo reported the rate of AKI at around 20% with 13% requiring RRT (5). Locally data on non-critically ill patients is lacking.

More than a quarter of hospitalized COVID-19 patients end up in ICU (10,23,23,30,31,40). Approximately 25-50% of these patients develop AKI, with around 15-50% needing RRT (5,10,11,13,18–23,40). A study in the United Kingdom by Lowe et al looking at 81 ICU patients reported the rate of AKI in COVID-19 in-patients at 44% with around 44% of them needing RRT (41). Silver et al in South Africa noted the pooled prevalence of AKI and RRT to be 46% and 19% respectively (19). Locally, data is limited to 40 critically ill patients reporting the rate at 24% with 40% requiring RRT (23). COVID-19 associated AKI rates have been noted to decline over the course of the pandemic due to early recognition and improved management of these patients (42).

Various studies have staged AKI based on the KDIGO severity stages with most of them showing that most of the COVID-19 in-patients who had AKI were in KDIGO stage 1. Increasing severity with adverse outcomes have been observed in patients in stage 3 (10,18). A large cohort study by Hirsch et al reported the AKI KDIGO stages of hospitalized COVID-19 patients at 46%, 22% and 31% in stages 1, 2 and 3 respectively (10). A retrospective study by Ng et al in New York reported the KDIGO stages of AKI in admitted COVID-19 patients at 42%, 21% and 35% in stages 1, 2 and stage 3 respectively (12). Data from Chan et al had similar results reporting the KDIGO severity stages of admitted COVID-19 patients at stage 1- 39%, 2- 19% and 3- 42% (11). In East Africa, the data on staging of in-patients with COVID-19 associated AKI is limited.

CLINICAL CHARACTERISTICS

Kidney damage mainly manifests clinically as deranged renal functions which includes an increase in SCr, a decrease in estimated glomerular filtration rate (eGFR), oliguria, electrolyte imbalance, hematuria and proteinuria (35,41,43,44).

COVID-19 associated AKI in hospitalized patients tends to develop within 2 weeks of admission or sooner especially in critically ill patients. Studies have reported that approximately a third of the hospitalized COVID-19 patients had preadmission AKI (10,17). A study by Pitre et al reported that more than half of the patients had preadmission AKI (18).

AKI in COVID-19 has been strongly associated with lung failure. Studies have reported that AKI usually develops around the time of intubation in these patients. Hirsch et al reported that 50% or more of COVID-19 in-patients with AKI who required mechanical ventilation, developed AKI in less than 24 hours of being intubated (10).

In critically ill in-patients with COVID-19, approximately 80% of these mechanically ventilated patients develop AKI in comparison to 20% of those not on mechanical ventilation. Of the mechanically ventilated patients 96% end up requiring RRT (10,18,19,41).

The commonly reported risk factors of in-patients with COVID-19 AKI are age (40-70 years), male sex, african race, high body mass index, comorbid conditions (diabetes mellitus, hypertension, cardiovascular disease), nephrotoxins and requirement for mechanical ventilation. Older age above 50 years, male sex and comorbidities (hypertension and diabetes) have been shown to have a greater probability of developing AKI in admitted COVID-19 patients (10,19). Diuretic use has been linked with higher risk of developing AKI. Renin angiotensin aldosterone blockers have not been linked to AKI in COVID-19 patients (10,15,39).

MECHANISMS

The pathophysiological mechanisms of COVID-19 leading to development of AKI are thought to be due to direct renal cytotoxicity and indirect mechanisms as a consequence of systemic inflammation due to viral infection or organ cross talk due to effects of the virus or mechanisms

related to its management (44–46). Direct cytotoxicity and systemic inflammation are thought to cause collapsing glomerulopathy mainly in Africans with the APOL1 gene (47,48). Nephrotoxic agents and mechanical ventilation also predispose to renal injury (44). Hypovolemia and dehydration are strongly correlated with AKI development in these patients (49).

OUTCOME

AKI development has been related with increased severity of illness, prolonged hospitalization, long-term complications like ESRD and cardiovascular disease, and increased mortality (5,10,12,14,18–23,34). The mortality rate of COVID-19 in in-patients with AKI is around 20-40% compared to 5-10% in those without AKI. The mortality rate is even higher in the critically ill patients and those requiring RRT (5,12,18,21,23). Older age, male sex, comorbidities and AKI stage 3 have been reported as predictors for in hospital mortality (5,12,18). Studies have reported that the mortality risk in COVID-19 associated AKI increased with the increasing AKI stages (14,18). In a large US study the rate of death was reported at 35% (10). Pitre et al reported in hospital mortality at 24% (18). Locally the mortality rate in critically ill patients is 50% (23). Data on in hospital mortality in the general patients is lacking.

The admission duration in most hospitalized COVID-19 patients with AKI is around 11 to 14 days as compared to approximately 5 days in patients who do not develop AKI (10,12,41,49). Around 70 to 80% of these patients have full renal recovery at discharge, locally this is not determined. The rate of full recovery based on the severity staging 1 to 3 is approximately 85%, 75% and 55% (12). A study carried out in the United Kingdom study reported that more than 80% of COVID-19 in-patients with AKI had full recovery of their renal functions and did not require RRT at discharge (14). Ng et al reported that around 74% of the AKI survivors had full renal recovery at discharge while 30% of the survivors who were on RRT still required RRT at discharge (12).

1.3 STUDY JUSTIFICATION AND SIGNIFICANCE

COVID-19 has adversely affected developing countries resulting in various complications which led to increased mortality, prolonged hospitalizations and increased health care cost. Globally, AKI is of public health concern due to its various causes and increasing prevalence. This is specifically higher in low to middle income countries due to late presentation of patients to hospital and inadequate health care resources resulting in adverse outcomes (37). AKI is a major complication of COVID-19 associated with poor outcomes if not well managed. Therefore, prevention, early recognition and management of AKI in COVID-19 patients is important.

Whereas various studies have characterized AKI in hospitalized COVID-19 patients worldwide, there is limited data in East Africa. Locally, data is limited to 40 critically ill patients (23). Our study reports the prevalence and short-term outcomes of AKI in hospitalized COVID-19 patients.

Our findings may provide meaningful insights to help inform practice and policy. We will seek to publish our study results and also disseminate our results to the relevant departments.

STUDY QUESTION

What is the burden and short-term outcome of COVID-19 associated AKI?

OBJECTIVES

Broad Objective

To determine the prevalence and short term outcomes of AKI in hospitalized COVID-19 patients.

Specific Objectives

1. To determine the prevalence of AKI among hospitalized COVID-19 patients.
2. To stratify the severity of AKI among hospitalized COVID-19 patients according to the KDIGO criteria.
3. To determine the short-term outcomes of hospitalized COVID-19 patients associated AKI at discharge.

Secondary Objective

- To determine the association of AKI with the presence of selected risk factors (age, sex, hypertension, diabetes, coronary artery disease, heart failure, obesity and mechanical ventilation).

CHAPTER TWO

2. METHODS

2.1 STUDY DESIGN

Retrospective cohort study of hospitalized COVID-19 patients.

2.2 STUDY SETTING

The study was conducted at The Nairobi Hospital (TNH) medical records department. TNH is one of the leading private hospitals in Nairobi, Kenya. University of Nairobi (UoN) postgraduate students are trained in acute care medicine in TNH through a memorandum of understanding between the two facilities. It has partnered with the United Nations to run a 130 bed COVID-19 Hospital, with an 18 bed ICU capacity. TNH received quite a high number of patients during the pandemic.

2.3 STUDY POPULATION

These were laboratory-confirmed COVID-19 patients aged 18 years and above who were hospitalized in TNH between 1st January and 31st December 2021.

2.4 TARGET POPULATION

Our target population were admitted COVID-19 cases with at least 2 serum creatinine levels recorded in their charts. COVID-19 refers to a disease caused by SARS-CoV-2. The diagnosis was based on patient charts with positive PCR test (50).

2.5 PATIENT SELECTION CRITERIA

INCLUSION CRITERIA

1) Medical records of patients ≥ 18 years with PCR confirmed COVID-19 infection admitted at TNH between 1st January and 31st December 2021.

2) Hospitalized COVID-19 patients with at least 2 measured creatinine levels while in hospital.

EXCLUSION CRITERIA

1. Medical records of patients with confirmed end stage renal disease (eGFR <15 mL/min/1.73 m^2) at admission or chronic RRT prior to admission.

2.6 TIME LIMITED SAMPLE SIZE

Medical records (1499) of PCR confirmed COVID-19 patients admitted in TNH between 1st January and 31st December 2021 were reviewed and records of patients who met our selection criteria were included.

2.7 SAMPLING TECHNIQUE

Consecutive sampling method was done sequentially from the hospital records using the study eligibility criteria. A study number was allocated sequentially to the records of subjects who met the inclusion criteria.

2.8 STUDY PROCEDURES

Medical records of PCR-confirmed COVID-19 patients ≥ 18 years admitted between 1st January and 31st December 2021 were retrieved. Patient's records with ≥ 2 serum creatinine levels were included while those with renal failure or on chronic RRT prior to admission were excluded. Records of eligible patients were sourced by the study personnel using an electronic data collection tool. Information on demographics (age, sex, race); length of stay (days); existing comorbidities (hypertension, diabetes mellitus, obesity, heart failure, coronary artery disease (previous MI, PCI, CABG)); SCr levels; ICU admission; need for mechanical ventilation or RRT and outcomes (in hospital death and renal recovery) were captured.

2.9 DEFINITION OF STUDY VARIABLES

AKI was defined using KDIGO criteria as: SCr rise 1.5 times or more above the baseline in less than 7 days or SCr ≥ 26.5μmol/L in less than 48 hours. Baseline SCr refers to previous best SCr level within the last 3 months if available or the minimum SCr level during admission.

AKI severity was defined according to KDIGO severity as:

Stage 1: SCr rise by 1.5 to 1.9 times above the baseline SCr or ≥ 26.5micromole/L within 48 hours.

Stage 2: SCr rise by 2 to 2.9 times above the baseline SCr.

Stage 3: SCr rise ≥ 3 times above the baseline SCr or ≥ 354μmol/L or initiation of RRT. Stratification of AKI in-patients based on AKI stage attained was done by comparing the highest to the baseline creatinine level.

The short-term outcomes at hospital discharge were in hospital death and renal outcomes. Renal outcomes in AKI patients were determined at discharge and further categorized as full, partial or no recovery. Full recovery refers to return of discharge SCr to baseline SCr or to normal range. Partial recovery refers to discharge SCr decrease but above the baseline SCr or normal limits. No recovery refers to no decrease in SCr levels.

Data on selected risk factors such as age, sex, race, presence of multiple comorbidities, hypertension, diabetes, heart failure, coronary artery disease, HIV, obesity and mechanical ventilation were used to determine the predictors of AKI in hospitalized COVID-19 patients. The comorbidities were defined as disease documented in the file. Records of patients with CKD diagnosis stage 1-4 and prehospitalization SCr (previous 3 months) were evaluated.

2.10 DATA COLLECTION

An electronic data collection tool was used to collect data from patient records/charts. Logical checks and range checks were inbuilt on the digitized form to reduce major data entry errors. Records of each study subject was assigned a unique serial number to avoid data duplication.

2.11 STATISTICAL ANALYSIS

Data from Kobo Toolbox was downloaded as an excel file then transferred to STATA software version 13.1 for analysis. Collected data was screened for duplicate records, missing data and erroneous data. Duplicate records were removed. Logical errors, missing data and erroneously entered/transcribed data points were corrected through confirmation from the source patient document. For completely unavailable data, these were coded in the database to reflect that data was unavailable.

Descriptive statistics of means, medians, interquartile ranges (IQR), standard deviation for continuous variables as well as the use of frequency/proportion/percentages for categorical variables were used for profiling participants socio-demographics and clinical parameters. The means of eligible participants, that is with AKI and those without AKI were compared using Mann-Whitney U test and the Kruskal–Wallis test for continuous variables (age, length of stay and SCr). Chi square test was used for categorical variables: race, sex, comorbidities, AKI stages, ICU admission, disposition and nephrology consult. Multivariable logistic regression was used in testing the association between AKI and presence of selected risk factors. Prior to that, a bivariable logistic regression was fit for each of the predictor variable and only included in the multivariable logistic regression predictor variables that had a p-value of 0.20 and below with exception of age, sex, and race as possible confounders. P value of < 0.05 was considered statistically significant.

2.12 ETHICAL CONSIDERATION

Ethical approval to conduct the study was sought from the University of Nairobi (UoN) Department of Clinical Medicine and Therapeutics, the UoN/ Kenyatta National Hospital (KNH) and The Nairobi Hospital (TNH) Ethics and Research Committee. Authority to use the medical records was obtained from the TNH Head of Department, Health Management Information System. Medical records of COVID-19 patients admitted between 1st January and 31st December 2022 were reviewed and data of only those who met our inclusion criteria was extracted.

Medical records were handled with confidentiality by using coded identification numbers and the names of the patients were not indicated in the data collection forms. Soft copy data was securely stored using a password. Data was only accessed by the study staff. One assistant was trained on the study protocol by the Principal Investigator to assist with data collection.

CHAPTER 3

3. RESULTS

Recruitment Process

Figure 1 shows that, 365 out of 1,499 hospital records of patients admitted between 1st January and 31st December 2021 met the study inclusion criteria. Most of these patients were excluded because they had less than 2 serum creatinine (SCr) levels.

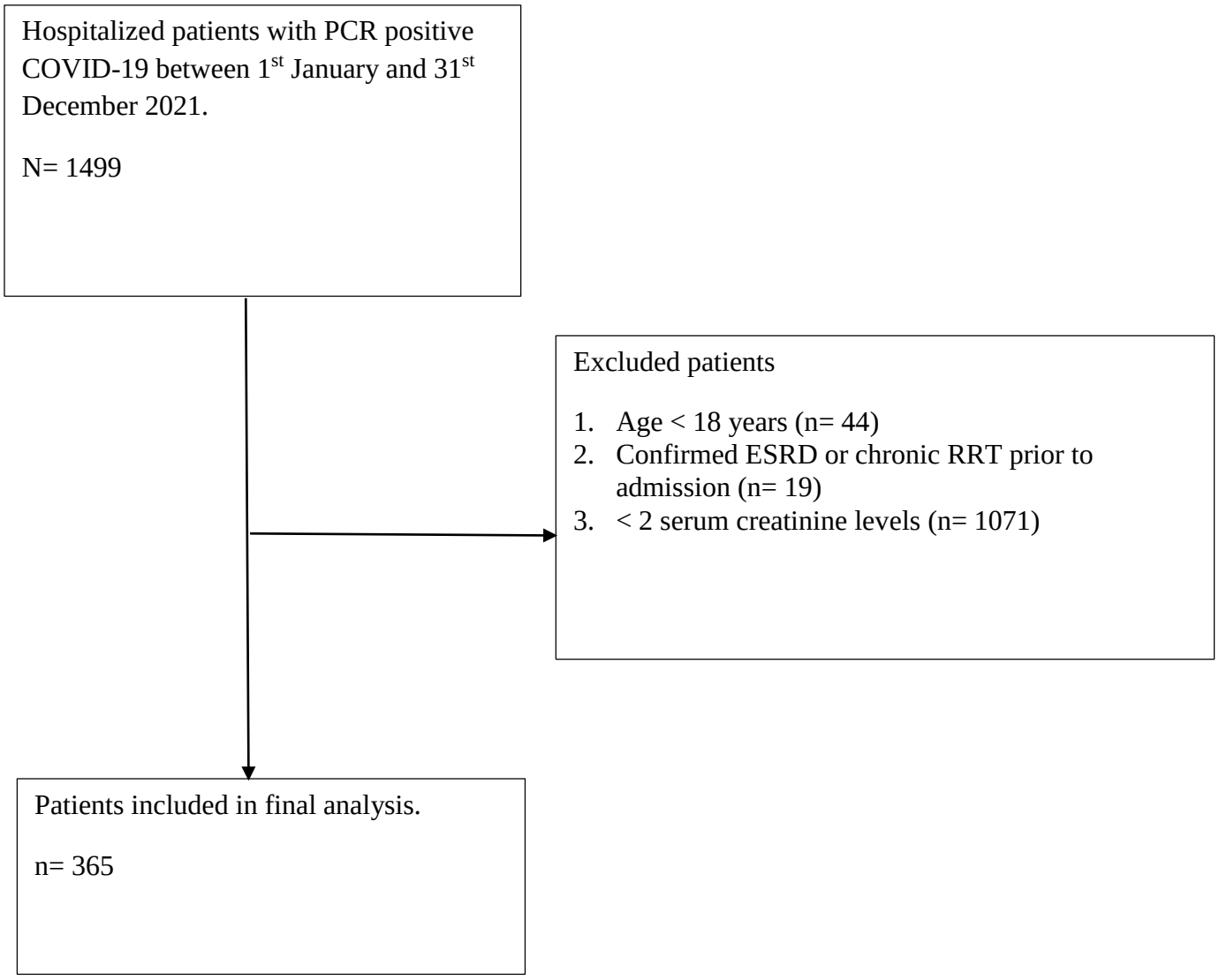

Figure 1 Study Flow Chart

Patient Characteristics

Table 1 shows patient characteristics. The median age of the eligible patients was 54 (IQR 44-65) with majority (26%) being between 50 to 59 years. Most of the patients were male 224 (61.4%). Africans accounted for most of the patient records 327 (89.6%). Among the eligible patients, 118 (32.3%) were admitted in the ICU. Fifty patients (13.7%) required mechanical ventilation at some point during their admission. Seventy-four patients (20.3%) had a BMI >30kg/m^2. The comorbidities were hypertension 185 (50.7%), diabetes 131 (35.9%), coronary artery disease 12 (3.3%), heart failure 8 (2.2%) and HIV 8 (2.2%).

The median admission serum creatinine (SCr) was 81.4 IQR (67.9-107.6) in these patients. The overall number of patients needing RRT were 10 (2.7%). Among the patients with baseline SCr, CKD was evident in 25 (6.9%) patients. The median duration of hospitalization was 10 days (IQR 6-19) in the general patients and 19 days (IQR 12-29) in ICU patients. Only 23 (6.3%) patients were vaccinated.

Table 1 Patient Characteristics

Variables	**Overall (n=365)**
Age in years (median)	54 (IQR 44, 65)
Age categories (years)	
< 30yrs	12 (3.3%)
30-<40	45 (12.3%)
40-<50	84 (23%)
50-<60	95 (26%)
60-<70	67 (18.4%)
70+	62 (17%)
Male	224 (61.4%)
Race	
African	327 (89.6%)
Asian	25 (6.8%)
Caucasian	13 (3.6%)
Comorbid Conditions	
Hypertension	185 (50.7%)
Diabetes	131 (35.9%)
Coronary Artery Disease (Previous MI, PCI, CABG)	12 (3.3%)
Heart failure	9 (2.5%)
HIV	8 (2.2%)
BMI >30 Kg/m^2	74 (20.3%)
Admission serum creatinine (µmol/L) (median)	81.4 (IQR 67.9, 107.6)
GFR <60 ml/min/1.73 m^2	25 (6.9%)
RRT	10 (2.7%)
ICU Admission	118 (32.3%)
Mechanical Ventilation	50 (13.7%)
Admission days	
General (median)	10 (IQR 6, 19)
ICU (median)	19 (IQR 12, 29)
Vaccinated	23 (6.3%)

Table 2, figure 2 and 3 show the prevalence of AKI in hospitalized COVID-19 patients and the various stages according to KDIGO criteria. The prevalence of AKI in COVID-19 admitted patients, based on KDIGO criteria was 20.3% (74 subjects). The AKI severity stages were: stage 1 (39 subjects, 52.7%), stage 2 (14 subjects, 18.9%) and stage 3 (21 subjects, 28.4%).

Table 2 Prevalence of AKI and AKI severity

	Prevalence n (%)
AKI	74 (20.3)
Stage 1	39 (52.7)
Stage 2	14 (18.9)
Stage 3	21 (28.4)
Non AKI	291 (79.7)

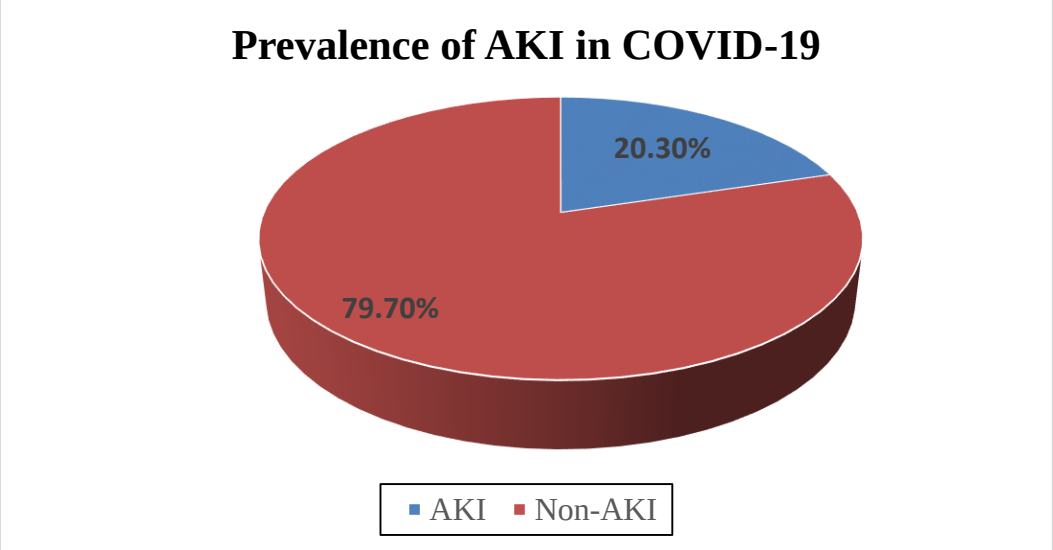

Figure 2 Prevalence of AKI in COVID-19

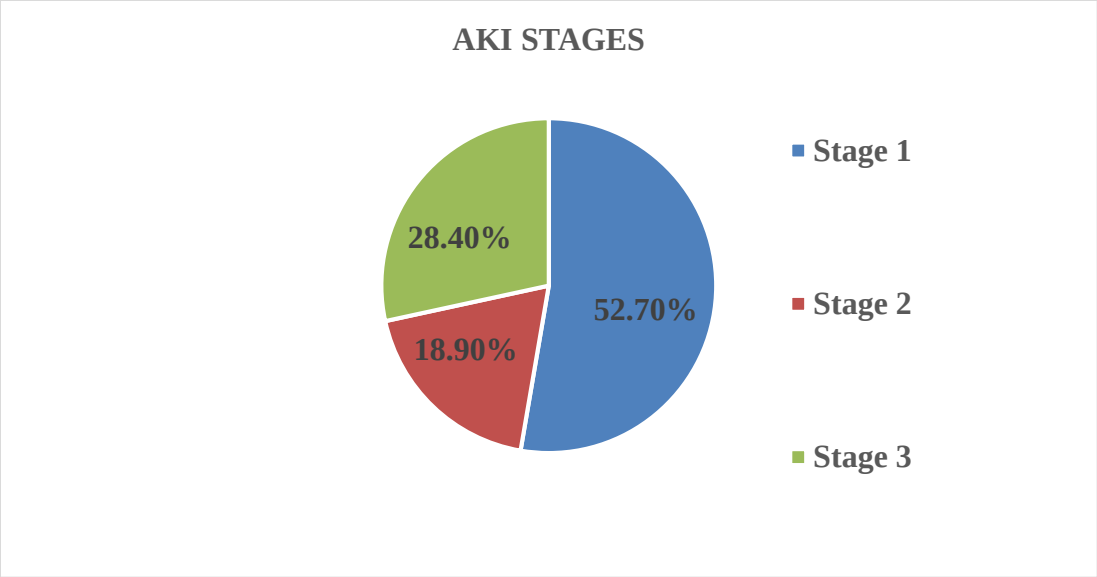

Figure 3 Percentages of AKI stages

Table 3 and 4 show the patient characteristics by AKI status. Of the AKI patients, 10 (13.5%) required RRT at some point during their hospitalization. Majority of the AKI group participants were male as compared to the non-AKI group and this was statistically significant (77.0% vs 57.4%, p 0.002). AKI group participants were older than the non-AKI group participants and this was statistically significant (62.1 years vs 52.8 years, $p < 0.001$). Among the AKI stages, age difference was statistically significant with subjects in stage 2 and 3 being older as compared to subjects in stage 1. Africans were the majority in both groups though this was statistically insignificant. The AKI group had a significantly higher tendency to present with multiple comorbidities compared to the non- AKI group (89.2% vs 69.1% $p < 0.001$). Both hypertension (AKI 68.9% vs non-AKI 46.0%) and diabetes (AKI 59.5% vs non-AKI 31.3%) were among the dominant comorbidities in both groups. Acute on chronic kidney disease was more common in the AKI group compared to the non-AKI group (23.0% vs 2.8% $p<0.001$).

AKI group were statistically significantly more likely to be admitted to ICU as compared to non-AKI group (43.2% vs 29.6% p 0.025). A higher proportion of patients with increased AKI severity Stage 2 (71.4%) and 3 (61.9%) were significantly more likely to require ICU care compared to stage 1 (23.1%) patients ($p <0.001$). A quarter (24.3%) of the AKI patients were mechanically ventilated compared to 11% of the non-AKI patients and this was significant. AKI stage 2 (35.7%) and 3 (38.1%) patients were more likely to be mechanically ventilated compared to patients in

stage 1 (12.8%). The median hospital admission days was 11 days (IQR 6, 19) in AKI and 10 days (IQR 6, 19) in non-AKI subjects (p = 0.4848).

Table 3 Patient Characteristics by AKI status

Continuous Variables	Non-AKI (n = 291) **Median (IQR)**	AKI (n = 74) **Median (IQR)**	Stages of AKI **Median (IQR)**			P value[¥] (non-AKI vs. AKI	P value[β] (AKI stages)
			1 (n = 39)	2 (n = 14)	3 (n = 21)		
Age	52.8 (42,63)	62.1 (54,73)	62 (54,70)	64 (52,77)	66 (53,74)	**<0.001**	**<0.001**
Admission days	10 (6,19)	11 (6,19)	8 (6,15)	15.5 (6,23)	11 (11,21)	0.4848	0.0871
BMI	27 (25,30)	29 (26,31)	29 (27,30)	28 (27,29)	29.5 (26,31)	0.1607	0.8674
Admission SCr (µmol/L)	76 (63.9,89.3)	145.6 (124.2,234.6)	142 (126.7,173.5)	150 (114,235.2)	265.1 (97,395.7)	**<0.001**	0.5696
Discharge SCr (µmol/L)	70.8 (61.3,82.4)	111.8 (89,169.5)	105 (88.7,139.7)	116.6 (103.8,171.5)	118 (81,316.7)	**<0.001**	0.3510
Peak SCr (µmol/L)	81.3 (69.9,96.1)	174.25 (142,274.4)	145.1 (134.6,173.5)	231.2 (149,269)	386.3 (265.1,498.5)	**<0.001**	**0.0001**
Lowest SCr (µmol/L)	66 (56,76)	92.55 (76.1,118)	94.6 (86.1,118)	99 (62.6,124.2)	78.1 (69.2,107.1)	**<0.001**	0.2247
Baseline eGFR	90 (90,90)	39.25 (24,52.2)	48 (35.6,62.7)	35.75 (24,47)	18.7 (14,28)	**<0.001**	**0.0001**
Discharge eGFR	90 (90,90)	71.2 (40.5,90)	73.4 (48,90)	55.05 (41.82.5)	63.8 (18.3,90)	**<0.001**	0.2701

[¥]*Comparisons between non AKI and AKI using nonparametric Wilcoxon (Mann–Whitney) rank-sum test for continuous variables.*

[β]*Comparisons are made across the AKI stages using Kruskal-Wallis rank sum test.*

Table 4 Patient Characteristics by AKI status (2)

Categorical Variables	Non-AKI (n=291) n (%)	AKI (n=74) n (%)	AKI Stages			P value[¥] (non-AKI vs. AKI	P value[β] (AKI stages)
			1 (n=39)	2 (n=14)	3 (n=21)		
Male	167 (57.4)	57 (77.0)	32 (82.1)	10 (71.4)	15 (71.4)	**0.002**	0.555
Comorbid Conditions							
None	90 (30.9)	8 (10.8)	6 (15.4)	0	2 (9.5)	**<0.001**	0.324
Presence of comorbidities (1-4)	201 (69.1)	66 (89.2)	33 (84.6)	14 (100.0)	19 (90.5)		
Hypertension	134 (46.0)	51 (68.9)	25 (64.1)	10 (71.4)	16 (76.2)	0.542	0.167
Coronary artery disease	8 (2.7)	4 (5.4)	1 (2.6)	3 (21.4)	0		
Heart failure	5 (1.7)	4 (5.4)	2 (5.1)	2 (14.3)	0		
Diabetes	91 (31.3)	40 (59.5)	19 (48.7)	7 (50.0)	14 (66.7)		
HIV	6 (2.1)	2 (2.7)	1 (2.6)	0	1 (4.8)		
Obesity	59 (20.3)	15 (20.3)	5 (12.8)	2 (14.3)	8 (28.1)		
ICU admissions	86 (29.6)	32 (43.2)	9 (23.1)	10 (71.4)	13 (61.9)	**0.025**	**<0.001**
Mechanical Ventilation	32 (11.0)	18 (24.3)	5 (12.8)	5 (35.7)	8 (38.1)	**0.003**	**0.051**
Nephrology consult	6 (2.1)	43 (58.1)	13 (33.3)	11 (78.6)	19 (90.5)	**<0.001**	**<0.001**
Vaccination	19 (6.5)	4 (5.4)	1 (2.6)	2 (14.3)	1 (4.8)	0.722	0.248
GFR<60ml/min/1.73 m^2	8 (2.8)	17 (23.0)	8 (20.5)	4 (28.6)	5 (23.8)	**<0.001**	0.823

[¥]*Comparisons between non AKI and AKI using Pearson chi test for categorical variables.*

[β]*Comparisons are made across the stages of AKI using the Pearson chi square test*

Table 5 shows the proportion of AKI patients who required mechanical ventilation. There was a statistically significant relationship between respiratory failure and development of AKI. AKI group were more likely to be mechanically ventilated compared to the non-AKI group (24.3% vs 11.0%, p 0.003). Mechanical ventilation was significantly associated with increased AKI severity, as most of the ventilated patients were in stages 2 (28%) and 3 (44%). A higher proportion of the patients who required RRT were mechanically ventilated (12.0% vs 1.3%, p <0.001).

Table 5 Proportion of AKI patients who required mechanical ventilation

	No use of invasive mechanical ventilation	**Required invasive mechanical ventilation**	***P* value**
Non- AKI (291)	259 (89.0)	32 (11.0)	**0.003**
AKI (74)	56 (75.7)	18 (24.3)	
Stage 1	34 (60.0)	5 (28.0)	**0.051**
Stage 2	9 (16.0)	5 (28.0)	
Stage 3	13 (23.0)	8 (44.0)	
Required RRT(10)	4 (1.3)	6 (12.0)	**<0.001**

Categorical variables compared using Fisher's exact test or chi-square

Outcomes

Table 6 shows outcomes of non-AKI and AKI patients. Twenty-eight (7.7%) patients died and 337 (92.3%) were discharged home. The all-cause mortality was significantly higher in the AKI group at 24.3% compared to 3.4% in non-AKI group (p <0.001). The case fatality rate in AKI stages was stage 1- 12.8%, stage 2- 35.7% and stage 3- 38.1%. Majority of the patients in both groups survived and were discharged home (AKI 75.7% vs non-AKI 96.6%) and this was statistically significant. Out of the 56 (75.7%) AKI survivors 42 (75%) achieved full renal recovery, 9 (16.1%) partial recovery while 5 (8.9%) had no recovery at discharge.

Table 6 Outcomes of Non-AKI and AKI patients

Outcome Variables	**Overall (n= 365)**	**Non-AKI (n=291) n (%)**	**AKI (n=74) n (%)**	**AKI Stages**			**P value[¥] (non-AKI vs. AKI**
				1 (n=39)	**2 (n=14)**	**3 (n=21)**	
Discharged	337 (92.3%)	281 (96.6)	56 (75.7)	34 (87.2)	9 (64.3)	13 (61.9)	**<0.001**
Full recovery			42 (75.0)	25 (73.5)	6 (66.7)	11 (84.6)	
Partial recovery			9 (16.1)	5 (14.7)	3 (33.3)	1 (7.7)	
No recovery			5 (8.9)	4 (11.8)	0	1 (7.7)	
Died	28 (7.7%)	10 (3.4)	18 (24.3)	5 (12.8)	5 (35.7)	8 (38.1)	**<0.001**

[¥]*Comparisons between non AKI and AKI using Pearson chi test for categorical variables.*

Figure 4 shows AKI severity and associated outcome. Across the AKI stages, majority achieved full renal recovery at discharge [stage 1- 25 patients (73.5%), stage 2- 6 patients (66.7%) and stage 3- 11 patients (84.6%)] as shown in table 6 and figure 4.

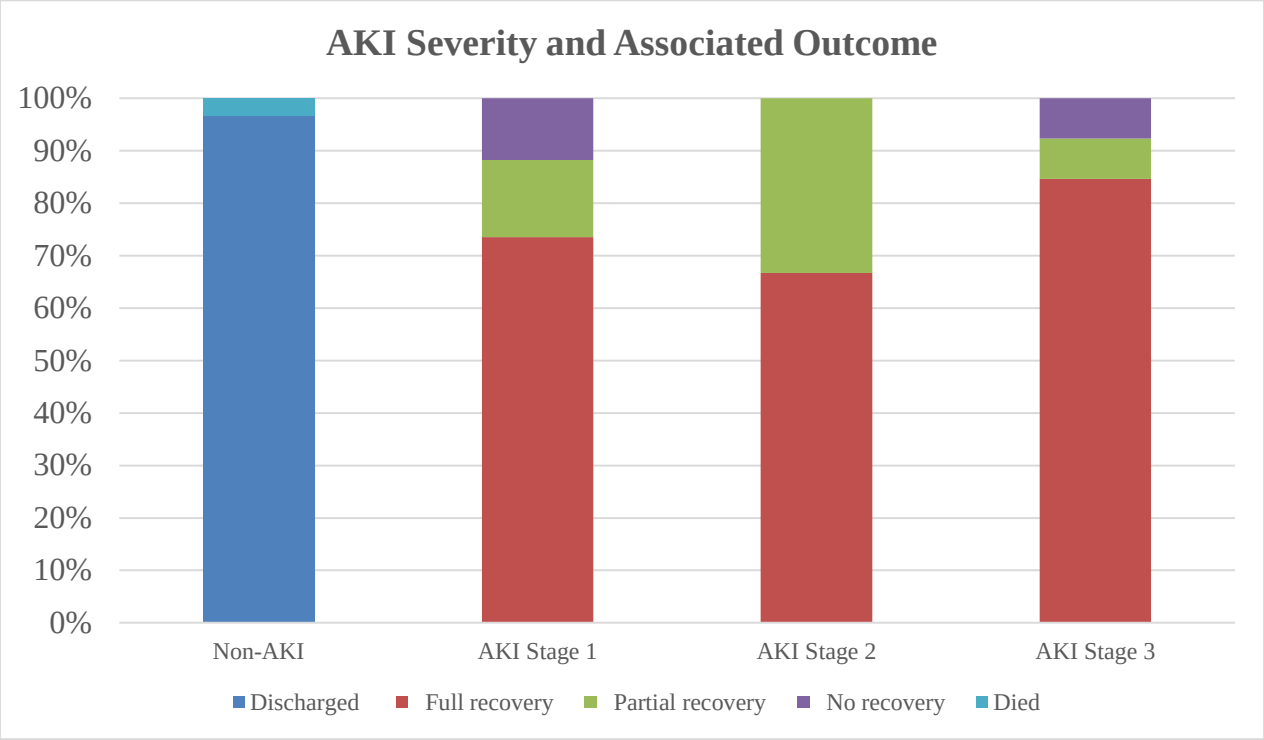

Figure 4 AKI severity and outcome

Factors associated with AKI in COVID-19

Table 7 shows the predictors of AKI development by univariate and multivariate logistic analysis. Risk factors found to be independently associated with AKI in COVID-19 patients by univariate logistic analysis include increased age (OR 1.046, 95%CI 1.026-1.065, p<0.001), male sex (OR 2.490, 95%CI 1.381-4.488, p=0.002), presence of multiple comorbidities (OR 3.694, 95%CI 1.702-8.016, p=0.001) and pre-existing CKD (OR 10.550, 95%CI 4.345-25.620, p<0.001). Amongst comorbidities that the patients had, hypertension and diabetes were independently associated with AKI. COVID-19 patients with hypertension (OR 2.598, 95%CI 1.509-4.474, p=0.001) or diabetes (OR 2.586, 95%CI 1.537-4.349, p<0.001) were twice likely to develop AKI compared to those without these comorbidities. In multivariate logistic analysis, only age (AOR

1.158, 95%CI 1.044-1.285, p=0.006) was found as a significant predictor associated with development of AKI in COVID-19 patients.

Table 7 Univariate and multivariate logistic analyses of predictors associated with AKI development

Characteristics	**Non-AKI (n=291) n (%)**	**AKI (n=74) n (%)**	**Univariate analysis**			**Multivariate analysis**		
			OR	95% CI	p Value	AOR[¥]	95% CI	p Value
Age median (IQR)	52.8 (42,63)	62.1 (54,73)	1.05	1.026-1.065	**<0.001**	1.2	1.044-1.285	**0.006**
Sex								
Female	124 (42.6)	17 (23.0)	Ref			Ref		
Male	167 (57.4)	57 (77.0)	2.5	1.381-4.488	**0.002**	1.2	0.222-6.821	0.812
Race								
Caucasian	9 (3.1)	3 (4.1)	Ref			Ref		
Asian	18 (6.2)	6 (8.1)	1	0.202-4.955	1.000	1.0	0.009-111.719	0.990
African	262 (90.0)	65 (87.8)	0.7	0.196-2.827	0.664	0.7	0.013-41.870	0.882
Comorbid								
None	90 (30.9)	8 (10.8)	Ref			Ref		
Multiple (1-4)	201 (69.1)	66 (89.2)	3.7	1.702-8.016	**0.001**	-		
Hypertension	134 (46.0)	51 (68.9)	2.6	1.509-4.474	**0.001**	0.9	0.138-7.004	0.986
Coronary Artery Disease	8 (2.7)	4 (5.4)	2.0	0.592-6.905	0.261	-		
Heart failure	5 (1.7)	4 (5.4)	3.3	0.855-12.489	0.083	0.1	0.003-6.582	0.311
Diabetes	91 (31.3)	40 (59.5)	2.6	1.537-4.349	**<.001**	0.2	0.031-1.627	0.140
HIV	6 (2.1)	2 (2.7)	1.3	0.261-6.674	0.737	-		
Obesity	59 (20.3)	15 (20.3)	1.0	0.530-1.886	0.999	-		
Mechanical ventilation	32 (11.0)	18 (24.3)	2.2	0.952-4.946	0.065	0.5	0.068-3.613	0.489

[¥]Variables were entered into the model when the α level of risk factor was less than 0.2.

CHAPTER 4

4. DISCUSSION

The purpose of this retrospective cohort study was to determine the prevalence and short term outcomes of AKI among hospitalized COVID-19 patients. To the best of our knowledge, there is limited data characterizing AKI in hospitalized COVID-19 patients especially in East Africa. To date, only one study looking at AKI in critically ill COVID-19 patients has been published though this was limited to few (40) critically ill patients (23).

Majority of our patients were male aged ≥ 50 years. The prevalence of AKI in COVID-19 was 20.3% with majority being in AKI stage 1 (52.7%), and 13.5% requiring RRT. Around 40% of the ICU patients were likely to have AKI with majority being in AKI stage 2 and 3. AKI patients had around a quarter chance of being mechanically ventilated, developing AOCKD and death. Majority of the AKI patients survived and achieved full renal recovery at discharge. In our analysis, the predictors of AKI in hospitalized COVID-19 patients were older age, male sex, multiple comorbidities (specifically hypertension and diabetes mellitus).

Our relatively lower prevalence of AKI in hospitalized COVID-19 patients could be attributed to our patients generally having less severe disease and also due to suboptimal testing.

Recent research has reported the rate of AKI in hospitalized COVID-19 patients at around 20-40% and this seems to be consistent with our data reporting the rate at 20.3% (5,10,19). Nlandu et al in DRC reported a similar prevalence of 20.3% (5). Hirsch et al reported a higher prevalence of AKI in COVID-19 at 36.6% (10). A systematic review and meta-analysis by Silver et al in South Africa reported a pooled prevalence of 28% (19). However, earlier reports from China reported lower rates of around 3-7% and this was thought to be due to differences in the populations and nephrology practices. Of note these patients also had lower rates of patients with comorbid conditions like hypertension and diabetes which are risk factors for AKI.

AKI in Sub-Saharan Africa is a public health concern because of the disease burden, late presentation of patients to hospital and inadequate resources. The prevalence of AKI in non-COVID-19 illnesses ranges between 5-11% and has been mainly attributed to infectious diseases (malaria, HIV, diarrhea amongst others), nephrotoxic agents, obstetric and surgical complications. Higher rates of up to 50% have been reported in critically ill patients (37). Locally Taiyebali et al

had similar results reporting the prevalence of community acquired AKI in hospitalized patients at 8.1% (8). The prevalence of AKI in hospitalized COVID-19 patients based on our study is higher than that of AKI in other non-COVID-19 diseases and therefore this high burden could be due to severity of COVID-19 disease.

Various studies have staged AKI based on the KDIGO severity stages with most of them showing that majority of the COVID-19 in-patients who had AKI were in KDIGO stage 1 (10–12). A large cohort study by Hirsch et al reported the AKI KDIGO stages of hospitalized COVID-19 patients at 46%, 22% and 31% in stages 1, 2 and 3 respectively. Hirsch et al had a similar pattern with majority being in AKI stage 1 (10). Chan et al reported a higher rate in AKI stage 3 (stage 1- 39%, 2- 19% and 3- 42%), this was because most of their patients had more severe disease (11). Our results mirror these findings and supports the theory that majority of the admitted COVID-19 patients had mild disease.

Our RRT rate of 13.5% was comparable to reports from other studies reporting the rate between 10% and 20% (5,10,19). A New York based study reported the rate at 14% (10). In Africa, a study by Nlandu et al in Democratic Republic of Congo reported the RRT rate at 13% (5).

AKI in critically ill patients is a marker of severe disease and could lead to adverse outcomes. Most studies have reported a higher rate of AKI in critically ill COVID-19 patients ranging between 40% and 50% with majority of patients being in AKI stage 3 (5,10,19,40,41). This is comparable to our data reporting the rate at 43.2% with 40.6% having AKI stage 3. This could suggest a relationship between increased inflammation associated with severe COVID-19 and developing AKI. Silver et al and Lowe et al reported a rate of 46% and 44% respectively (19,41). Locally, Bagha et al reported a lower rate of 24.4% though this study was limited to 40 critically ill patients over a 6-month period.

Development of AKI in hospitalized COVID-19 patients has been strongly associated with respiratory failure. Hirsch et al reported that AKI occurred in majority of the mechanically ventilated patients, who were mainly in AKI severity stage 2 and 3, and lastly that most of these patients required RRT (10). Our findings confirm this relationship in that a higher proportion of our AKI patients were mechanically ventilated compared to the non-AKI patients and secondly majority of the patients who required RRT were mechanically ventilated.

AKI development has been associated with increased severity of illness, prolonged hospitalization, increased mortality and long-term complications like ESRD. The overall in-patient mortality was 24.3% in AKI patients and 3.4% in non-AKI patients. Increasing severity of AKI as shown in our data has been linked with adverse outcomes, especially in patients with stage 2 and 3 disease as also shown in various studies (5,12,18,23).

The mortality rate in these patients has been reported to range between 20 and 40% in general patients and can go up to 50% in critically ill patients (5,10,18,23). Lowe et al had a similar result with 25% mortality in AKI group versus 6.7% in non-AKI group (41). This was comparable to our data as we found a mortality rate of 24.3% in the AKI group versus 3.4% in non-AKI group with majority being in AKI stages 2 and 3. Chan et al also reported a higher mortality rate of 50% in AKI group versus 8% in non-AKI group, this was due to increased severity of AKI and COVID-19 (11). Our lower rate was thought to be due to less severe disease in our patients.

Knowledge on renal recovery is important as it provides insight on nephrology follow-up post discharge and probable cause of AKI. More than half of the AKI survivors who were discharged home had achieved full renal recovery. This further supports the theory that our patients had less severe disease. Our results were similar to those of a study done by Ng et al who also reported that majority of the patients who were discharged had achieved full renal recovery (12). In contrast, a study by Chan et al reported a low recovery rate which they attributed to the severity of AKI and COVID-19 (11).

Our results are comparable to previous studies which report older age, male sex and comorbidities mainly hypertension and diabetes mellitus as predictors of AKI in COVID-19. A UK based study reported similar results with age and diabetes as being part of the major risk factors (10). Bagha et al also reported hypertension and diabetes as major risk factors (23). Individuals with older age had a higher likelihood of developing AKI and this was associated with presence of multiple comorbidities like hypertension and diabetes. Kidney function decreases with increasing age due to decreased renal mass, increased incidence of sclerotic glomeruli and presence of multiple comorbidities. Ageing is also associated with an increase in other risk factors e.g. cardiovascular risk.

5. CONCLUSION

AKI in hospitalized COVID-19 patients is common. The prevalence is predominantly higher in critically ill patients and is associated with a higher chance of mortality. Majority of the patients have mild disease with most of them achieving full renal recovery at discharge.

6. STUDY LIMITATIONS AND DELIMITATIONS

Due to the retrospective nature of this study, we were unable to obtain all data related to the parameters of interest. However, data validation was adequate as we went through both physical and electronic medical records before selection of records. Patients with less than two serum creatinine readings may have had AKI but would be missed resulting in majority of their records being excluded, this may have introduced a selection bias. The study was limited to in-patients in a private facility; therefore, this may limit the generalizability of the study findings.

7. STUDY RECOMMENDATIONS

Based on our findings we recommend frequent monitoring of renal functions especially in patients who had severe disease. Further research is required to better characterize the predictors associated with in hospital mortality in AKI in COVID-19 patients. Secondly, the AKI in COVID-19 patients could be followed up to determine the implications of post-acute on chronic kidney disease.

9. APPENDICES

9.1 Ethical Approval Forms

THE NAIROBI HOSPITAL

REF: TNH/DCS/DMSR/ERC/24/05/22 24th May 2022

TO: Dr. Oganga Maureen Alexandria
Principal Investigator

Dear Dr. Oganga,

RE: THE PREVALENCE AND SHORT TERM OUTCOME OF ACUTE KIDNEY INJURY IN PATIENTS HOSPITALIZED WITH COVID-19 INFECTION: A RETROSPECTIVE STUDY

This is to inform you that ***The Nairobi Hospital Ethics & Research Committee*** has reviewed and approved your above research proposal. Your application approval number is ***TNH-ERC/DMSR/ RP/027/22***. The approval period is ***24th May, 2022 – 24th May, 2023.***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***The Nairobi Hospital Ethics & Research Committee***
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***The Nairobi Hospital Ethics & Research Committee*** within 24 hours of notification
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***The Nairobi Hospital Ethics & Research Committee*** within 72 hours
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***The Nairobi Hospital Ethics & Research Committee.***
viii. Compliance with the guidelines and regulations stipulated by the study site authorization

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Healthcare with a difference!

Yours sincerely,
FOR: THE NAIROBI HOSPITAL

Dr. Morris Muhinga
CHAIRMAN, TNH-ETHICS & RESEARCH COMMITTEE

CC Chief Executive Officer
Director, Medical Services & Research
Ag. Director Nursing Services
ChN. Renal Unit
Ag. A&E and OPCs Coordinator
Chief Medical Records Officer

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/283

22nd July, 2022

Dr. Maureen Alexandria Oganga
Reg. No. H58/34310/2019
Dept. of Clinical Medicine andTherapeutics
Faculty of Health Sciences
University of Nairobi

Dear Dr. Oganga,

RESEARCH PROPOSAL: THE PREVALENCE AND SHORT TERM OUTCOMES OF ACUTE KIDNEY INJURY IN PATIENTS HOSPITALIZED WITH COVID-19 INFECTION; A RETROSPECTIVE STUDY (P219/03/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P219/03/2022.** The approval period is 22nd July 2022 – 21st July 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept., KNH
The Chair, Dept. of Clinical Medicine and Therapeutics, UoN
Supervisors: Prof. S.O.Mcligeyo, Dept. of Clinical Medicine and Therapeutics, UoN
Dr. A.S.Mohammed, Dept. of Clinical Medicine and Therapeutics, UoN
Dr. B.M.Wambugu, Consultant Physician and Nephrologist, KNH
Dr. K.B. Soki, Consultant Physician and Nephrologist, The Nairobi Hospital

9.2 Budget

Item	Quantity	Unit Cost (Kshs)	Total (KShs)
Training and remuneration of Study Assistants	2	30,000	60,000
Stationery and Printing	Data collection forms, research booklets		40,000
Statistician Allowance	1	50,000	50,000
Ethics committee review fee	2	2,000	4,000
Contingency		30,000	30,000
Total (Kshs)			184,000

10. REFERENCES

1. Coronavirus disease (COVID-19) [Internet]. Accessed February 1st, 2022. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019

2. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region — Case Series. N Engl J Med. 2020 May;382(21):2012–22.

3. Bialek S, Boundy E, Bowen V, et al. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020 Mar;69(12):343–6.

4. Gupta A, Madhavan MV, Sehgal K, et al. Extrapulmonary manifestations of COVID-19. Nat Med. 2020 Jul;26(7):1017–32.

5. Nlandu Y, Mafuta D, Sakaji J, et al. Predictors of mortality in COVID-19 patients at Kinshasa Medical Center and a survival analysis: a retrospective cohort study. BMC Infect Dis. 2021 Dec 20;21(1):1272.

6. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Accessed May 11th 2021. Available from: http://www.kidney-international.org

7. Makris K, Spanou L. Acute Kidney Injury: Definition, Pathophysiology and Clinical Phenotypes. Clin Biochem Rev. 2016 May;37(2):85–85.

8. Taiyebali MM. Prevalence, severity and outcomes of community acquired acute kidney injury in medical patients at Kenyatta National Hospital University of Nairobi 2012;62–62.

9. Fisher M, Prudhvi K, Brogan M, et al. Providing Care to Patients with AKI and COVID-19 Infection: Experience of Front Line Nephrologists in New York. Kidney360. 2020 Jun;1(6):544–8.

10. Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int. 2020 Jul;98(1):209–18.

11. Chan L, Chaudhary K, Saha A, et al. AKI in hospitalized patients with COVID-19. J Am Soc Nephrol. 2021 Jan;32(1):151–60.

12. Ng JH, Hirsch JS, Hazzan A, et al. Outcomes Among Patients Hospitalized with COVID-19 and Acute Kidney Injury. Am J Kidney Dis. 2021 Feb;77(2):204-215.e1.

13. Grasselli G, Greco M, Zanella A, et al. Risk Factors Associated with Mortality among Patients with COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med. 2020 Oct;180(10):1345–55.

14. Jewell PD, Bramham K, Galloway J, et al. COVID-19-related acute kidney injury; incidence, risk factors and outcomes in a large UK cohort. BMC Nephrol. 2021 Nov 1;22(1):359.

15. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA - J Am Med Assoc. 2020 Mar;323(11):1061–9.

16. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020 Feb;395(10223):507–13.

17. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020 May;97(5):829–38.

18. Pitre T, Dong AHT, Jones A, et al. Incidence and Outcomes of Acute Kidney Injury in Patients Admitted to Hospital with COVID-19: A Retrospective Cohort Study. Can J Kidney Health Dis. 2021 Jul 11; 8:20543581211027759.

19. Silver SA, Beaubien-Souligny W, Shah PS, et al. The Prevalence of Acute Kidney Injury in Patients Hospitalized with COVID-19 Infection: A Systematic Review and Meta-analysis. Kidney Med. 2021 Jan;3(1):83-98. e1.

20. Mohamed MMB, Lukitsch I, Torres-Ortiz AE, et al. Acute Kidney Injury Associated with Coronavirus Disease 2019 in Urban New Orleans. Kidney360. 2020 Jul;1(7):614–22.

21. Paek JH, Kim Y, Park WY, et al. Severe acute kidney injury in COVID-19 patients is associated with in-hospital mortality. PLoS ONE. 2020 Dec;15(12 December): e0243528–e0243528.

22. Naser MN, Al-Ghatam R, Darwish AH, et al. Risk factors, predictions, and progression of acute kidney injury in hospitalized COVID-19 patients: An observational retrospective cohort study. PLOS ONE. 2021 Sep 29;16(9): e0257253.

23. Bagha H, Ahmed S, Gajjar N, Bajaber A. POS-005 acute kidney injury in critically ill COVID-19 patients admitted at a private hospital. Kidney Int Rep. 2021 Apr;6(4): S2–S2.

24. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med J. 2021 May;97(1147):312–20.

25. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb;382(8):727–33.

26. Ritchie H, Mathieu E, Rodés-Guirao L, et al. Coronavirus Pandemic (COVID-19). Our World Data [Internet]. Accessed on February 1st 2022; Available from: https://ourworldindata.org/covid-vaccinations

27. Li H, Liu L, Zhang D, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. The Lancet. 2020 May;395(10235):1517–20.

28. Zhang C, Wu Z, Li JW, et al. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents. 2020 May;55(5).

29. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020 Apr;8(4):420–2.

30. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020 Feb;395(10223):497–506.

31. Guan W jie, Ni Z yi, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr;382(18):1708–20.

32. Ombajo LA, Mutono N, Sudi P, et al. Epidemiological and clinical characteristics of COVID-19 patients in Kenya. medRxiv. 2020 Nov;2020.11.09.20228106-2020.11.09.20228106.

33. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020 Mar;395(10229):1054–62.

34. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area. JAMA. 2020 May;323(20):2052–9.

35. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. The BMJ [Internet]. 2020 May;369.

36. Argenzian MG, Bruc SL, Slate CL, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: Retrospective case series. The BMJ [Internet]. 2020 May;369.

37. Kahindo CK, Mukuku O, Wembonyama SO, et al. Prevalence and Factors Associated with Acute Kidney Injury in Sub-Saharan African Adults: A Review of the Current Literature. Int J Nephrol. 2022 Mar 15;2022:5621665.

38. Hoste EAJ, Kellum JA, Selby NM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol 2018 1410. 2018 Aug;14(10):607–25.

39. Hirsch JS, Ikizler TA, Sharma S, et al. Acute Kidney Injury and Advanced Kidney Disease in the COVID-19 Pandemic: Proceedings from a National Kidney Foundation Symposium. Kidney Med. 2021 May-Jun;3(3):426-432.

40. Doher MP, Torres de Carvalho FR, Scherer PF, et al. Acute Kidney Injury and Renal Replacement Therapy in Critically Ill COVID-19 Patients: Risk Factors and Outcomes: A Single-Center Experience in Brazil. Blood Purification. 2021;50(4-5):520-530. 2021. p. 520–30.

41. Lowe R, Ferrari M, Nasim-Mohi M, et al. Clinical characteristics and outcome of critically ill COVID-19 patients with acute kidney injury: a single centre cohort study. BMC Nephrol 2021 221. 2021 Mar;22(1):1–9.

42. Charytan DM, Parnia S, Khatri M, et al. Decreasing Incidence of Acute Kidney Injury in Patients with COVID-19 Critical Illness in New York City. Kidney Int Rep. 2021 Apr;6(4):916–27.

43. Almeida DC de, Franco M do CP, Santos DRP dos, et al. Acute kidney injury: Incidence, risk factors, and outcomes in severe COVID-19 patients. PLOS ONE. 2021 May 25;16(5): e0251048.

44. Legrand M, Bell S, Forni L, et al. Pathophysiology of COVID-19-associated acute kidney injury. Nat Rev Nephrol 2021. 2021 Jul;1–14.

45. Diao B, Wang C, Wang R, et al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 infection. Nat Commun. 2021 Dec;12(1):1–9.

46. Nadim MK, Forni LG, Mehta RL, et al. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. Nat Rev Nephrol. 2020 Dec;16(12):747–64.

47. Nlandu YM, Makulo JRR, Pakasa NM, et al. First Case of COVID-19-Associated Collapsing Glomerulopathy in Sub-Saharan Africa. Case Rep Nephrol. 2020;2020.

48. Peleg Y, Kudose S, D'Agati V, et al. Acute Kidney Injury Due to Collapsing Glomerulopathy Following COVID-19 Infection. Kidney Int Rep. 2020 Jun;5(6):940–5.

49. Tarragón B, Valdenebro M, Serrano ML, et al. Acute kidney failure in patients admitted due to COVID-19. Nefrol Engl Ed. 2021 Jan;41(1):34–40.

50. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med. 2020 Dec 17;383(25):2451–60.