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Research Article

Acute Kidney Injury during the COVID-19 Pandemic – Experience from Two Tertiary Centres in South Africa

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ABSTRACT

Background: The first case of SARS-CoV-2 in South Africa [SA] was documented in March 2020. By October, the total cases for the Western Cape and Gauteng Provinces were 331,425 with 8456 fatalities. The aim of this study was to describe the prevalence of acute kidney injury [AKI] in hospitalized patients with COVID-19 in two tertiary centres in SA.

Methods: SARS-CoV-2 positive patients admitted to two tertiary centres in SA between 18 March and 31 August 2020 were included in the study. Demographic data, pre-existing comorbidities, admission variables, laboratory data, management and hospital outcomes were captured. Exclusion criteria included age <18 years, pre-existing Stage 4 or 5 chronic kidney disease and prior renal transplant. Outcomes assessed were the need for acute dialysis, recovery from AKI, discharge and death.

Results: AKI occurred in 374/1102 (33.9%) patients admitted to the two hospitals. Within the AKI cohort, 91 (24.3%) patients required intensive care unit [ICU] management, and 32 (8.6%) received kidney replacement therapy. Older age ($P = 0.001$), pre-existing hypertension [HPT] ($P = <0.0001$) 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. AKI Stage 3 had a higher mortality and lower rates of renal recovery upon discharge. AKI was significantly associated with an increased utilization of ICU resources, prolonged length of stay and mortality.

Conclusion: This study reports the largest cohort of COVID-19-associated AKI in Africa. Older age, HPT and severe COVID-19 infection were significantly higher in patients with COVID-19 who developed AKI. This cohort had high rates of AKI which was associated with adverse outcomes, including mortality.

Keywords: COVID-19, South Africa, Acute kidney injury

INTRODUCTION

The first documented case of SARS-CoV-2 in South Africa [SA] took place in March 2020. The peak of the pandemic was reached in mid-July 2020. At the time of publication the Gauteng Province [GP] and Western Cape [WC] Province had reported a total of 220,365 and 111,060 cases, respectively, and the fatalities in the two provinces were 4260 [GP] and 4196 [WC].(1,2) The large influx of critically ill patients required considerable resource consideration. Guidelines were developed to assist the selection of patients requiring admission to an intensive care unit [ICU].(3)

Although COVID-19 predominantly affects the respiratory system, there is multisystem involvement, including the gastrointestinal, cardiovascular, nervous system and the kidneys. Multiple organ disturbances interact with each other to culminate in disease severity and contribute to adverse outcomes.(4,5)

The pathogenesis of acute kidney injury [AKI] in COVID-19 is multifactorial. Prerenal AKI has been associated with increased insensible loses or renal hypoperfusion from myocardial dysfunction (cardio-renal syndrome type 1).(6) Intra-renal failure may develop from direct SARS-CoV-2 entry into renal tissue via angiotensin converting enzyme-2 receptors causing direct viral cytopathic effects or acute tubular necrosis [ATN] following cytokine release, septic shock and rhabdomyolysis.(6) Endotheliitis, thrombotic events and intravascular coagulation have also been associated with AKI in severe COVID-19 infection.(6) Kidney biopsies have demonstrated areas of segmental fibrin thrombi within glomerular capillary loops associated with severe injury to the endothelium.(7) Importantly, nephrotoxicity from concomitant antibiotics and other drugs should not be overlooked as a potential cause.(6)

The latest evidence suggests that AKI is a common complication of COVID-19 infection.(8) It frequently develops in critically ill patients and is associated with a poor prognosis.(9–11) A recent systematic review and meta-analysis of 22 observational studies from China and the United States reported on renal complications in 17,391 hospitalized patients with COVID-19. The pooled incidence for AKI ($n = 22$ studies) was 11.0% (7.4–15.1) with 6.8% (1–17) requiring kidney replacement therapy [KRT]. Although AKI was the common outcome reported by studies; hyperkalaemia was the most frequent renal complication with an incidence of 12.5%. AKI incidence was comparable in younger (<60 years) and older (>60 years) individuals.(4)

The prevalence of AKI resulting in the need for KRT ranges from 0.8% in China to 20% of hospitalized patients in New York.(12,13) In a large New York cohort AKI was commonly seen in association with respiratory failure and mechanical ventilation.(10) Patients developing AKI in the setting of COVID-19 have poor outcomes, irrespective of their age.(11) The worldwide mortality of AKI associated with COVID-19 has ranged from 22% to 100%.(10,11,13–16) Zhou et al. described a 100% mortality of those requiring acute KRT in a cohort from China.(16) Identified risk factors for AKI included older age, diabetes mellitus, cardiovascular disease, black race, hypertension [HPT] and need for mechanical ventilation and vasopressor support.(10)

There is a paucity of data regarding SARS-CoV-2 infection and AKI from the African continent. The primary aim of this study was to describe the clinical, biochemical features and outcomes of patients who were polymerase chain reaction positive for SARS-CoV-2 and developed AKI from two tertiary referral centres in SA. The secondary aim was to determine pre-existing conditions which were associated with AKI.

METHODS

Patients who tested positive for SARS-CoV-2 between 18 March and 31 August 2020 admitted to Groote Schuur Hospital [GSH], Cape Town and Charlotte Maxeke Johannesburg Academic Hospital [CMJAH] were included in the study. Exclusion criteria included age <18 years, pre-existing 4 or 5 chronic kidney disease [CKD] and patients with a prior renal transplant. Patients who did not have admission data on kidney function were excluded. The study received ethics approval from the University of Cape Town and the University of the Witwatersrand.

Information collected included demographic data (age, sex, weight, smoking status) and clinical data, including presenting symptoms, medical comorbidities (human immunodeficiency virus [HIV] status, diabetes mellitus, HPT, pre-existing cardiac and respiratory diseases, CKD), blood pressure [BP] and oxygen requirements at admission. The need for ICU admission and dialysis was also documented. Outcomes that were analysed included the need for acute dialysis, recovery from AKI, discharge and death.

Biochemical parameters were analysed using standard methods by the hospitals' accredited central laboratories. This included creatinine (μmol/L), estimated glomerular filtration rate (mL/min/1.73 m^2), sodium (mmol/L), potassium (mmol/L), hs-troponin T (ng/L), C-reactive protein [CRP] (mg/L), ferritin (μg/L), glycated haemoglobin [HbA1c] (%) and lactate dehydrogenase [LDH] (U/L) performed on the Roche Cobas 6000, full blood count on the Sysmex XN-9000 and d-dimer (mg/L) on the Beckman ACL-TOP 500. Laboratory data were extracted from the laboratory information system (TrakCare). For each patient, data analysis was performed using Excel (Microsoft) and Stata (StataCorp LLC). Background data were analysed to determine a diagnosis of diabetes mellitus (random glucose, HbA1c) and HIV [viral load (copies/mL), CD4 (cells/μL)].

AKI was defined according to Kidney Disease: Improving Global Outcomes [KDIGO] criteria as follows: Stage 1 – increase in serum creatinine by 0.3 mg/dL (26.4 μmol/L) within 48 h or 1.5–1.9 times increase in

serum creatinine from baseline within 7 days; Stage 2 – 2–2.9 times increase in serum creatinine within 7 days; Stage 3 – 3 times or more increase in serum creatinine within 7 days or initiation of KRT.(17) Patients were stratified according to the highest AKI stage attained during their hospital stay. The baseline creatinine was defined as the last creatinine preceding the diagnosis of COVID-19. When there was no baseline creatinine available, an estimated baseline creatinine was calculated using a previously described method.(13) Recovery was defined as the difference between discharge creatinine and baseline creatinine of <26.4 μmol/L and a creatinine change of <25%.

STATISTICAL ANALYSIS

As the Shapiro–Wilk normality test initially indicated that the data reported that were not normally distributed non-parametric statistical tests were used for all the analyses. The Mann–Whitney test was used to compare continuous variables between two groups and the Kruskal–Wallis test used for comparison between three groups. Pearson's chi-square test was used to analyse categorical data between the groups and if the frequency was ≤5, a Fisher's exact (two-tailed) test was used. Continuous variables are presented as medians with an interquartile range [IQR] and categorical variables as numbers and percentages. A *P*-value <0.05 was considered statistically significant and results that are reported in the tables as statistically significant are highlighted in bold black text. Box and whisker plots displayed comparative data between groups. Owing to time constraints and significant burden of illness during the peak of the COVID pandemic, some of the clinical data were missing from the clinical cohort analysed. For clinical variables, in particular admission to ICU and KRT, we assumed missing data (i.e. not marked as present or absent) to be negative. This was considered a reasonable assumption given data recording by busy healthcare workers was pragmatic in nature and is in-line with common practice in epidemiological research.

RESULTS

During the study period, 1102 patients were included into the cohort from 2 sites: GSH, Cape Town ($n = 500$) and CMJAH ($n = 602$). The cohort characteristics are described in Table 1. The median age of the cohort was 52 years, with a slight female predominance (54.2%). The three leading comorbidities included HPT (42.7%), diabetes mellitus (27.5%) and HIV (15.5%).

The clinical characteristics of the cohort included a median admission BP of 127/77 mmHg. High-flow nasal oxygen was required in 8.4% (89/1063), mechanical ventilation in 8.7% (96/1102) and inotropic support was required in 7.1% (45/634) of admissions. Dialysis was commenced in 2.9% (32/1102) of admitted patients, and high-dose steroids were provided to 39.7% (437/1102) of patients. Laboratory data demonstrated a low median lymphocyte count (1.3×10^9/L) and elevated CRP (85 mg/L), d-dimer (0.69 mg/L), LDH (482 U/L) and ferritin (594 μg/L). These results reflected disease severity. The median creatinine of the entire cohort on admission was 85 μmol/L with a median peak creatinine of 114 μmol/L. The median length of admission was 7 days; however, it ranged from 1 to 70 days. There was a mortality rate of 21% attributed directly to COVID-19.

Table 2 describes the differences between the cohort of patients that developed AKI versus those that did not. The total number of patients who developed AKI was 374 / 1102 (33.9%). There was a significantly higher number of patients with pre-existing HPT (52.7% vs 37.6%; $P = <0.0001$) and older age (54% vs 50%; $P = 0.001$) in the AKI versus the non-AKI cohort. There was a trend towards an increased number of diabetic patients in the AKI cohort, but it did not reach statistical significance (31.2% vs 25.8%, $P = 0.06$). The diastolic BP was lower in the AKI group (74.5 vs 77 mmHg, $P = 0.0285$). Laboratory markers indicating a more severe COVID-19 illness in patients with AKI; serum ferritin, LDH, d-dimer and CRP were statistically higher (Figures 1–3). Serum creatinine was higher in the AKI cohort on admission, peak and at discharge. More patients with AKI required inotropic support (17.3% vs 1.5%; $P = <0.0001$), mechanical ventilation (19% vs 3.4%; $P = <0.0001$) and ICU admission (24.3% vs 8.8%; $P = <0.0001$). Death was more common in those with AKI (33.5% vs 14.5%; $P = <0.0001$) and the AKI patients had longer hospitalization (8 vs 7 days; $P = 0.0002$) (Figure 4).

Table 3 describes the characteristics of patients with KDIGO AKI Stages 1–3. There were few significant differences in parameters between the patients in each stage. The haemoglobin and potassium were lower in AKI Stages 2 and 3. Kidney function deteriorated during hospitalization in 63.1% of those who developed Stage 3 AKI. Those patients with AKI Stage 3 required more intensive care resources in the form of dialysis, ICU admission, ventilation and inotropic support. They were also more likely to die. Of the 204 AKI patients in whom serum creatinine results were available at time of discharge; 150 (73.5%) recovered renal function – 104/122 (85%) of the Stage 1 patients, 20/36 (55.6%) of the Stage 2 patients and 26/46 (56.5%) of the Stage 3 patients.

DISCUSSION

To our knowledge, this is the largest cohort describing AKI associated with COVID-19 on the African continent. AKI was significantly associated with an increased utilization of ICU resources, prolonged length of stay and mortality. At discharge, 26.5% of patients with AKI did not recover renal function.

The prevalence of AKI in COVID-19 is well documented and ranges from 0.5% to 46%.(12,13). This wide prevalence distribution is most likely due to heterogeneity in cohorts studied, including the severity of illness, rates of

Table 1: Baseline characteristics for hospitalized patients admitted with PCR positive SARS-COV-2

Patient characteristics	All ($n = 1102$)
Age (years), median (IQR)	52 (40–62)
Gender, *n* (%)	
Male	505 (45.8)
Female	597 (54.2)
Comorbidities, *n* (%)	
Hypertension	470 (42.7)
Myocardial infarction	26 (2.4)
Stroke	25 (2.3)
Diabetes mellitus	304 (27.6)
Human immunodeficiency virus positive	171 (15.5)
Admission symptoms associated with AKI, *n* (%)	
Diarrhoea ($n = 1061$)	78 (7.4)
Admission vitals, median (IQR)	
Systolic blood pressure (mmHg) ($n = 1026$)	127 (115–140)
Diastolic blood pressure (mmHg) ($n = 1026$)	77 (68–86)
SaO_2 (%) ($n = 1009$)	91 (85–96)
Admission laboratory investigations, median (IQR)	
Haemoglobin (g/dL) ($n = 1045$)	13.3 (11.9–14.6)
Lymphocyte count $\times 10^9$/L ($n = 806$)	1.3 (0.89–1.88)
LDH (U/L) ($n = 339$)	482 (350–666)
CRP (mg/L) ($n = 847$)	85 (30–182)
D-dimer (mg/L) ($n = 753$)	0.69 (0.37–1.81)
Ferritin (μg/L) ($n = 488$)	594 (262.8–1363)
Potassium (mmol/L) ($n = 809$)	4.5 (4.1–4.95)
HbA1c (%) ($n = 576$)	7.1 (6.2–10.3)
Creatinine (μmol/L), median (IQR)	
Admission creatinine	85 (65–115)
Peak creatinine ($n = 621$)	114 (83–178.5)
Discharge creatinine ($n = 668$)	79 (63–105)
Dialysis, *n* (%)	32 (2.9)
Inotropes ($n = 634$)	45 (7.1)
High-dose steroids, *n* (%)	437 (39.7)
ICU admission, *n* (%)	155 (14.1)
Respiratory support, *n* (%)	
Invasive mechanical ventilation	96 (8.7)
High-flow nasal cannula ($n = 1063$)	89 (8.4)
Outcome measures, *n* (%)	
Death	223 (21)
Length of stay (days) ($n = 999$)	7 (4–11)

PCR, polymerase chain reaction; IQR, interquartile range; HbA1c, glycated haemoglobin; AKI, acute kidney injury; SaO_2, oxygen saturation; LDH, lactate dehydrogenase; CRP, C-reactive protein; ICU, intensive care unit.

Table 2: Comparison of patient characteristics in those developing AKI vs non-AKI

Patient characteristics	**AKI**	**Non-AKI**	***P***
N	374	728	
Age (years), median (IQR)	54 (42–64)	50 (38–61)	0.001
Gender, *n* (%)			0.58
Male	167 (44.7)	338 (46.4)	
Female	207 (55.3)	390 (53.6)	
Comorbidities, *n* (%)			
Hypertension	196 (52.4)	274 (37.6)	<0.0001
Myocardial infarction	9 (2.4)	17 (2.34)	0.94
Stroke	7 (1.9)	18 (2.5)	0.54
Diabetes mellitus	116 (31.2)	188 (25.8)	0.06
Human immunodeficiency virus positive	63 (27.9)	108 (24)	0.27
Admission symptoms associated with AKI, *n* (%)			
Diarrhoea	29 (8.7)	49 (6.7)	0.26
Admission vitals, median (IQR)			
Respiratory rate (bpm)	24 (20–30)	24 (20–28)	0.08
Heart rate (bpm)	99 (88–113)	100 (87–113)	0.77
Systolic blood pressure(mmHg)	125 (113–140)	129 (116–141)	0.08
Diastolic blood pressure (mmHg)	74.5 (67–85)	77 (69–86.8)	0.0285
SaO_2 (%)	90 (84–96)	91 (85–95.7)	0.23
Admission laboratory investigations, median (IQR)			
Haemoglobin (g/dL)	13.1 (11.4–14.3)	13.4 (12.1–14.7)	0.0019
Lymphocyte count × 10^9/L	1.2 (0.9–1.8)	1.3 (0.9–1.9)	0.22
LDH (U/L)	565 (407.3–726.8)	454 (324–625)	<0.0001
CRP (mg/L)	101 (36.5–217.5)	80.5 (26.8–164)	0.0028
D-dimer (mg/L)	0.8 (0.4–1.9)	0.7 (0.3–1.7)	0.0028
Ferritin (μg/L)	789.5 (346.8–1543)	532.5 (217–1302)	0.0020
Potassium (mmol/L)	4.5 (4.1–5)	4.4 (4.1–4.9)	0.19
HbA1c (%)	7.1 (6.3–10.2)	7.1 (6.2–10.4)	0.39
Creatinine (μmol/L), median (IQR)			
Admission creatinine	128 (87–174)	76 (62–93)	<0.0001
Peak creatinine	179 (132–302)	85 (71–106)	<0.0001
Discharge creatinine	102 (76–171)	70 (59–83)	<0.0001
Dialysis, *n* (%)	32 (8.6)	0	<0.0001
Inotropes	39 (17.3)	6 (1.5)	<0.0001
High dose steroids, *n* (%)	153 (40.1)	284 (39)	0.60
ICU admission	91 (24.3)	64 (8.8)	<0.0001
Respiratory support, *n* (%)			
Invasive mechanical ventilation	71 (19)	25 (3.4)	<0.0001
High flow nasal cannula	28 (8.36)	61 (8.38)	0.99
Outcome measures, *n* (%)			
Death	122 (33.5)	101 (14.5)	<0.0001
Length of stay (days)	8 (5–13)	7 (4–11)	0.0002

IQR, interquartile range; HbA1c, glycated haemoglobin; SaO_2, oxygen saturation; LDH, lactate dehydrogenase; CRP, C-reactive protein; ICU, intensive care unit.

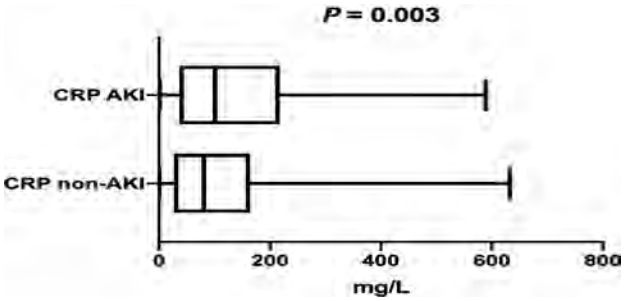

Fig 1: Differences in CRP levels between AKI and non-AKI

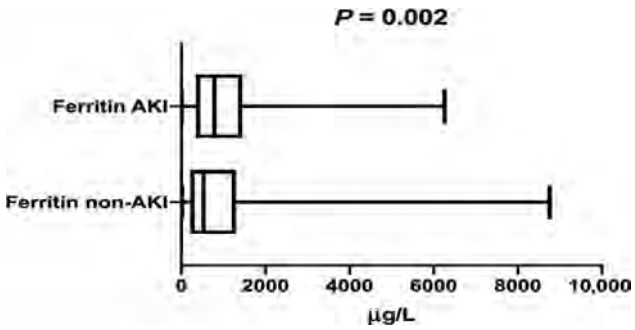

Fig 2: Differences in ferritin levels between AKI and non-AKI

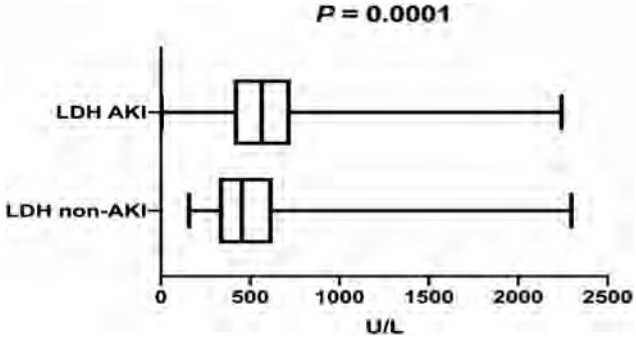

Fig 3: Differences in LDH levels between AKI and non-AKI

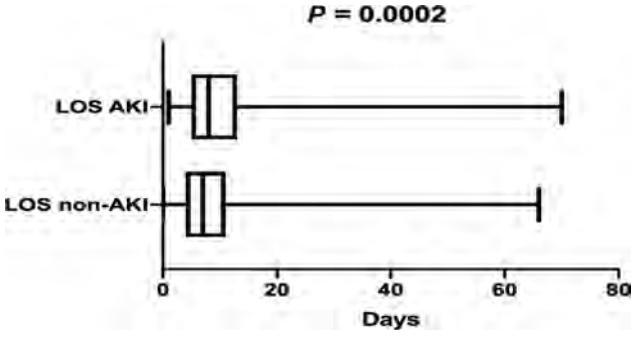

Fig 4: Differences in length of stay (LOS) between AKI and non-AKI

comorbid illnesses and the definitions for AKI used. The 33.9% prevalence of AKI reported in our cohort is much higher than that reported in China but similar to 36.6% reported in New York, United States.(10) Although our cohort was younger, the high rates of AKI may reflect the degree of comorbidities seen in our cohort. The Chinese data report lower rates of comorbidities known to be risk factors for more severe COVID-19 disease, such as diabetes and HPT.

The higher rate of AKI in this study can partially be explained by the fact that both GSH and CMJAH are main referral hospitals for COVID-19 as well as nephrology services. This may have created a bias with the more severely ill patients being referred to GSH and CMJAH. Some studies have used ICU admission as a marker of severity of disease in their cohorts. One hundred and fifty-five (14.1%) of our patients were admitted to ICU. However, in our centres, ICU admission was limited by bed availability and resource constraints. Hence, this is likely to be an underestimation of the true reflection of COVID-19 disease severity.

The degree of AKI and mortality associated with COVID-19 infection has differed between regions, with AKI-associated mortality rates ranging from 7.4% to 100%.(18) We noted that with an increasing severity of AKI stage, there was a significant increase in the associated mortality rate; Stage 1 – 25.5%, Stage 2 – 36.2% and Stage 3 – 48.5%. These are similar to mortality rates reported by Hirsch et al. with 22.4%, 34% and 54%, respectively.(10)

In comparison to our non-AKI cohort, the patients with AKI were significantly older and more likely to have pre-existing HPT. There was no statistical difference with respect to HIV positivity rates between the two groups. HIV has not been shown to be a risk factor for COVID-19-related AKI in other studies.(19) Patients who developed AKI had elevated markers consistent with severe COVID-19, including higher levels of serum CRP, LDH, ferritin and d-dimer. They also had clinical indicators of severity, including high rates of ICU admission and mechanical ventilation. These finding are in keeping with the published literature and point towards a common pathophysiological mechanism resulting in severe respiratory and renal disease. (6,20) Similar to the reported literature, 32/374 (8.6%) of our patients with AKI required dialysis.(10,11)

The majority (56.1%) of our AKI cohort developed AKI Stage 1, which is concordant with the international literature on COVID-19-related AKI.(18) One hundred and thirty-eight (39.8%) patients' renal function deteriorated following admission for COVID-19. Chan et al. also reported a delay in the diagnosis of AKI in hospitalized patients with COVID-19 [median 1 (IQR 1–4 days)]. (13) Within our cohort of patients we documented significantly lower serum potassium in the AKI Stage 3 patients. Admission, and not peak, potassium levels were documented in our patients. Of note, 65 patients during their admission deteriorated to AKI Stage 3, accounting

Table 3: Comparison of patient characteristics in those with acute kidney injury, divided into KDIGO Stages 1–3

Patient characteristics	**AKI Stage 1**	**AKI Stage 2**	**AKI Stage 3**	***P***
N	210	61	103	
Age (years), median (IQR)	54.5 (42–64)	58 (44–69.5)	51(42–62)	0.12
Gender, *n* (%)		0.67		
Male	98 (46.7)	30 (44.7)	43 (42)	
Female	112 (55.3)	37 (55.3)	60 (58)	
Comorbidities, *n* (%)				
Hypertension	106 (50.5)	36 (59)	54 (52.9)	0.49
Myocardial infarction	5 (2.4)	2 (3.3)	2 (2)	0.28
Stroke	3 (1.4)	2 (3.3)	2 (2)	0.54
Diabetes mellitus	67 (31.9)	24 (39.4)	25 (24.5)	0.45
Human immunodeficiency virus positive	35 (25.7)	9 (23.1)	19 (38)	0.192
Admission symptoms associated with AKI, *n* (%)				
Diarrhoea	19 (9.3)	7 (11.9)	3 (4.3)	0.28
Admission vitals, median (IQR)				
Respiratory rate (bpm)	24 (20–30)	24 (20–28)	24 (20–32)	0.75
Heart rate (bpm)	98 (86–111)	100 (93–110.5)	106 (86–118)	0.12
Systolic blood pressure (mmHg)	126 (114.5–140)	125.5 (111.5–138.3)	124 (112.8–140)	0.74
Diastolic blood pressure (mmHg)	75 (67–85.5)	73.5 (66.5–83)	74 (66–86.25)	0.95
SaO_2 (%)	90 (84–96)	90 (84–94)	92 (85–97)	0.31
Admission laboratory investigations, median (IQR)				
Haemoglobin (g/dL)	13.4 (11.7–14.7)	12.85 (11.6–14.3)	12.5 (10.05–13.9)	**0.003**
Lymphocyte count × 109/L	1.27 (0.9–1.95)	1.11 (0.805–1.708)	1.23 (0.75–1.68)	0.14
LDH (U/L)	546 (390–748.3)	607 (474.5–689)	570 (407–741)	0.88
CRP (mg/L)	112 (41–233)	129 (59–173)	67 (22–204)	0.06
D-dimer (mg/L) (RR 0–0.25)	0.72 (0.42–1.88)	0.78 (0.42–1.76)	0.86 (0.48–2.07)	0.78
Ferritin (μg/L) (30–400)	767.5 (309.3–1526)	1097 (386–1998)	808 (481.3–1299)	0.70
Potassium (mmol/L) (RR 3.5–5.1)	4.6 (4.2–5.2)	4.5 (4.1–5.0)	4.3 (3.9–4.7)	**0.009**
HbA1c	7.15 (6.3–10.4)	7.5 (6.1–9.8)	7.0 (6.3–10.0)	0.87
Creatinine (μmol/L), median (IQR)				
Admission creatinine	126 (92.75–157.3)	166 (102.5–222.5)	109 (69–303)	**0.029**
Peak creatinine	137 (115.3–166)	219 (166.5–285.5)	421.5 (282.8–658)	**0.001**
Discharge creatinine	89 (71–118)	102 (77–163)	209 (91.75–413.3)	**0.001**
Dialysis, *n* (%)	0	0	32 (31.7)	**0.001**
Developed worsening AKI in hospital	50 (23.8)	23 (37.8)	65 (63.1)	
Acute Kidney Injury Recovery				0.001
Dialysis, *n* (%)	0	0	32 (31.7)	0.001
Developed worsening AKI in hospital	50 (23.8)	23 (37.8)	65 (63.1)	
Acute Kidney Injury Recovery				0.001
AKI recovery	104 (85)	20 (55.6)	26 (56.5)	
AKI no/incomplete recovery	18 (15)	16 (44.4)	20 (43.5)	
Inotropes	5 (4)	5 (16.13)	29 (41.4)	**0.0001**

(*Continued*)

Table 3: Comparison of patient characteristics in those with acute kidney injury, divided into KDIGO Stages 1–3 (*Continued*)

Patient characteristics	AKI Stage 1	AKI Stage 2	AKI Stage 3	*P*
High dose steroids, *n* (%)	95 (45.23)	22 (36.1)	36 (51.4)	**0.0021**
Intensive care unit (ICU) admission	39 (18.6)	9 (14.75)	43 (41.8)	**0.001**
Respiratory support, *n* (%)				
Invasive mechanical ventilation	22 (10.5)	9 (14.75)	40 (38.8)	**0.001**
High flow nasal cannula	21 (10.2)	2 (3.4)	5 (7.1)	0.23
Outcome measures, *n* (%)				
Death	52 (25.5)	21 (36.2)	49 (48.5)	**0.0003**
Length of stay (days)	8 (5–13)	8 (5–13)	9 (4–14)	0.92

IQR, interquartile range; HbA1c, glycated haemoglobin; SaO_2, oxygen saturation; LDH, lactate dehydrogenase; CRP C-reactive protein.

for 63.1% of the total AKI Stage 3 cohort. This may explain why our AKI Stage 3 patients did not have higher potassium levels. In contrast, Chan et al. reported higher serum potassium levels at admission to be predictive of AKI severity.(13) There was no difference with respect to frequency of diarrhoea between the AKI stages indicating that gastrointestinal loss, a known risk factor for AKI, was not likely a contributing factor to AKI development. AKI Stage 3 was associated with worse COVID-19 disease severity, reflected by the significantly higher numbers of ICU admissions, mechanical ventilation and inotropic support and was associated with higher mortality rates.

There were few patients who had urinalysis. However, in those where it was performed almost all had abnormalities, including proteinuria, haematuria and leukocyturia. Urine abnormalities in COVID-19 are well described. From numerous publications, the commonest findings were proteinuria which ranged between (43.9%–65.8%) and haematuria (26.7%–41.7%).(9,21) Autopsies of patients with COVID-19 with renal dysfunction suggest that ATN is one of the major forms of intra-renal AKI in COVID-19, consistent with the earlier mentioned urinalysis findings.(7) The high reported rate of resolution (68.5%) of proteinuria and haematuria after 3 weeks is keeping with resolving ATN.(21) Patients without AKI have also been documented to have urine abnormalities and it has been postulated that urinalysis may be a potential early identifier of AKI.(22)

AKI associated with COVID-19 has a lower recovery rate compared to other types of AKI, in which most patients attain renal recovery within 10 days.(23) This may be attributed to the extensive tubular injury, microthrombi in renal capillaries and the overall severity of AKI in COVID-19 patients.(7) Renal recovery following COVID-19 is not well documented with renal recovery ranging from 18.2% to 65%.(13,21,24) In our cohort, 150/204 (73.5%) of AKI patients with available discharge creatinine values recovered from poor renal function. However, those patients who developed AKI Stage 3 were significantly less likely to recover ($P < 0.001$). In a country with limited access to chronic dialysis, persistent renal disease following COVID-19 may have deleterious long-term consequences.

LIMITATIONS

There was an inherent limitation with the retrospective study design. This study only included hospitalized patients at two large tertiary referral centres in Cape Town and Johannesburg and thus may have included patients with more severe disease. However, GSH had a testing centre from which patients could be directly admitted to the hospital when required. Numerous patients had missing urinalysis data. Available urine results were likely to have been obtained for a clinical reason and thus likely to represent a bias subset. Patients with CKD Stage 4 or 5 were excluded and therefore baseline CKD status could not fully be assessed as a risk factor. Follow-up data were limited by the patient's length of hospital stay; renal recovery rates may change with an extended follow-up period.

CONCLUSION

This study of 1102 SARS-CoV-2 positive hospitalized patients from 2 tertiary referral centres in SA noted a younger cohort with high rates of AKI (33.9%). Older age, HPT and severe COVID-19 infection were significantly higher in the cohort of patients with AKI. AKI Stage 3 was associated with adverse outcomes, including lack of renal recovery at time of discharge and a higher mortality. This study adds to the paucity of data about COVID-19 associated AKI from the African Continent.

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