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Brief Report

Acute Kidney Injury in COVID-19 Patients: A Single Center Experience in an Inner City Hospital

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Abstract

Although patients with coronavirus disease 19 (COVID-19) predominantly present with acute respiratory failure, involvement of other organs including the kidneys has been reported. We present a case series of 8 critically ill COVID19-patients, predominantly African-Americans, who developed moderate to severe oliguric acute kidney injury (AKI). The serum creatinine values peaked within one week consistent with the rise of inflammatory markers and disease progression. All the patients required mechanical ventilation, and 25% needed continuous renal replacement therapy with an in-hospital death rate of 75%. All patients had microhematuria and pyuria, and majority of the urine electrolytes were of pre-renal pattern. Possible AKI mechanisms include direct cytopathic effect of the virus, deposition of immune complexes and cytokine-mediated effect in the form of rhabdomyolysis, hypoxia, and shock. Awareness that AKI is a significant poor prognostic marker of mortality among COVID-19 patients will enable clinicians to risk stratify patients early in the course of the disease process in order to provide appropriate interventions.

Keywords: Coronavirus; COVID-19, Acute Kidney Injury (AKI)

Introduction

A recent number of pneumonia cases in Wuhan, China were caused by a novel beta coronavirus, now called coronavirus disease of 2019 (COVID-19) [1]. The COVID-19 virus was shown to affect multiple organs including the lungs, kidneys, heart and esophagus by binding to their angiotensin-converting enzyme 2 (ACE2) receptors [2]. Of note, in 2005, 6.7% of patients with severe acute respiratory syndrome (SARS) were found to have AKI with mortality rate as high as 91.7% with kidney involvement [3]. Similarly, the incidence of AKI ranges from 17% to 29% among hospitalized COVID-19 patients in different regions including China, United States of America and Europe [4-7]. Combined data from the above studies showed that critically ill patients admitted to the intensive care unit (ICU) have a higher incidence of AKI (19-29%) than those who are hospitalized in non-ICU units (0-19%).

In this clinical case series, we describe our single center experience in an underserved inner city hospital with a predominance of African-American patients. We included 8 critically ill COVID-19 patients who were admitted to our ICU and developed moderate to severe oliguric AKI. Findings from these cases can help generate awareness among clinicians about the burden of AKI and their associated severe clinical outcomes among COVID-19 patients, especially African-American patients, in the ICU.

Results

We included 8 critically ill COVID-19 patients, admitted to the intensive care unit of an inner city tertiary hospital, who developed moderate to severe oliguric AKI. The median age was 77.5 IQR (69-79), and 62% were male. Majority were African-Americans (87.5%), and more than half of these patients were admitted directly from home. The mean baseline estimated glomerular filtration rate (eGFR) was 59.14 ± 8.67 cc/min/1.73m^2, and the mean serum creatinine value was 2.0 mg/dL. All patients had hypertension, 88% had baseline chronic kidney disease (CKD), and 75% had diabetes. Three patients were on angiotensin-converting enzyme inhibitors/angiotensin receptor blockers prior to hospitalization, and three were on diuretics which were discontinued due to hypotension. Majority (75%) of the patients showed AKI upon admission, with serum creatinine values peaking over an average of about 6 days (Table 1 and Figure 1). Inflammatory markers such as serum ferritin and D-dimer as well as oxygen requirements (FiO2) trended higher as serum creatinine peaked, with serum ferritin showing a statistically significant difference from admission values (2790 ng/ml *vs.* 7028 ng/ml) with P value of <0.001 (Table 2). All patients had sub-nephrotic proteinuria, microhematuria and pyuria on the urine analysis. Majority (87.5%) had hyaline casts on examination of urine sediment, and 75% of the urine fractional excretion of sodium(FE_{Na}) or urea(FE_{Urea})

profile was prerenal in character. Majority (88%) of the patients had septic shock requiring at least one vasopressor. Half of the patients also required contrast administered intravenously for diagnostic imaging studies with an average contrast dose of 87.5 ml. All the patients required mechanical ventilation, and a fourth needed continuous renal replacement therapy (CRRT). While one (12.5%) patient remains admitted and one (12.5%) was discharged after nearly 4 weeks stay in the ICU, six patients (75%) succumbed to complications of COVID-19 infection (Figure 1).

Characteristics	**Total (N=8)**
Median age (IQR) – yr	77.5 (69-79)
Sex	
Male – no. (%)	5 (62.5)
Female – no. (%)	3 (37.5)
Race or ethnic group – no (%)	
African American	7 (87.5)
Caucasian	1 (12.5)
Asian	0
Hispanic	0
Residence – no. (%)	
Nursing home	3 (37.5)
Home	5 (62.5)
Comorbidities– no. (%)	
Hypertension	8 (100)
Diabetes mellitus	6 (75)
Chronic Kidney Disease – no. (%)	7 (87.5)
Stage 1	1 (14.2)
Stage 2	4 (57.1)
Stage 3a	2 (28.5)
Stage 3b	0
Stage 4	0
Stage 5	0
Baseline eGFR (mean±SD)	59.14±8.67
Chronic Systolic Heart Failure	2 (25)
Benign Prostatic Hyperplasia	1 (12.5)
Home medications – no. (%)	
Diuretics	3 (37.5)
NSAIDs	2 (25)
ARBs	2 (25)
ACEi	1 (12.5)
Admission data – no. (%)	
Contrast exposure	4 (50)
Inpatient medications – no. (%)	
Vancomycin	8 (100)
Proton pump inhibitors	8 (100)
Allopurinol	1 (12.5)
Nonsteroidal anti-inflammatory drugs	2 (25)
Sepsis/Septic shock	7 (87.5)
Urinary tract infection	2 (25)
Rhabdomyolysis	1 (12.5)
Multiorgan failure	1 (12.5)
AKI Staging (KDIGO) – no. (%)	
Stage 1	1 (12.5)
Stage 2	3 (37.5)
Stage 3	4 (50)
Days to AKI diagnosis – no. (%)	
0	6 (75)
1-7	1 (12.5)
>7	1 (12.5)
Urine output (ml/24 h) at AKI – no. (%)	
>400	2 (25)
100-400	6 (75)
<100	0
Mean days to peak of creatinine level (IQR)	6.25 (1-16)
Inflammatory markers on admission – (mean)	
Ferritin (ng/mL)	2790
LDH (IU/l)	462
D-dimer (ng/mL)	5733
CRP (mg/L)	
Inflammatory markers at creatinine peak – (mean)	
Ferritin (ng/mL)	7028
LDH (IU/l)	790
D-dimer (ng/mL)	11956
CRP (mg/L)	
FiO2 requirement on admission – (mean)	31
FiO2 requirement at creatinine peak – (mean)	81
Diagnostic findings – no. (%)	
BUN-Creatinine ratio	
>20:1	4 (50)
<20:1	4 (50)
Urine osmolality (mOsm/kg H2)	395.13±71.29
Urine Na (mEq/L)	
<20	3 (37.5)
>20	5 (62.5)
FE_{Na} or FE_{Urea}	
<1% or ≤35%	6 (75)
>1% or >35%	2 (25)
Specific gravity – no. (%)	
>1.020	1 (12.5)
<1.020	7 (87.5)
(urine protein: creatinine ratio mg/g) – no. (%)	
≤150 mg/g	0
>150 mg/g	8 (100)
Glycosuria – no. (%)	0
Ketonuria – no. (%)	0
Hematuria – no. (%)	8 (100)
Pyuria – no. (%)	8 (100)
Bacteriuria – no. (%)	4 (50)
Cast – no. (%)	
Hyaline	7 (87.5)
Granular	1 (12.5)
Imaging Findings – no. (%)	
hydronephrosis	0
Decreased kidney size	0
Increased echogenicity	0
Need for CRRT – no. (%)	2 (25)
Days to CRRT – no. (%)	
0	0
1-7	2 (25)
>7	0
COVID-19 treatment – no. (%)	
Mechanical ventilation	8 (100)
Medications – no. (%)	
Hydroxychloroquine	6 (75)
Tocilizumab	2 (25)
Glucocorticoids	5 (62.5)
Length of ICU stay – days (mean)	10
Discharged – no. (%)	1 (12.5)
Remains admitted – no. (%)	1 (12.5)
Death in the hospital – no. (%)	6 (75)

Table 1: Characteristics of 8 patients with COVID-19 with AKI.

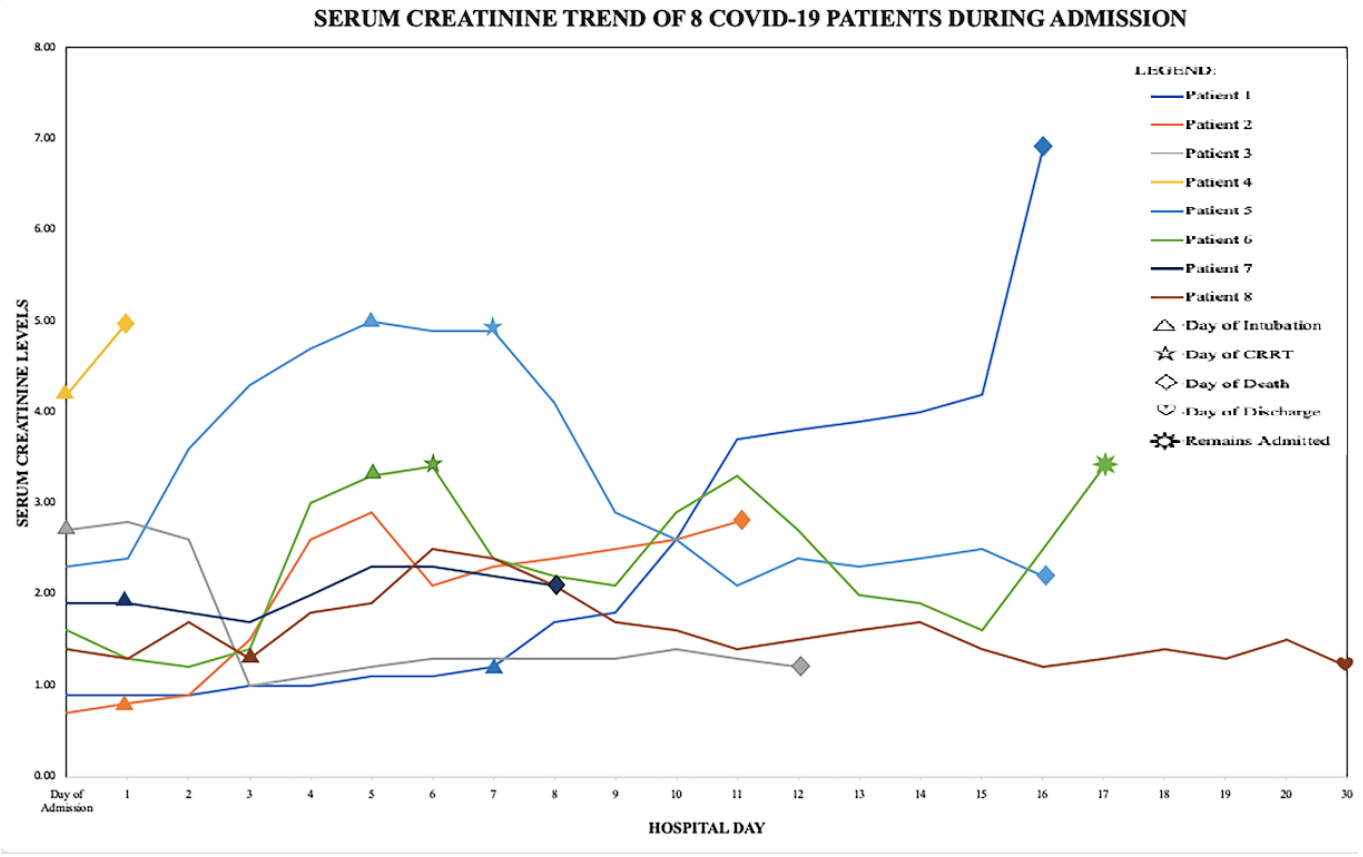

Figure 1: Serum creatinine trend of COVID-19 patients during admission.

	Admission	Peak of kidney injury	p value
Ferritin	2789.88 ± 4011.65	7027.63 ± 13376.92	<0.0001
D-dimer	5732.50 ± 7980.13	11956.25 ± 9668.48	0.188
FiO2%	30.88 ± 20.36	81.25± 21.0	0.549

Table 2: Comparison of markers of disease on admission and on the peak of the kidney injury.

Discussion

In this clinical case series, we describe eight critically-ill patients with COVID-19 who developed moderate to severe AKI. The serum creatinine values peaked within a span of over 1 week consistent with the rise of inflammatory markers, particularly the serum ferritin, and disease progression. This is highly suggestive that the disease activity and severity correlates with the course of kidney injury.

Little is known about the mechanisms of AKI among COVID-19 patients; however, several factors can be traced to link the pathophysiology of AKI in this cohort of patients. First, the COVID-19 virus is known to induce direct cytopathic effects on resident renal cells, substantiated by the detection of coronavirus fragments in blood and urine among COVID-19 patients [1]. Recently, the virus is shown to employ the angiotensin converting enzyme 2 (ACE2) as a cell entry receptor which is extensively expressed in the kidneys particularly in the podocytes and proximal tubular epithelial cells [2,8]. Recent human tissue RNA-sequencing data revealed that the ACE2 expression in the kidneys was nearly 100-fold higher than in the lungs [9]. Another protease family, transmembrane protease serine 2 (TMPRSS2), which is co-expressed with ACE2 in the proximal tubule S3 of the kidney has been observed to be directly involved in "priming" the coronavirus to activate its peptides and eventually amplify its damaging effects on the kidneys [10]. It is hypothesized that severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) potentially induces direct tubular injury based on the fact that SARS-CoV2 nucleocapsid protein and viral particles were detected in the tubular epithelium and podocytes [11]. Autopsies of kidney tissues of COVID-19 patients revealed severe acute tubular necrosis with macrophage infiltration of the tubulointerstitium and diffuse proximal tubule injury with erythrocyte aggregates obstructing the peritubular capillaries [11]. These histopathologic reports are reflective of the urinalysis findings which include hematuria, proteinuria, pyuria, coarse granular, and leukocyte casts seen in our patients. Second, virus-induced cytokines or inflammatory mediators exert an indirect effect on the kidneys as a result of hypoxia and shock, which were the clinical sequelae seen in our patients needing mechanical ventilation, vasopressors, stress dose steroids and fluid resuscitation. In the same vein, pigmented casts containing high levels of creatine

phosphokinase and elevated serum creatine kinase, consistent with rhabdomyolysis, were reported in some cases of COVID-19 [11]. All of these may have contributed to AKI worsening in our patients. Furthermore, in the setting of cytokine storm and septic shock, other factors such as nonsteroidal anti-inflammatory drug (NSAID) use, poor oral intake from the viral prodrome, and volume depletion can potentially decrease GFR that could explain the low calculated FE_{Na} and/or FE_{Urea} suggestive of prerenal etiology present in our patients. However useful, FE_{Na} has significant limitations as FE_{Na} of less than 1% can be also seen in clear-cut causes of intrinsic kidney disease such as contrast-induced nephropathy, acute interstitial nephritis, rhabdomyolysis and early tubular obstruction which are possible complications present in our patients as well [12]. These patients may actually have both pre-renal and intrinsic AKI due to the combined net pathologic effect of COVID-19 infection.

The high prevalence of comorbidities in our patients inherently place them at a higher risk of developing severe forms of COVID-19 infection. In particular, 25% of our patients who had CKD at baseline eventually needed CRRT with mortality rate as high as 75%. This is supported by previous studies reporting the rates to as high as 39% among ICU patients undergoing CRRT and the occurrence of in-hospital death of approximately 16% of hospitalized patients [4,7,13]. Indeed, AKI is a poor prognostic marker for mortality among COVID-19 patients.

Of note, most of the data on COVID-19 related AKI comes from China and Europe. We present a clinical series that involve a significant number of African-American patients who are sometimes known to possess variants of armadillo repeat containing 5 (ARMC5) gene potentially causing low renin phenotype and consequently suppressed renin-angiotensin-aldosterone system (RAAS), a pathway SARS-CoV2 can potentially impact [14]. It would theoretically be expected that a low renin state in this specific population may confer a benefit with respect to the severity of the course of COVID-19 given the potential for increased risk of acute respiratory distress syndrome (ARDS) with angiotensin-1 (AT1) receptor activation; however this experience indicates that African-American patients are at very high risk for severe COVID-19 including AKI. This emphasizes the need for more research on race-based differences in susceptibility to COVID, especially with African-American patients who are high risk for preexisting cardiorenal disease [15]. A case of an African-American COVID-19 patient with a high-risk apolipoprotein L1 (APOL1) gene who developed severe collapsing glomerulopathy was recently reported, with biopsy findings of tubular injury, collapsed glomerular tuft with epithelial hyperplasia, foot process effacement, and tubuloreticular inclusions within the endothelial cells [16]. More cases of this type of glomerulopathy triggered by the coronavirus may be reported as we are seeing more African-American patients who are affected by the pandemic.

Although findings of this study are consistent with the results of previous large, multicenter prospective and retrospective cohort studies, its main limitation is the lack of external validity given the nature of the study design. Apart from AKI, other factors that were not accounted for must have contributed to the deterioration of our patients. Also, we only included a limited number of patients and the sample is only representative of 2 ethnicities at most.

In a case series of predominantly elderly African American patients with COVID-19 who developed moderate to severe oliguric AKI, AKI may potentially herald poorer outcomes such as need for mechanical ventilation, CRRT and mortality. More studies are needed to further elicit mechanisms and outcomes of AKI in the setting of COVID-19 in a larger sample of patients belonging to different ethnicities.

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Conflict of interest

None of the authors have any conflicts of interest to disclose.

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