

Acute Kidney Injury Incidence, Stage, and Recovery in Patients with COVID-19

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Purpose: To determine the incidence, mortality, stage, and recovery of acute kidney injury (AKI) in COVID-19 patients and further analyze the effect of patient demographics and comorbidities on AKI incidence.

Study Design: Our study looked at 1545 charts of patients over 18 years old who presented to BronxCare Hospital in NY with a positive SARS-CoV-2 PCR test. Using the KDIGO criteria, any patient presenting with a creatinine of 1.5 times the baseline or that had an increase in creatinine of 0.3mg/dL in 48 hours was diagnosed with AKI. Pregnant patients, patients with end-stage renal disease (ESRD), and patients with a history of renal transplant were excluded.

Results: The incidence of AKI in COVID-19 patients was 39% (608), and the mortality rate was 58.2% (354). Of the 254 survivors, 74.8% recovered. Moreover, 42.6% (259) of patients with AKI were admitted to the ICU. Twenty-six of our patients received hemodialysis during admission. There was a statistically significant association between AKI and age, race, hypertension (HTN), diabetes mellitus (DM), hepatitis C (HCV), congestive heart failure (CHF), CKD, patient outcome, and days spent in the hospital. Of the 608 patients with AKI, 294 (48.4%), 185 (30.4%) and 129 (21.2%) had AKI stage 1, 2 and 3, respectively.

Conclusion: Early resource planning is necessary when admitting COVID-19 patients. Nephrology should be consulted early, and measures should be in place to optimize outpatient follow-up in the nephrology clinic. Lastly, the use of nephrotoxic agents should be carefully considered and, if possible, avoided from the time of admission in patients with COVID-19.

Keywords: acute kidney injury, AKI, COVID-19, hemodialysis, chronic kidney disease, CKD

Introduction

According to the CDC, COVID-19 cases have totaled over 70 million in the United States as of January 2022.¹ Many studies have described pulmonary and extrapulmonary presentations of COVID-19 including but not limited to vasculitis in several organ systems. Although a renal phenotype has not yet been clearly defined, hematuria, proteinuria, and elevated creatinine levels have been reported in several studies.^{2,3} Several articles have been published worldwide and the incidence of AKI varies greatly. A meta-analysis on 20 articles published in June 2020 shows the incidence of AKI was approximately 9% in COVID-19 patients.⁴ However, in an article published in January 2021, analyzing over 3000 patients across New York City, AKI was found to be present in 46% of the patients.⁵ In our study, we look at AKI throughout the first year of the pandemic on our local and underserved patient population in the Bronx, New York.

AKI is defined by a change in either serum creatinine, by 0.3mg/dL or more within 48 hours, an increase in serum creatinine 1.5 times more than the baseline within the last 7 days, or urine output less than 0.5mL/kg/hr for 6 hours.⁶ Clinically, we often look at urine output for diagnosis, as this does not require any prior patient data.

AKI can be isolated or superimposed on chronic renal disease. Risk factors for AKI include age above 65 and the presence of specific comorbidities such as hypertension, heart disease, liver disease, chronic kidney disease (CKD), peripheral artery disease, and diabetes.⁷ The causes of AKI can be distributed into pre-renal, renal, and post-renal causes. Different serum blood urea nitrogen to serum creatinine ratios can help localize the patient's AKI etiology.

To assess the severity of AKI, one must determine the ratio of creatinine to the baseline creatinine or the stage of AKI. If the creatinine at the time of AKI is 1.5 to 1.9 times the baseline, it is AKI Stage 1. If the creatinine is 2–2.9 times

the baseline, it is AKI stage 2, and if the creatinine is above 2.9 times the baseline, it is AKI Stage 3. The stage of AKI is essential as it affects the treatment plan and prognosis of a patient. High-risk patients and stage 1 patients are treated preventatively by ensuring proper volume status, avoiding hyperglycemia and nephrotoxic agents, and monitoring creatinine and urine output. Stage 2 and 3 patients, however, require more aggressive measures. ICU admission and renal replacement therapy may be necessary.⁸ Although the underlying pathogenesis of AKI in patients with COVID-19 remains a subject of debate, associated comorbidities, medications, and viral insult to kidney cells are all possible causes.

Method

In our study, we retrospectively analyzed 1546 patient charts above 18 who were admitted to BronxCare hospital and tested positive for COVID-19 through a SARS-CoV-2 PCR test from March 2020 through December 2020. Pregnant patients, patients with end-stage renal disease on dialysis, and patients with a history of renal transplant were excluded. We then applied the KDIGO AKI criteria described in the introduction to the remaining patients to determine which patients had AKI and what stage of AKI they had. The baseline creatinine used was the most recent creatinine level recorded between 7 and 365 days prior to admission. If no such number was present in the patient's medical records, we calculated a standardized baseline using a GFR of 75 mL/min/1.37m² through the MDRD equation (see below).

MDRD Equation:⁹

$$GFR\left(\frac{ml}{min/1.37m^2}\right) = 186 \times S.Cr^{-1.154} \times age^{-0.203} \times GenderCoefficient \times RaceCoefficient$$

The gender coefficient is 1 for males, 0.742 for females.

The race coefficient was 1.21 for African-Americans and 1 for any other race.

Reversed MDRD Equation

$$S.Cr = \left[\frac{GFR(ml/min/1.37m^2)}{186 \times age^{-0.203} \times GenderCoefficient \times RaceCoefficient} \right]^{(-1/1.154)}$$

We further stratified our data to analyze the incidence, stage, and outcome of these AKI patients based on their demographics, comorbidities, and whether or not they were admitted into the ICU.

We calculated frequency and percentages for all qualitative variables. We used the Mann–Whitney *U*-test for continuous variables and the chi-squared test for nominal variables. A p-value less than 0.05 was considered significant. Univariate logistic regression models adjusted for covariates (age; sex; race; comorbidities including human immunodeficiency virus (HIV), hypertension, diabetes, obstructive airway disease, hepatitis B, hepatitis C, congestive heart failure, coronary artery disease and CKD) were used to estimate the adjusted odds ratio (AOR) for deaths in patients with AKI versus without AKI. The data obtained was analyzed on IBM's statistical package for the social sciences (SPSS) version 21.

Results

Our study analyzed 1545 patient charts of patients admitted to BronxCare hospital from March 2020 through December 2020 with a positive SARS-CoV-2 PCR test. Five of those patients were readmitted after their initial discharge with a positive SARS-CoV-2 PCR test. These charts were counted individually in our statistics. In total, 401 charts had a baseline creatinine from 7 to 365 days prior to admission. For all other patients, we used the MDRD equation to calculate baseline creatinine.

The results of our study analysis show that 608 patients (39.3%) developed AKI either on admission or during their admission. Of these patients, 137 had underlying chronic renal disease (CKD). A total of 354 patients (58% of the patients with AKI) expired during their admission, and 190 patients (31% of the patients with AKI) fully recovered from AKI at the time of discharge. The remaining patients were discharged with AKI, primarily stage 1, as determined by the KDIGO criteria. Of our 608 AKI patients, 259 spent time in the ICU.

Table 1 Patient Demographics, Comorbidities, and Outcome

	All (n =1545)	AKI (n=608)	No AKI (n=937)	p Value
Age (Avg ± SD)	62.63 ± 15.72	68.48 ± 13.04	58.82 ± 16.14	<0.001
BMI (Avg ± SD)	30.11 ± 7.84	29.95 ± 7.83	30.22 ± 7.85	0.304
Sex, n (%)				
Women	627 (40.6)	229 (36.5)	398 (63.5)	0.060
Men	918 (59.4)	379 (41.3)	539 (58.7)	
Race/ethnicity, n (%)				
Asian	6 (0.4)	0	6(0.6)	<0.001
Black	407 (26.3)	194 (31.9)	213 (22.7)	
Caucasian	27 (1.7)	10 (1.6)	17 (1.8)	
Hispanic	968 (62.7)	353 (58.1)	615 (65.6)	
Other or unknown	137 (8.9)	51 (8.4)	86 (9.2)	
Comorbidities, n (%)				
HIV	89 (5.8)	40 (6.6)	49 (5.2)	0.266
HTN	979 (63.4)	457 (75.2)	522 (55.7)	<0.001
DM	732 (47.4)	342 (56.3)	390 (41.6)	<0.001
OAD	292 (18.9)	119 (19.6)	173 (18.5)	0.586
HBV	46 (3.0)	18 (3.0)	28 (3.0)	0.975
HCV	64 (4.1)	32 (5.3)	32 (3.4)	0.075
CHF	167 (10.8)	86 (14.1)	81 (8.6)	0.001
CAD	179 (11.6)	93 (15.3)	86 (9.2)	<0.001
CKD	198 (12.8%)	137 (22.5)	61 (6.5)	<0.001
Outcome, n (%)				
Discharged	1103 (71.4)	254 (41.8)	849 (90.6)	<0.001
Expired	442 (28.6)	354 (58.2)	88 (9.4)	
Day in the hospital (Avg ± SD)	9.56 ± 8.72	11.48 ± 10.42	8.31 ± 7.15	<0.001

Abbreviations: Avg, average; SD, standard deviation; HTN, hypertension; DM, diabetes mellitus; OAD, obstructive airway disease; HBV, hepatitis B virus; HCV, hepatitis C virus; CHF, congestive heart failure; CAD, coronary artery disease; CKD, chronic kidney disease.

Patient Demographics and Comorbidities

The majority of the patients in our study were either Hispanic (62.7%) or black (26.3%). About 47.6% of the black patients developed AKI, while only 36.4% of the Hispanic patients developed AKI. Out of the 608 patients with AKI 75.2% of the patients had hypertension and 56.3% of the patients had diabetes mellitus. Patient demographics, comorbidities, clinical outcomes, and the number of days spent in the hospital are presented in [Table 1](#).

Our results show that there was a statistically significant association between AKI and age, race, hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD) congestive heart failure (CHF), CKD, patient outcome, and days spent in the hospital.

AKI Stages and ICU Admissions

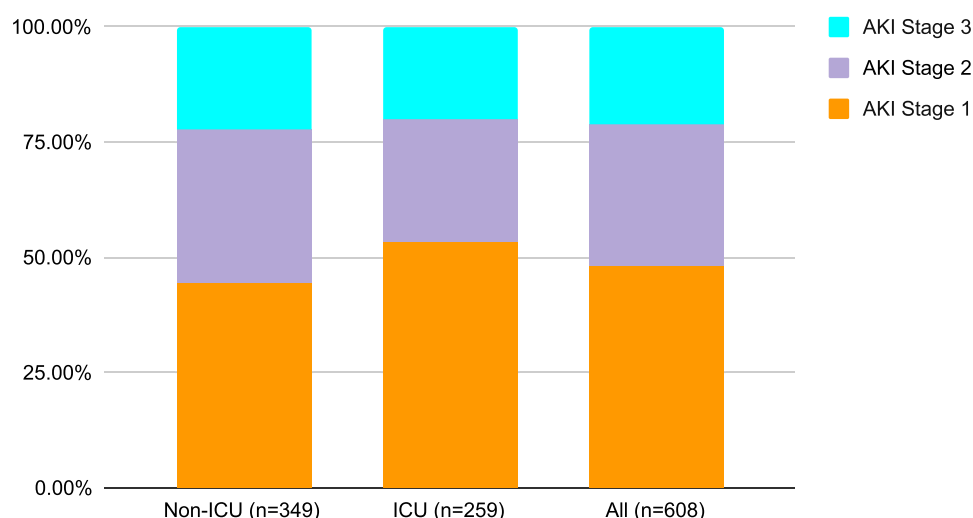


Figure 1 Acute kidney injury (AKI) stages and intensive care unit (ICU) admission.

Abbreviation: n, number of patients.

ICU and AKI Stages

We further compartmentalized our data looking at how many of our COVID-19 patients with AKI were admitted into the intensive care unit (ICU). Moreover, 42.6% (259) of patients with AKI were admitted to the ICU. The mean duration of stay in ICU for patients admitted with AKI was 6.17 ± 5.46 . There was no significant and clinical difference between the stage of AKI and length of ICU stay. Of the 608 patients with AKI, 294 (48.4%), 185 (30.4%) and 129 (21.2%) had stage 1, 2 and 3, respectively. This is presented in Figure 1.

Table 2 Patient Demographics and Characteristics for AKI Patients with and without Prior CKD History

	AKI without CKD (n= 471)	AKI with CKD (n= 137)	p Value
Age (Avg ± SD)	67.52 ± 13.3	71.76 ± 11.5	0.001
Sex (Avg ± SD)			
Male	285	94	0.085
Female	186	43	
BMI (Avg ± SD)	29.91 ± 7.9	30.10 ± 7.7	0.565
Days in hospital (Avg ± SD)	11.78 ± 10.7	10.48 ± 11.5	0.12
HD performed during admission			
Yes	20	6	0.946
No	451	131	
Patient outcome			
Discharged	182	72	< 0.001
Expired	289	65	

Abbreviations: Avg, average; SD, standard deviation; HD, hemodialysis.

Table 3 Patient Characteristics Associated with Mortality After Adjustment for Age, Sex, Comorbidities, AKI Stage, ICU Admission, and Number of Days Spent in Hospital

	Adjusted Odds Ratio	Lower 95% CI	Upper 95% CI
Age	0.974	0.959	0.989
Male	1.606	1.114	2.317
HIV	2.948	1.274	6.819
HTN	0.967	0.619	1.51
DM	0.718	0.499	1.035
OAD	1.613	1.004	2.593
HBV	0.357	0.118	1.081
HCV	0.754	0.329	1.728
CHF	0.897	0.52	1.548
CAD	1.125	0.666	1.9
CKD	0.501	0.324	0.774
AKI Stage I	0.743	0.593	0.932
ICU Admission	2.879	1.925	4.304
Days in Hospital	1.040	1.021	1.059

Abbreviations: HTN, hypertension; DM, diabetes mellitus; OAD, obstructive airway Disease; HBV, hepatitis B virus; HCV, hepatitis C virus; CHF, congestive heart failure; CAD, coronary artery disease; CKD, chronic kidney disease.

AKI vs AKI on CKD

In this branch of our study, we noted patients with a history of CKD and looked at factors such as age, sex, BMI, days spent in the hospital, hemodialysis, and patient outcome.

AKI Survivors at Discharge (n=254)

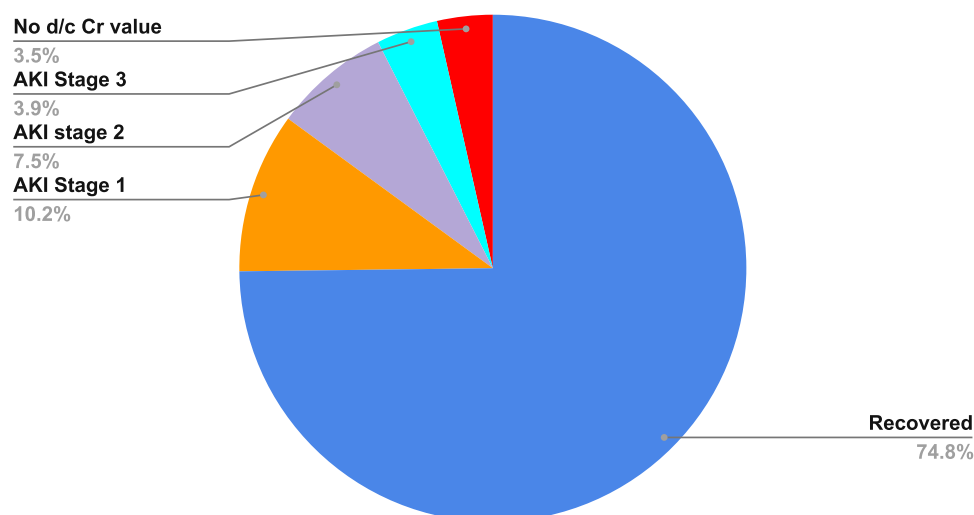


Figure 2 AKI survivors at discharge (n=254).

Abbreviations: n, number of patients; D/c, discharge; Cr, creatinine.

We found that out of the 608 patients with AKI, 471 had no prior history of CKD. Twenty-six patients required hemodialysis (HD) during the hospitalization, four of them expired.

The mortality rate was 58.2% (354). Of those with acute on chronic kidney injury, 47.4% expired, while 61.36% of AKI patients without prior CKD expired. Results comparing AKI and AKI on CKD can be seen in [Table 2](#).

AKI and Mortality Rates

Approximately 58.2% of AKI patients expired. We adjusted specific demographics and comorbidities associated with mortality in [Table 3](#). Male gender, history of HIV, history of OAD and ICU admissions were significantly associated with mortality.

The adjusted odds ratio for death was 13.0 (95% CI, 7.2 to 18) for all patients with AKI versus no AKI. Of the 254 patients who survived, 74.8% of the patients had a complete recovery. Seventy-two of the discharged patients had CKD at baseline and the majority (63.8%) made a complete recovery. We stratified the remaining patients by AKI stage at discharge based on the ratio of baseline creatinine to discharge creatinine. Nine of our patients did not have a discharge creatinine value within 48 hours of discharge. Results are in [Figure 2](#).

Discussion

In approximately 1500 patients admitted to BronxCare Hospital with COVID-19, 39% developed AKI, and 58.2% of those patients expired during their time in the hospital. Of the patients who survived, the majority made a full recovery, determined by creatinine levels returning to baseline. Moreover, 42.6% of AKI patients were admitted to the ICU. The rate of AKI in our patient population was significantly higher than that reported in studies across the globe.⁴ However, when looking at the results of other studies performed locally, we find that our numbers are comparable. This could be due to the high prevalence of AKI risk factors in our patient population, such as age, race, hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), congestive heart failure (CHF) and CKD which all showed a statistically significant association in our results.

The incidence of AKI in COVID-19 is higher than in the most recent respiratory pandemic: influenza A H1N1 in 2009. According to a meta-analysis performed on 20 studies and looking at over 3000 patients with H1N1 who developed AKI, 33% of the patients admitted with H1N1 developed AKI. The study demonstrated results comparable with ours, showing an association with specific comorbidities such as obesity and diabetes.¹⁰ Furthermore, the histology assessment of the kidneys of H1N1-infected patients also demonstrated acute tubular necrosis (ATN), DIC, and myoglobin pigments,¹¹ showing that tubular necrosis may be the common mechanism of renal injury of patients infected with these respiratory illnesses.

The pathogenesis of AKI in COVID-19 is multifactorial. The most common cause of acute kidney injury in COVID-19 patients was acute tubular injury that resulted from.¹² Direct viral infection and replication in podocytes and tubules of kidney cells was shown to cause tubular injury. Prominent acute proximal tubular necrosis was observed by light microscopy, with loss of brush border, non-isometric vacuolar degeneration and even frank necrosis.¹³ Subsequently, endothelial injury, microvascular thrombi, local inflammation and immune cell infiltration have been repeatedly observed in patients with COVID-19 AKI.¹⁴ The overloaded immune response and cytokine storm cause acute tubular necrosis and endothelial injury that may result in a thrombus.¹³ This in conjunction with observed erythrocyte aggregates obstructing the lumen of capillaries indicates that abnormal coagulation may also participate in the pathogenesis of AKI in COVID-19.¹³ Multiple indirect causes or insulting events also play a role in contributing to AKI in COVID-19 patients, such as medications, hemodynamic instability, hypoxia, acute respiratory distress syndrome, rhabdomyolysis, excessive diuresis, and secondary infections.¹⁵

Our study has a few limitations, the first being that more than half of the charts we analyzed did not have a baseline creatinine value. We therefore resorted to the MDRD equation to calculate one and determine whether or not the patient had AKI. Additionally, certain discharged patients were excluded from the final numbers tracking recovery status due to a lack of creatinine values for comparison. Lastly, if a patient did not have AKI upon admission, in that case, it is impossible to ascertain whether the renal injury was caused by COVID-19, the multitude of medications they received during admission or/and any acute events they may have suffered from while in the hospital. However, it can be assumed that many patients worldwide have received similar antiviral and antibiotic treatments.

Conclusion

The results of our study incite us to believe that there may be a correlation between COVID-19 and the development of AKI. Preventative measures should be considered for patients admitted with COVID-19. As the long-term effects on the kidneys are unknown, resource planning and strategies to improve the long-term understanding and kidney care are necessary. Nephrologists should be consulted early and nephrotoxic agents should be avoided. Finally, discharge planning with a follow-up nephrology appointment should be considered to mitigate the onset of AKI.

Ethics Statement

The BronxCare Health System Institutional Review Board (IRB) reviewed and approved our study. A waiver of the HIPAA authorization was granted by the IRB as this is a minimal risk retrospective chart study. Therefore, informed consent was not required. The guidelines noted in the Declaration of Helsinki were followed.

Disclosure

The authors report no conflicts of interest in this work.

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