Acute kidney injury in patients hospitalized with COVID-19

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The rate of acute kidney injury (AKI) associated with patients hospitalized with Covid-19, and associated outcomes are not well understood. This study describes the presentation, risk factors and outcomes of AKI in patients hospitalized with Covid-19. We reviewed the health records for all patients hospitalized with Covid-19 between March 1, and April 5, 2020, at 13 academic and community hospitals in metropolitan New York. Patients younger than 18 years of age, with end stage kidney disease or with a kidney transplant were excluded. AKI was defined according to KDIGO criteria. Of 5,449 patients admitted with Covid-19, AKI developed in 1,993 (36.6%). The peak stages of AKI were stage 1 in 46.5%, stage 2 in 22.4% and stage 3 in 31.1%. Of these, 14.3% required renal replacement therapy (RRT). AKI was primarily seen in Covid-19 patients with respiratory failure, with 89.7% of patients on mechanical ventilation developing AKI compared to 21.7% of non-ventilated patients. 276/285 (96.8%) of patients requiring RRT were on ventilators. Of patients who required ventilation and developed AKI, 52.2% had the onset of AKI within 24 hours of intubation. Risk factors for AKI included older age, diabetes mellitus, cardiovascular disease, black race, hypertension and need for ventilation and vasopressor medications. Among patients with AKI, 694 died (35%), 519 (26%) were discharged and 780 (39%) were still hospitalized. AKI occurs frequently among patients with Covid-19 disease. It occurs early and in temporal association with respiratory failure and is associated with a poor prognosis.

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Since late 2019, when the severe acute respiratory coronavirus 2, and the resulting illness, acute respiratory syndrome with coronavirus 2 (coronavirus disease 2019 [COVID-19]), developed in Wuhan, China,[1] COVID-19 has become a worldwide pandemic, with 2.3 million cases reported as of April 19, 2020.[2] In late January 2020, the United States had its first COVID-19 case in Washington state,[3] followed by massive growth of infections in New York, the current epicenter.[2,4] As had been observed in China and Italy, the disease resulted in a large number of hospitalizations, respiratory failure, and intensive care unit (ICU) admissions.[5,6] The New York metropolitan area began to see a rapid increase in COVID-19 cases in February 2020. Our health system, with 23 hospitals in counties in and around New York City, rapidly experienced a surge in COVID-19 hospitalizations, with over 9000 at the time of this writing. As we cared for patients with COVID-19, we noticed an alarming number of patients who developed acute kidney injury (AKI), at rates higher than had been reported from China.

Early reports from China and Italy found the rate of AKI to range widely from 0.5% to 29%, with most estimates on the lower end.[7–15] U.S. data has been limited to critically ill patients in the ICU in a Seattle hospital showing a 19% rate of AKI.[16] Differences may have resulted from definitions of AKI and the populations studied. Little to date has been published on AKI in COVID-19 beyond rate; for example, wider descriptions of the timing, urine studies, relationship to respiratory failure, detailed analysis of renal replacement therapy (RRT) requirements, risk factors, and outcomes post-AKI are lacking.

Northwell Health is uniquely situated to study COVID-19 based on its location in metropolitan New York and because it has 23 hospitals, with a combination of urban and suburban areas and academic tertiary and community hospitals. In this study, we sought to define the rate of AKI among patients hospitalized with COVID-19 and to describe various aspects of the phenomenology of AKI in this patient population.

RESULTS

From March 1, 2020, to April 5, 2020, 6477 patients were admitted to 13 Northwell Health hospitals with a diagnosis of COVID-19 present on admission or made during the hospitalization. Of these, 5449 were used as the analysis cohort

(Figure 1). The baseline characteristics of patients at hospital admission are provided in Table 1. A total of 1190 patients (21.8%) were treated with mechanical ventilation at some point during the hospitalization. Among the 5449 patients, 888 (16.3%) died, 3280 (60.2%) were discharged to home or to a rehabilitation facility, and 1281 (23.5%) were still in treatment.

Overall, 1993 of 5449 patients (36.6%) developed AKI during their hospitalization. The peak stages of AKI were stage 1 in 46.5%, stage 2 in 22.4%, and stage 3 in 31.1% (Table 2). The baseline laboratory data of patients are shown in Supplementary Table S1. The timing of initial development of AKI with respect to hospital admission is displayed in Figure 2. Most cases developed early in the course, with 37.3% either arriving with AKI or developing it within 24 hours of admission. The number of patients requiring dialytic support at some point was 285 (overall 5.2% of all patients, representing 14.3% of those with AKI). The modality utilized was intermittent hemodialysis only in 154 patients (54% of all patients requiring RRT), continuous RRT only in 70 (24.6%) and requirement of both treatments at some point in 61 (21.4%). The median time of initiation of dialytic support from hospital admission was 2.0 (interquartile range [IQR]: −1.63, 141) hours. The median number of hours from AKI diagnosis to initiation of dialysis was 0.0 (IQR: 0.0, 79.6).

The relationship between respiratory failure and development of AKI was substantial and is displayed in Table 3. Among patients who required mechanical ventilation, 1068 of 1190 (89.7%) developed AKI compared with 925 of 4259 (21.7%) in nonventilated patients. The majority of severe (stage 3) AKI (518 of 619 [83.6%]) and most patients requiring dialytic support (276 of 285 [96.8%]) occurred in patients on mechanical ventilation. RRT was required in 9 of 4259 nonventilated patients (0.2%) compared with 276 of 1190 patients on ventilators (23.2%).

There was a substantial clustering of AKI events at the time of intubation and initiation of mechanical ventilation (Figure 3). Of patients who required ventilation and developed AKI, 52.2% had the onset of AKI within 24 hours of intubation. The median time from mechanical ventilation to initiation of dialytic therapy was 0.3 (IQR: −41.1, 92.3) hours.

Urine studies were available within 24 hours before or 48 hours after the development of AKI in up to 646 of 1993 patients with AKI (Table 4). The median urine-specific gravity was 1.020 (IQR: 1.010, 1.020). By urine dipstick, 36.2% had no heme and 46.1% had 2+ to 3+ positivity. Urine protein was negative in 26.0%, but 2+ to 3+ positive in 42.1%. Automated microscopy detected significant leukocyturia or hematuria in 36.5% and 40.9%, respectively. The urine sodium concentration was <35 mEq/l in 65.6% of patients.

We studied various baseline characteristics as potential predictors of AKI in COVID-19 (Table 5). By univariate analysis, increased age, male sex, diabetes mellitus, hypertension, history of cardiovascular disease, increased body
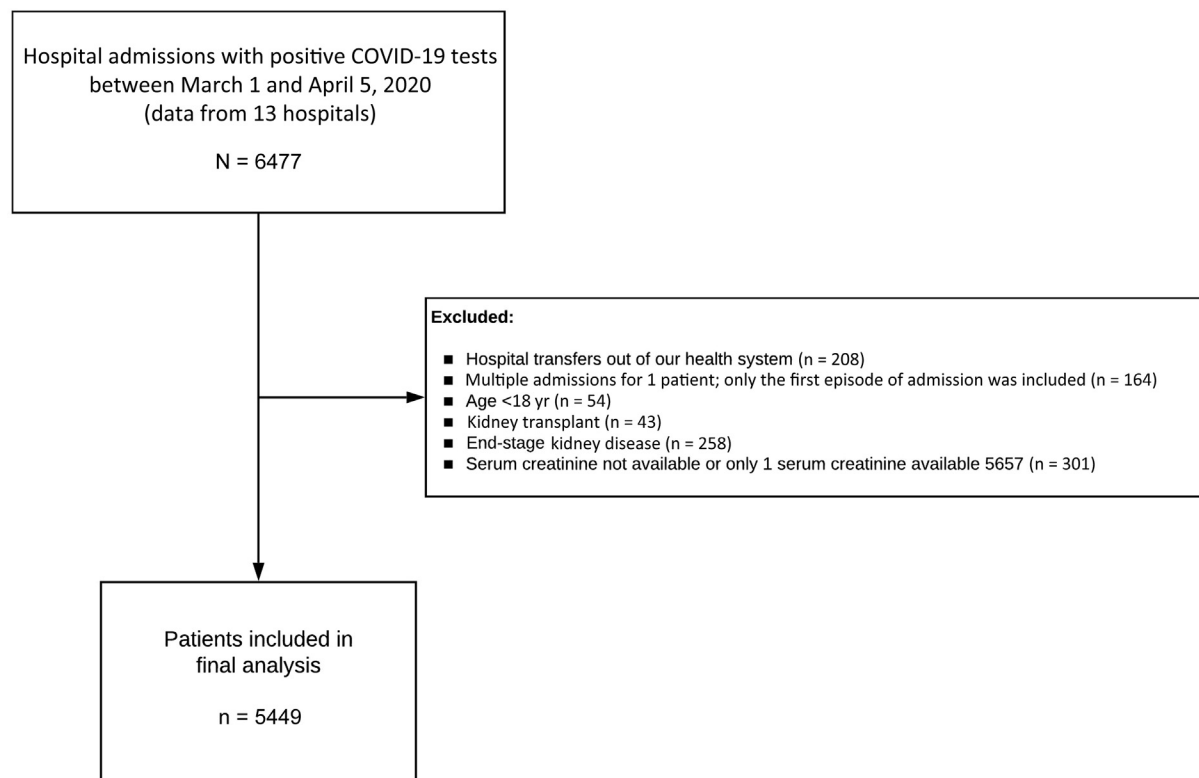

Figure 1 | Flowchart of the study. COVID-19, coronavirus disease 2019.

Table 1 | Clinical characteristics of the study cohort

Variables	Overall (n = 5449)
Age (yr)	64.0 (52.0, 75.0)
Male	3317 (60.9)
Race	
Asian	466 (8.6)
Black	1123 (20.6)
White	2112 (38.8)
Declined	32 (0.6)
Other/multiracial	1494 (27.4)
Other/unknown	222 (4.1)
Ethnicity	
Hispanic/Latino	1145 (21.0)
Not Hispanic/Latino	3953 (72.5)
Other/unknown	351 (6.4)
Language	
English	4433 (81.4)
Spanish	640 (11.7)
Other	376 (6.9)
Insurance status	
Commercial	1856 (34.1)
Medicaid	1141 (20.9)
Medicare	2292 (42.1)
Self-pay	114 (2.1)
Other	46 (0.8)
Hospital type	
Tertiary	3765 (69.1)
Community	1684 (30.9)
Comorbid conditions[a]	
HTN	3037 (55.7)
CAD	600 (11.0)
HF	349 (6.4)
PVD	98 (1.8)
Diabetes	1797 (33.0)
HIV	35 (0.6)
Chronic liver disease	114 (2.1)
COPD	296 (5.4)
Asthma	460 (8.4)
OSA	164 (3.0)
Cancer	327 (6.0)
Obesity	1475 (27.1)
Morbid obesity	456 (8.4)
BMI (kg/m^2)	28.6 (25.4, 33.1)
Admission SCr (mg/dl)	1.01 (0.80, 1.34)
Medications	
No. of medications	4 (1, 8)
ACE-I	654 (13.3)
ARB	902 (18.3)
ICU	1395 (25.6)
Mechanical ventilator	1190 (21.8)
ECMO	10 (0.2)
Inotropes[b]	54 (1.0)
Vasopressor[c]	1168 (21.4)
CCI	4 (2, 6)
Length of stay (d)	
Discharged/expired	5.7 (3.3, 8.7)
Currently hospitalized	12.0 (9.3, 16.0)

Table 1 | (Continued)

Variables	Overall (n = 5449)
Disposition	
Discharged	3280 (60.2)
Expired	888 (16.3)
Currently admitted	1281 (23.5)

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCI, Charleson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; HF, heart failure; HTN, hypertension; ICU, intensive care unit; OSA, obstructive sleep apnea; PVD, peripheral vascular disease; SCr, serum creatinine.

[a]Chronic kidney disease was not included as a comorbid condition because pre-hospitalization estimated glomerular filtration rate was available only in 15% of patients.
[b]Inotropes include dobutamine and milrinone.
[c]Vasopressors include norepinephrine, epinephrine, vasopressin, dopamine, and angiotensin-2 infusion.
Values are median (interquartile range) or n (%).

and use of vasopressor medications. In this analysis, renal-angiotensin-aldosterone–inhibiting drugs were no longer an AKI predictor. As BMI data were missing in 1138 of 4211 patients (27%), we compared 2 multivariate logistic regression models, one including BMI and the other excluding BMI (Supplementary Table S2), with no appreciable change in the risk factors for AKI observed.

Among 1993 patients who developed AKI during the hospitalization, a total of 780 (39%) were still hospitalized, 519 patients (26%) were discharged and 694 (35%) died. Of those who died, 34% had stage 1, 64% stage 2, and 91% stage 3 (Figure 4). Among the 285 patients who required RRT, 157 died and 9 were discharged from the hospital. Another 119 were still undergoing treatment in the hospital, with 108 still on RRT (90.8%). For patients who developed AKI and survived to hospital discharge, the median peak serum creatinine was 2.34 (IQR: 1.42, 4.25) mg/dl with median at hospital discharge of 1.70 (IQR: 0.96, 3.58).

DISCUSSION

Infection with COVID-19 is primarily a respiratory illness, but other organs including the kidneys are often affected.[9] We found that in a large cohort of hospitalized patients at both tertiary care and community hospitals the rates of AKI were higher than were reported previously in the literature.

The important relationship between AKI and respiratory failure is indicated by the following findings. First, severe AKI occurred most commonly in close temporal proximity to the time of intubation and mechanical ventilation. Second, the rate of AKI was 89.7% among patients on ventilators compared with 21.7% among other patients. Third, severe (stages 2 and 3) AKI occurred in 65.5% of patients on ventilators compared with 6.7% of nonventilated patients. Finally, almost all of the patients requiring RRT were on ventilator support (276 of 285 [96.8%]). Taken together, these data strongly suggest that AKI, particularly when severe, is a condition that occurs among patients with COVID-19 who also have respiratory failure.

mass index (BMI), mechanical ventilation, vasopressor medications, and a history of treatment with renal-angiotensin-aldosterone–inhibiting medications were predictors of AKI. Treatment in a tertiary care hospital was associated with marginally reduced risk. Independent predictors, by multivariate analysis included older age, black race, diabetes, hypertension, cardiovascular disease, mechanical ventilation,

Table 2 | Baseline characteristics of study cohort, by AKI status

Variables	No AKI (n = 3456)	AKI (n = 1993)	Stages of AKI 1 (n = 927)	2 (n = 447)	3 (n = 619)	P value[a] (no AKI vs. all AKI)	P value[b] (trend)
Age (yr)	61.0 (50.0, 72.0)	69.0 (58.0, 78.0)	69.0 (58.0, 79.0)	71.0 (58.5, 79.0)	67.0 (58.0, 76.0)	<0.001	<0.001
Male	2047 (59.2)	1270 (63.7)	556 (60.0)	266 (59.5)	448 (72.4)	0.001	<0.001
Race						0.04	0.04
Asian	304 (8.8)	162 (8.1)	72 (7.8)	35 (7.8)	55 (8.9)		
Black	708 (20.5)	415 (20.8)	190 (20.5)	106 (23.7)	119 (19.2)		
White	1294 (37.4)	818 (41.0)	393 (42.4)	191 (42.7)	234 (37.8)		
Other/multiracial	988 (28.6)	506 (25.4)	232 (25.0)	92 (20.6)	182 (29.4)		
Other/unknown	138 (4.0)	84 (4.2)	38 (4.1)	21 (4.7)	25 (4.0)		
Declined	24 (0.7)	8 (0.4)	2 (0.2)	2 (0.4)	4 (0.6)		
Ethnicity						0.03	0.03
Hispanic/Latino	765 (22.1)	380 (19.1)	159 (17.2)	85 (19.0)	136 (22.0)		
Not Hispanic/Latino	2474 (71.6)	1479 (74.2)	711 (76.7)	330 (73.8)	438 (70.8)		
Other/unknown	217 (6.3)	134 (6.7)	57 (6.1)	32 (7.2)	45 (7.3)		
Language						0.52	0.12
English	2825 (81.7)	1608 (80.7)	764 (82.4)	353 (79.0)	491 (79.3)		
Spanish	402 (11.6)	238 (11.9)	96 (10.4)	53 (11.9)	89 (14.4)		
Other	229 (6.6)	147 (7.4)	67 (7.2)	41 (9.2)	39 (6.3)		
Insurance status						<0.001	<0.001
Commercial	1329 (38.5)	527 (26.4)	247 (26.6)	98 (21.9)	182 (29.4)		
Medicaid	792 (22.9)	349 (17.5)	159 (17.2)	78 (17.4)	112 (18.1)		
Medicare	1238 (35.8)	1054 (52.9)	495 (53.4)	260 (58.2)	299 (48.3)		
Self-pay	67 (1.9)	47 (2.4)	19 (2.0)	8 (1.8)	20 (3.2)		
Other	30 (0.9)	16 (0.8)	7 (0.8)	3 (0.7)	6 (1.0)		
Hospital type						0.06	0.04
Tertiary	2420 (70.0)	1345 (67.5)	635 (68.5)	312 (69.8)	398 (64.3)		
Community	1036 (30.0)	648 (32.5)	292 (31.5)	135 (30.2)	221 (35.7)		
Comorbid conditions[c]							
HTN	1745 (50.5)	1292 (64.8)	624 (67.3)	287 (64.2)	381 (61.6)	<0.001	<0.001
CAD	311 (9.0)	289 (14.5)	136 (14.7)	72 (16.1)	81 (13.1)	<0.001	<0.001
HF	141 (4.1)	208 (10.4)	112 (12.1)	47 (10.5)	49 (7.9)	<0.001	<0.001
PVD	37 (1.1)	61 (3.1)	22 (2.4)	18 (4.0)	21 (3.4)	<0.001	<0.001
Diabetes	967 (28.0)	830 (41.6)	368 (39.7)	193 (43.2)	269 (43.5)	<0.001	<0.001
HIV	25 (0.7)	10 (0.5)	5 (0.5)	4 (0.9)	1 (0.2)	0.42	0.36
Chronic liver disease	72 (2.1)	42 (2.1)	27 (2.9)	8 (1.8)	7 (1.1)	1.00	0.11
COPD	149 (4.3)	147 (7.4)	74 (8.0)	36 (8.1)	37 (6.0)	<0.001	<0.001
Asthma	317 (9.2)	143 (7.2)	74 (8.0)	35 (7.8)	34 (5.5)	0.012	0.02
OSA	99 (2.9)	65 (3.3)	27 (2.9)	20 (4.5)	18 (2.9)	0.46	0.31
Cancer	194 (5.6)	133 (6.7)	65 (7.0)	25 (5.6)	43 (6.9)	0.13	0.30
Obesity	916 (26.5)	559 (28.0)	244 (26.3)	132 (29.5)	183 (29.6)	0.23	0.25
Morbid obesity	276 (8.0)	180 (9.0)	81 (8.7)	42 (9.4)	57 (9.2)	0.20	0.57
BMI (kg/m^2)	28.4 (25.3, 32.8)	29.0 (25.4, 33.5)	28.7 (25.5, 33.2)	28.7 (24.7, 33.6)	29.5 (25.9, 34.0)	0.09	0.04
Kidney function							
Admission SCr (mg/dl)	0.95 (0.77, 1.16)	1.24 (0.91, 1.82)	1.26 (0.91, 1.83)	1.30 (0.95, 1.86)	1.19 (0.90, 1.79)	<0.001	<0.001
Discharge SCr (mg/dl)	0.80 (0.66, 0.98)	1.42 (0.84, 3.16)	1.02 (0.72, 1.57)	1.38 (0.80, 2.26)	4.00 (2.21, 6.12)	<0.001	<0.001
Peak SCr (mg/dl)	0.98 (0.80, 1.20)	2.23 (1.40, 4.12)	1.50 (1.10, 2.16)	2.13 (1.59, 2.91)	5.20 (3.40, 7.24)	<0.001	<0.001
Median SCr (mg/dl)	0.86 (0.70, 1.03)	1.20 (0.82, 2.00)	1.04 (0.75, 1.53)	1.10 (0.80, 1.53)	2.05 (1.11, 3.55)	<0.001	<0.001
Admission eGFR (ml/min/1.73 m^2)	82.5 (62.0, 98.0)	56.0 (34.0, 80.0)	54.0 (33.0, 81.0)	53.0 (32.0, 79.0)	62.0 (37.0, 81.0)	<0.001	<0.001
Discharge eGFR (ml/min/1.73 m^2)	94.0 (77.0, 107.0)	45.0 (17.0, 86.0)	69.0 (39.0, 97.0)	50.0 (27.0, 89.0)	14.0 (8.0, 27.0)	<0.001	<0.001
Medications							
No. of medications	3 (1, 7)	6 (2, 10)	6 (2, 10)	6 (2, 10)	5 (1, 9)	<0.001	<0.001
ACE-I	385 (11.9)	269 (15.9)	119 (14.4)	51 (13.4)	99 (20.2)	<0.001	<0.001
ARB	516 (16.0)	386 (22.8)	184 (22.3)	84 (22.1)	118 (24.0)	<0.001	<0.001
ICU	335 (9.7)	1060 (53.2)	320 (34.5)	244 (54.6)	496 (80.1)	<0.001	<0.001
Mechanical ventilator	122 (3.5)	1068 (53.6)	288 (31.1)	262 (58.6)	518 (83.7)	<0.001	<0.001
ECMO	0 (0.0)	10 (0.5)	3 (0.3)	5 (1.1)	2 (0.3)	<0.001	<0.001
Inotropes[d]	3 (0.1)	51 (2.6)	10 (1.1)	12 (2.7)	29 (4.7)	<0.001	<0.001
Vasopressor[e]	119 (3.4)	1049 (52.6)	278 (30.0)	252 (56.4)	519 (83.8)	<0.001	<0.001
CCI	3.0 (1.0, 5.0)	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	5.0 (3.0, 7.5)	4.0 (3.0, 6.0)	<0.001	<0.001
Length of stay (d)							
Discharged/ expired	4.9 (3.0, 7.6)	7.8 (5.0, 11.6)	7.4 (4.8, 10.9)	7.2 (4.2, 12.1)	8.6 (5.8, 12.3)	<0.001	<0.001
Currently hospitalized	10.3 (8.5, 13.0)	13.2 (10.2, 17.3)	12.2 (9.4, 16.2)	14.0 (11.0, 18.1)	14.0 (11.0, 18.23)	<0.001	<0.001

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Table 2 | (Continued) **Baseline characteristics of study cohort, by AKI status**

Variables	No AKI (n = 3456)	AKI (n = 1993)	Stages of AKI			P value[a] (no AKI vs. all AKI)	P value[b] (trend)
			1 (n = 927)	2 (n = 447)	3 (n = 619)		
Disposition						<0.001	<0.001
Discharged	2761 (79.9)	519 (26.0)	397 (42.8)	87 (19.5)	35 (5.7)		
Expired	194 (5.6)	694 (34.8)	208 (22.4)	152 (34.0)	334 (54.0)		
Currently hospitalized	501 (14.5)	780 (39.1)	322 (34.7)	208 (46.5)	250 (40.4)		

ACE-I, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCI, Charleson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; HF, heart failure; HTN, hypertension; ICU, intensive care unit; OSA, obstructive sleep apnea; PVD, peripheral vascular disease; SCr, serum creatinine.
[a]Comparisons are made between no AKI and AKI using Fisher exact test for categorical variables and or nonparametric Kruskal-Wallis test for continuous variables.
[b]Comparisons are made across the stages of AKI using Kruskal-Wallis rank sum test.
[c]Chronic kidney disease was not included as a comorbid condition because prehospitalization estimated glomerular filtration rate was only available in 15% of patients.
[d]Inotropes include dobutamine and milrinone.
[e]Vasopressors include norepinephrine, epinephrine, vasopressin, dopamine, angiotensin-2 infusion.
Values are median (interquartile range) or n (%).

AKI is a common complication among patients hospitalized for a wide range of diagnoses. Among patients hospitalized with COVID-19, we found that 36.6% developed AKI during their hospitalization. This is a higher rate than has been reported previously from China and other areas, from smaller studies, and including various stages of disease. For example, the rate of AKI reported to date has ranged from 0.5% to 29%.[7–15] In particular, Cheng *et al.*[13] reported from Wuhan, China, a rate of AKI of only 5.1% of 701 patients. While we cannot completely explain this difference, it must be noted that significantly lower rates of comorbidities such as diabetes and hypertension were reported in their patients. In addition, the respiratory disease severity appeared to be less, as only 13.4% of their patients required mechanical ventilation compared with 21.8% of our population. The greater

rate found in our study seems consistent with anecdotal reports emerging from other U.S. hospitals.[17]

In our analysis, the clearest risk factors for the development of AKI were indicators of severe COVID-19, specifically the need for ventilator support or vasopressor drug treatment. Reported risk factors for generally poor outcomes of COVID-19, such as increased age, male sex, and higher BMI[12,18–21] were varied in their relationship to AKI risk. Older individuals and men were at greater risk, but there was less of an association to BMI. Individuals from minority communities, particularly African Americans and Hispanics have been disproportionately affected by and have had worse outcomes with COVID-19,[22,23] and we found black race to be associated with increased risk for AKI. There has been interest in the role of blockers of the renin-angiotensin and
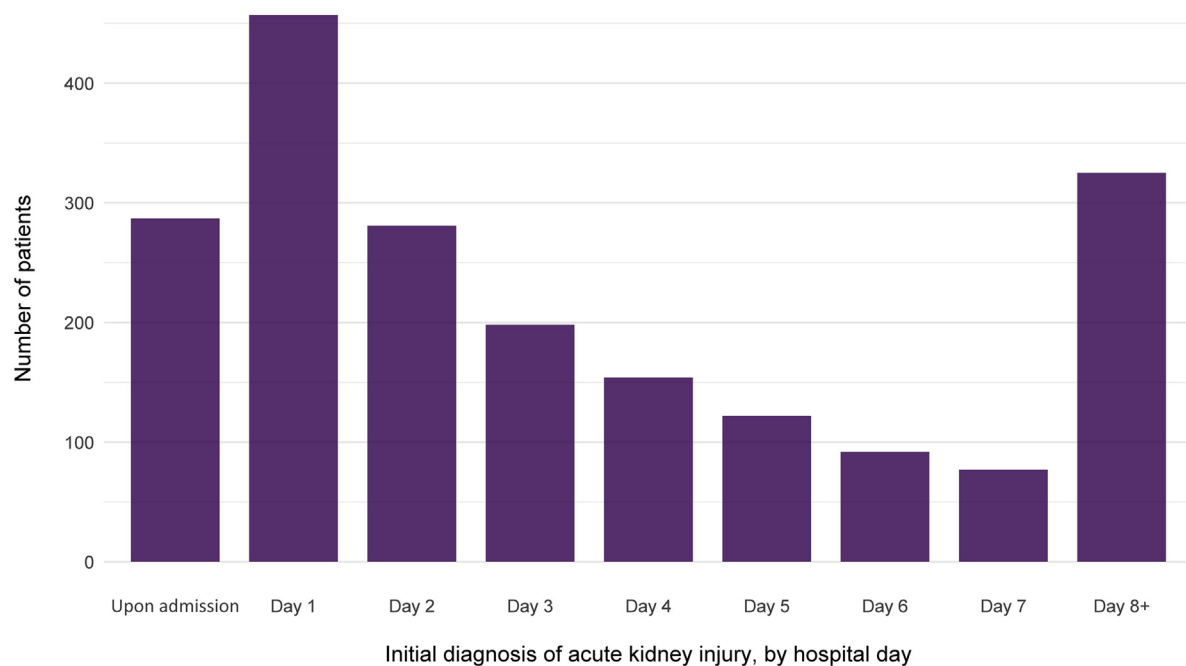

Figure 2 | **The number of patients with initial diagnosis of acute kidney injury, by hospital day of admission.**

Table 3 | The proportion of patients with AKI, by requirement for invasive mechanical ventilation

	No use of invasive mechanical ventilation (n = 4259)	Required invasive mechanical ventilation (n = 1190)	P value[a]
No AKI	3334 (78.3)	122 (10.3)	<0.001
AKI			
Any stage	925 (21.7)	1068 (89.7)	<0.001
Stage 1	639 (15.0)	288 (24.2)	<0.001
Stage 2	185 (4.3)	262 (22.0)	<0.001
Stage 3	101 (2.4)	518 (43.5)	<0.001
Required renal replacement therapy[b]	9 (0.2)	276 (23.2)	<0.001

AKI, acute kidney injury.
[a]Data were compared using the Fisher exact test.
[b]Renal replacement therapy includes intermittent hemodialysis and continuous renal replacement therapy.
Values are n (%).

aldosterone system and COVID-19.[24–27] We did not find that use of these drugs at hospital admission was related to greater AKI risk.

The etiology of AKI in COVID-19 cases has not been fully elucidated. The close temporal relationship between AKI and respiratory failure occurrence is somewhat suggestive of ischemic acute tubular necrosis, which often happens concordant with systemic collapse. However, other etiologies must continue to be considered. The prothrombotic state that has been observed among patients with COVID-19 suggests other renal pathogenic factors. Our urinary results are provocative. We found a high median urine-specific gravity and a majority of patients with urinary sodium <35 mEq/l at the time of development of AKI. Traditionally these findings are most indicative of prerenal states, but they may also be found with glomerulonephritis and even certain forms of acute tubular necrosis. Because a cytokine storm often occurs in close temporal proximity to respiratory failure, it is possible that circulating substances or other related factors could contribute to AKI. It was beyond the scope of the current work to evaluate for these possibilities. In addition, our findings of fairly high rates of proteinuria and hematuria are noteworthy, but inferences are limited as we were unable to ascertain indwelling urethral catheter status at the time of urine collection. It should be noted that, Su *et al.*,[28] in a study from Wuhan, China, determined autopsy findings among 26 patients, with tubular injury as the primary renal finding.

Although not a primary purpose of this study, we found that the development of AKI among our patients portended a particularly dire prognosis. Of 1993 who developed AKI, 35% of them died. For patients requiring dialytic support, the prognosis appears bleaker. Of 285 patients, 157 died and only 9 were discharged from the hospital at the time of analysis. Another 119 were still hospitalized, but 108 of them were still receiving RRT. The early censoring precludes definitive inferences, but it can be seen that the prognosis of patients on RRT who have COVID-19 is quite guarded.

Our study has certain strengths. To date, this is by far the largest cohort of hospitalized patients with COVID-19 with a focus on AKI. The multicenter design and mixture of community and tertiary hospitals allows examination of a breadth of presentations. To increase the validity of the data, we had prespecified operational definitions for variables and
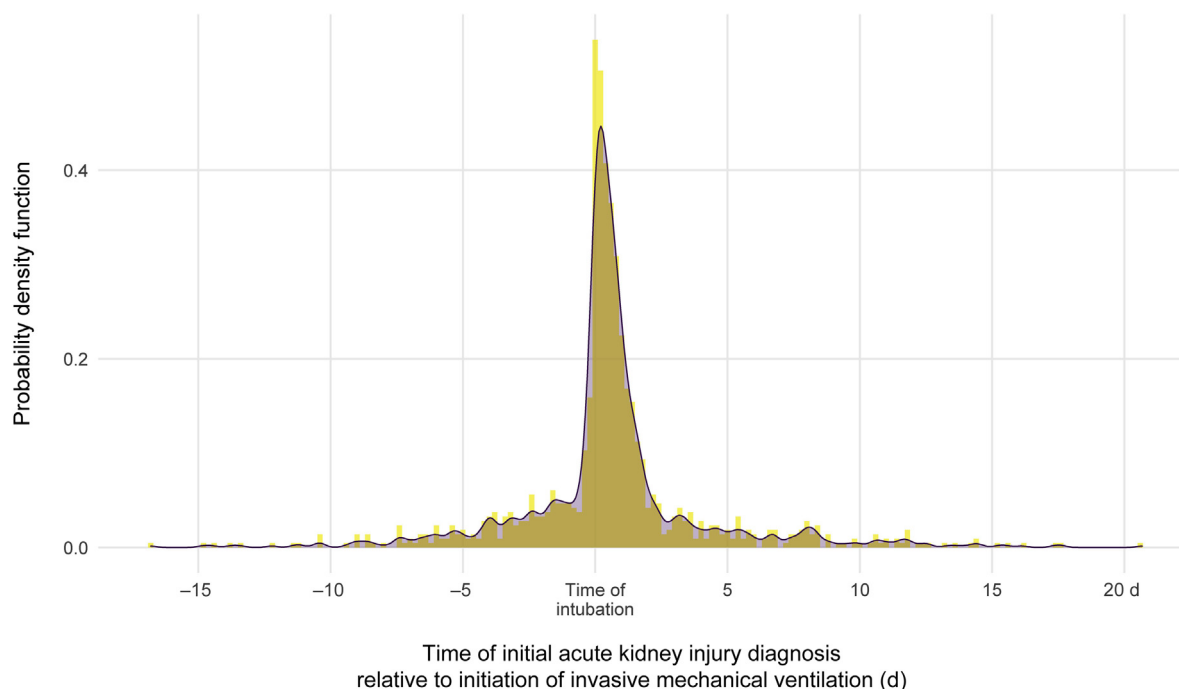

Figure 3 | The probability of acute kidney injury diagnosis relative to time of mechanical ventilation.

Table 4 | Urine tests results obtained 24 hours before up to 48 hours after the development of acute kidney injury

Urine studies	n (%)
Urine sodium (mEq/l)	
<35[a]	187 (65.6)
35–50	47 (16.5)
>50	51 (17.9)
Specific gravity	1.020 (1.010, 1.020)
Blood	
0, negative or trace	196 (36.2)
1+, small	96 (17.7)
2+, moderate	148 (27.3)
3+, large	102 (18.8)
Protein	
0, negative, trace, or <30	168 (26.0)
1+, 30–99	206 (31.9)
2+, 100–299	194 (30.0)
3+, 300–999	78 (12.1)
Urine microscopy, automated	
Positive with white blood cells, >5	221 (36.5)
Positive with red blood cells, >5	249 (40.9)

Values are n (%) or median (interquartile range).
[a]Urine sodium was reported as <20 mEq/l in a few of the enterprise hospitals.

outcomes. Our definition and identification of AKI is consistent with national and international guidelines, is well-validated, and has been automatically calculated in real time for almost 1 year.

The present study has limitations. First, because this is an observational study, we cannot make inferences regarding causal relationships between exposures and AKI. Second, although we have adjusted for potential confounders, there may be potential unmeasured confounders. Third, we relied exclusively on electronic health information systems as the source of data, including identification of AKI. However, the amount of data validation, cleaning, auditing, and quality assurance was substantial. Fourth, we cannot generalize our findings in the outpatient AKI settings because nonhospitalized patients were not part of the present study. In addition, the lack of baseline chronic kidney disease status does not allow us to specifically look at that factor as a risk factor. Finally, the data we presented may not represent the true rate of AKI as the denominator may be different if we had included other health system hospitals in the area.

In conclusion, we found that AKI was a relatively common finding among patients hospitalized with COVID-19. It was strongly linked to the occurrence of respiratory failure and was rarely a severe disease among patients who did not require ventilation. The development of AKI in patients hospitalized for COVID-19 conferred a poor prognosis. Further study will be needed to better understand the causes of AKI and patient outcomes.

METHODS

Study design and cohort

This was a retrospective observational cohort study of a large New York health system. Data for this study was obtained from the 13 hospitals using the enterprise inpatient electronic health record Sunrise Clinical Manager (Allscripts, Chicago, IL). All adult patients (age ≥18 years) who tested positive by polymerase chain reaction testing of a nasopharyngeal sample for COVID-19 and were hospitalized from March 1, 2020, to April 5, 2020, were eligible. For patients who had multiple qualifying hospital admissions, we included only the first hospitalization. Patients who were transferred between hospitals within the health system were treated as 1 hospital

Table 5 | Univariate and multivariate logistic regression analyses of risk factors associated with the development of AKI

Variable	Unadjusted OR	95% CI	P value	Adjusted OR[a]	95% CI	P value
Age (yr)	1.03	1.02–1.03	<0.001	1.03	1.03–1.04	<0.001[b]
Male	1.21	1.08–1.35	0.001	1.14	0.97–1.33	0.10
White race	Reference	Reference	Reference	Reference	Reference	Reference
Asian	0.84	0.68–1.04	0.11	0.83	0.61–1.12	0.23
Black	0.93	0.80–1.08	0.32	1.23	1.01–1.50	0.04[b]
Other/mixed	0.81	0.71–0.93	0.003	0.84	0.69–1.03	0.09
Unknown	0.9	0.69–1.18	0.44	0.74	0.50–1.11	0.15
Tertiary hospital	0.89	0.79–1.00	0.05	0.90	0.77–1.06	0.20
Diabetes	1.84	1.64–2.06	<0.001	1.76	1.49–2.07	<0.001[b]
Hypertension	1.81	1.61–2.02	<0.001	1.25	1.04–1.50	0.02[b]
Cardiovascular disease[c]	2.05	1.77–2.37	<0.001	1.48	1.22–1.80	<0.001[b]
Respiratory disease[d]	1.09	0.93–1.26	0.29	—	—	—
Obesity, BMI ≥30 kg/m²	1.12	1.00–1.26	0.05	1.11	0.94–1.31	0.22
HIV	0.69	0.33–1.44	0.33	—	—	—
Cancer	1.2	0.96–1.51	0.11	1.09	0.82–1.45	0.54
Chronic liver disease	1.01	0.69–1.49	0.95	—	—	—
Mechanical ventilation	31.60	25.80–38.60	<0.001	10.7	6.81–16.70	<0.001[b]
Vasoactive medication[e]	31.40	25.60–38.40	<0.001	4.53	2.88–7.13	<0.001[b]
ACE-I or ARB use	1.61	1.42–1.82	<0.001	0.87	0.73–1.04	0.12

ACE-I, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; BMI, body mass index; CI, confidence interval; OR, odds ratio.
[a]Variables were entered into the model when the α level of risk factor was less than 0.15. Age, sex, and race were added into the model regardless of α level.
[b]Independent risk factors include increased age, black race, diabetes, hypertension, cardiovascular disease, mechanical ventilation, and vasoactive medication.
[c]Cardiovascular diseases include coronary artery disease, heart failure, and peripheral vascular disease.
[d]Respiratory diseases include asthma and chronic obstructive pulmonary disease.
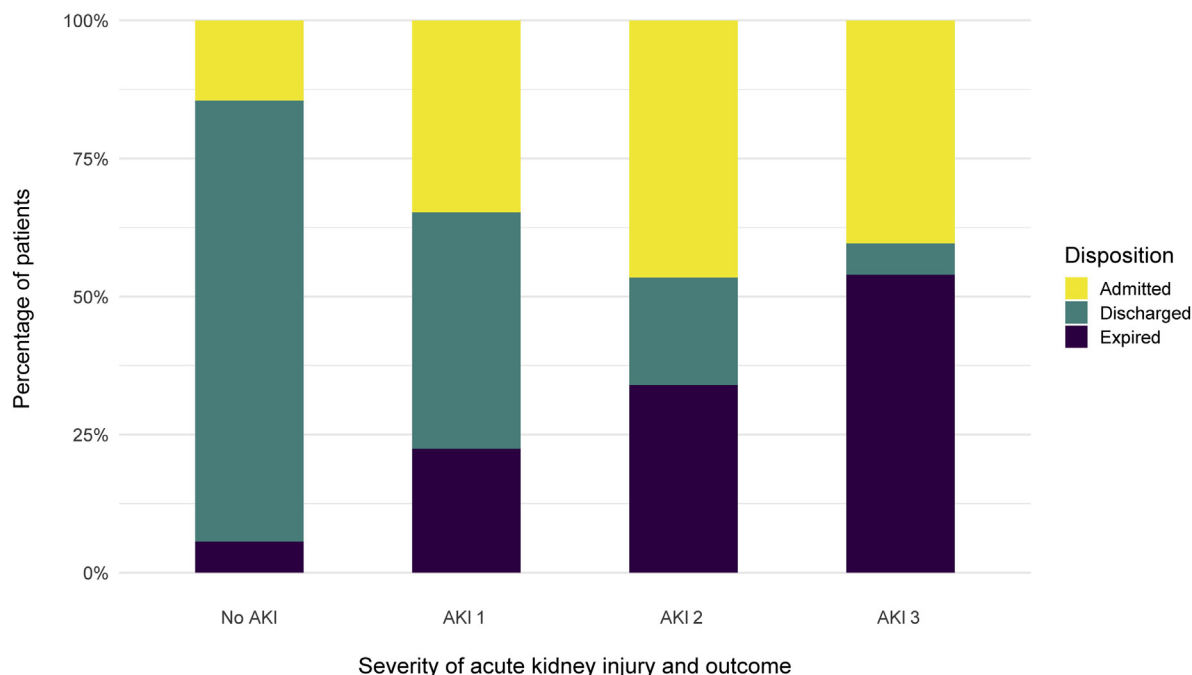[e]Vasoactive medications include inotropes and vasopressors.

Figure 4 | The proportion of disposition type, by stages (1–3) of acute kidney injury (AKI).

encounter. Patients were excluded if they were transferred to hospitals out of the health system for which we were unable to obtain data, had end-stage kidney disease (ESKD), had prior kidney transplant, or had <2 serum creatinine levels during the admission.

The Institutional Review Board of Northwell Health approved the study protocol before the commencement of the study. In a previous publication,[29] we reported an initial case series on the broad spectrum of clinical characteristics and outcomes among patients hospitalized with COVID-19. In that article, we reported preliminary information on AKI and RRT for the first 2634 patients who died or were discharged from our hospitals.

Data cleaning and preparation process
The electronic health record data were screened for duplicate records and missing data; range checks were done to assess for outliers and erroneous data. Outliers were excluded and duplicate records were removed. To ensure accurate exclusion of ESKD and kidney transplant, additional verification was performed. ESKD diagnosis was defined using International Classification of Diseases, Tenth Revision code N18.6. One study investigator (JSH) adjudicated the ESKD diagnosis through manual chart review of hospital admission notes for the following key search terms: "ESRD," "ESKD," "end stage renal," and "end stage kidney." Kidney transplant was defined using International Classification of Diseases, Tenth Revision codes T86.1, T86.10, T86.11, T86.12, T86.13, T86.19, and Z94.0. The study investigator (JSH) adjudicated kidney transplant diagnosis using the following key search terms: "kidney transplant," "renal transplant," "kidney txp," "renal txp," "DDRT," "LRRT," and "LURT."

Definitions and measurements
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 within 48 hours or a 1.5 to 1.9 times increase in serum creatinine from baseline within 7 days; stage 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 RRT.[30] Patients were stratified according to the highest AKI stage attained during their hospital stay.

Baseline serum creatinine and adjudication of AKI was automatically calculated from a prebuilt operational algorithm that was available internally since June 2019 (Supplementary Figure S1). This algorithm was based on KDIGO AKI criteria and the U.K. National Health Service AKI algorithm.[31] It attempts to calculate baseline kidney function from prehospitalization serum creatinine values and simultaneously recalculates baseline to determine AKI based on the aforementioned KDIGO criteria. The baseline creatinine was defined as the median serum creatinine within 8 to 365 days prior to hospital admission. When there were no prior serum creatinine records, we used the serum creatinine on the day of admission as the baseline serum creatinine, with subsequent baseline recalculated with each new serum creatinine according to a predefined algorithm (Supplementary Figure S1). As only 15% of patients had prehospital baseline serum creatinine measurements available, the baseline was retrospectively adjusted to the median serum creatinine value from the entirety of the hospitalization (this value was chosen, rather than the nadir or final creatinine to provide a more conservative estimate to adjudicate AKI). A ratio of >1.5 from peak to median was classified as AKI. Any patient requiring RRT, regardless of automated AKI stage reporting, was defined as stage 3 AKI, as per KDIGO criteria. We did not use the urine output criteria to define AKI as the documentation of urine output in the electronic health record was unreliable. The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.[32]

We additionally collected urine test results including urine electrolytes and urinalysis with automated microscopy that were obtained within 24 hours before or 48 hours after the initial development of AKI. Ascertainment of indwelling urethral catheter information was not available for this study.

Outcomes

The primary outcome was the development of AKI. Secondary outcomes included need for RRT and hospital disposition (i.e., discharge or death). The RRT modalities offered to patients with AKI in our health system were intermittent hemodialysis or continuous CRRT. All patients were followed up through April 12, 2020.

Covariates

We collected data on patient demographics, baseline history of co-morbid conditions, and home medications. Comorbid conditions and home medications were determined from provider-entered past medical history and admission medication reconciliation. Chronic kidney disease was not included as a comorbid condition because the diagnosis of chronic kidney disease using electronic health record has low sensitivity and low positive predictive value.[33] Moreover, pre-hospitalization estimated glomerular filtration rate was available only in 15% of the patients and thus precludes ascertainment of the diagnosis of chronic kidney disease based on estimated glomerular filtration rate. In addition to baseline clinical data, we collected details of hospital admission such as ICU stay, mechanical ventilation, extracorporeal membrane oxygenation, vasopressor support, and baseline laboratory test results within 48 hours of hospital admission. Due to the COVID-19 pandemic, many additional ICUs were created in nontraditional hospital areas and units. Hence, ICU stay was defined as one of the following: need for invasive mechanical ventilation, need for vasopressor or inotrope support, care from an ICU service, or care in a known ICU location.

Statistical analysis

We performed descriptive statistics including means and SDs for normally distributed continuous measures, medians and IQRs for skewed continuous measures, and proportions for categorical measures. We compared baseline patient characteristics between patients with or without AKI using Fisher exact tests for categorical variables and nonparametric Kruskal-Wallis test for continuous variables. To compare the clinical characteristics of patients across different stages of AKI, we performed Kruskal-Wallis test. To identify risk factors associated with the development of AKI, we performed a logistic regression model, with adjustment for risk factors that differed between those who developed AKI and those who did not. The models were built using stepwise procedure, and variables were entered into the models when the α level of risk factor was <0.15. All statistical tests were 2-sided, and a P value <0.05 was considered statistically significant. We performed sensitivity analysis for missing data. The statistical analyses were performed using R (version 3.6.3; R Foundation for Statistical Computing, Vienna, Austria).

To ensure a clear and complete report of the study's design, conduct, and findings, this study followed the Enhancing the Quality and Transparency of Health Research (EQUATOR) reporting guidelines, Reporting of Studies Conducted Using Observational Routinely Collected Health Data (RECORD).[34,35]

APPENDIX

List of Northwell Nephrology COVID-19 Research Consortium

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Northwell Nephrology COVID-19 Consortium authors and affiliations.

Figure S1. Algorithm for detecting AKI using electronic health records.

Table S1. Baseline laboratory blood results within 48 hours of admission.

Table S2. Comparison analysis of risk factors associated with the development of acute kidney injury when including BMI in the multivariate logistic regression model versus excluding BMI in the model.

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