RESEARCH LETTER

COVID-19–Associated Acute Kidney Injury: A Case Series

To the Editor:

During the peak of the coronavirus disease 2019 (COVID-19) pandemic in the New York area, nephrology consults in our intensive care units (ICUs) nearly tripled. The clinical epidemiology of COVID-19–associated acute kidney injury (AKI) across our health system has been reported,[1] but we highlight our experience from 1 hospital (Mount Sinai Hospital), in which we saw an unprecedented number of highly catabolic AKI cases, all due to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Data collection was approved by the Institutional Review Board (approval number 20-00523) at the Icahn School of Medicine at Mount Sinai.

All patients in this series were critically ill in the ICU with pneumonia caused by COVID-19 (COVID PNA) requiring ventilatory support. All experienced rapid increases in serum urea nitrogen (SUN) and serum creatinine levels, with striking elevations in uric acid, phosphorus, and potassium levels; lactate-negative anion gap; metabolic acidosis; and rapid decreases in serum albumin levels. This could not be explained by low glomerular filtration rate alone and there was no evidence of tumor lysis syndrome or rhabdomyolysis.[2,3]

At 1 particular day near the peak of the COVID-19 crisis (April 9, 2020), of 138 COVID-19–positive ICU cases, 49 of 52 nephrology consult cases had AKI. We present 3 that typify the hypercatabolic state.

1. A 64-year-old man with no preexisting conditions presented with COVID PNA. Creatinine and SUN levels increased from 1.2 and 21 mg/dL, respectively, to 9.9 and 160 mg/dL by day 4. Serum phosphorus level at that time was 11.7 mg/dL. Creatine kinase (CK) level was normal.
2. A 67-year-old man with background hypertension presented with COVID PNA. Over 4 days, serum creatinine level increased from 1 to 7.1 mg/dL, SUN level increased from 12 to 94 mg/dL, and calcium level decreased from 8.1 to 5.8 mg/dL, whereas serum phosphorus level was 9.7 mg/dL (day 2) and peaked at 12.2 mg/dL on day 3.
3. A 50-year-old man with a history of asthma developed COVID PNA. Serum creatinine level increased from 0.8 to 7.8 mg/dL, and SUN level increased from 20 to 102 mg/dL over 3 days. During that period, serum phosphorus level increased to 7.9 mg/dL.

We considered the hyperphosphatemia and rapid increase in SUN level to represent a highly catabolic state and sought to determine how prevalent this was in our COVID-19–infected ICU cohort. Not having a non–COVID-19–infected patient population as comparators, we arbitrarily chose serum phosphorus level > 10 mg/dL early in the course of AKI as sufficiently unique to warrant reporting. We found 9 of 49 such patients with AKI, with a mean AKI duration before phosphorus levels reached 10 mg/dL of only 6 days. No patients were eating or receiving enough nutritional support that could explain exogenous phosphate loads. As summarized in Table 1, there was striking hyperuricemia and hypoalbuminemia, whereas SUN and creatinine reached levels that under ordinary circumstances take weeks to develop, not days. These changes can only come from muscle breakdown. CK levels were normal or only slightly elevated. We reevaluated the same parameters in our nephrology ICU census 2 weeks later, for patients not included in Table 1, and the frequency and degree of biochemical abnormalities were similarly abnormal.

In this report, we highlight a unique phenotype in a subset of critically ill COVID-19–infected patients. None of our patients required vasopressors or had elevated CK levels and only a few received steroids. Hypercatabolic patients in an ICU setting is not an unprecedented event, but such a high proportion of patients, all caused by the same infectious agent and with an intact muscle cell membrane is unprecedented. It supports the hypothesis of a unique cytokine release profile in COVID-19.[4]

Both interleukin 6 and tumor necrosis factor α have a direct effect on muscle protein breakdown.[5,6] There is a large literature supporting their role in muscle wasting associated with other inflammatory disorders.[7,8] The increased release of muscle phosphorus and uric acid could cause or contribute to worsening AKI through intratubular deposition and tubular obstruction.[2,3] We cannot definitely exclude other contributors to the laboratory abnormalities in individual patients, but as a group, the marked increase in phosphorus levels, urea nitrogen levels, and nonlactate acidosis all point toward COVID-19–associated tissue breakdown.

We considered whether such a hypercatabolic state could be useful as a marker for disease severity, predicting pulmonary or kidney outcomes, all-cause mortality, or potentially a stratifier for selecting high-risk patients to clinical trials. Given the wide range of COVID-19 disease severity, the wide range of AKI disease severity, and the inherent limitations of clinical observations from a cross-sectional cohort, there simply is not enough power from this select cohort to make meaningful disease associations. Of the 9 patients, 6 died, 2 recovered, and 1 had no change. Daily dialysis to manage hyperkalemia in the ICU cohort was often necessary.

Better understanding of the pathophysiologic causes of COVID-19–associated AKI is needed, particularly the role of cytokines. In anticipation of COVID-19 surges elsewhere, providers should be prepared for this hypercatabolic syndrome. Conventional intermittent hemodialysis alone may become a limited resource because of an increased number of patients and increased dialysis demands.

Table 1. Average Serum Laboratory Values in a Select Sample of COVID-19–Positive Patients With AKI in the ICU

Serum Electrolytes[a]	
Sodium, mEq/L	138 ± 5
Potassium, mEq/L	5.6 ± 0.7
Chloride, mEq/L	99 ± 6
Total carbon dioxide, mEq/L	17.6 ± 2.2
SUN, mg/dL	125 ± 25
Creatinine, mg/dL	8.3 ± 1.7
Calcium, mg/dL	7.4 ± 1
Phosphorus, mg/dL	13.2 ± 2.3
Inflammatory Markers and Other Laboratory Values[b]	
Lactate, mmol/L	1.3 ± 1.1
Albumin, g/dL	1.8 ± 0.5
IL-6, pg/mL	1,466 ± 2,939
TNF-α, pg/mL	37 ± 21
CK, U/L	819 ± 650
LDH, U/L	1,142 ± 570
Urate, mg/dL	13.3 ± 3.3
CRP, mg/L	311 ± 73

Note: Mean ± standard deviation in a group of 9 COVID-19–positive patients with AKI evaluated in the hospital ICU who had a serum phosphorus level > 10 mg/dL (reached after a mean of 6 days postdiagnosis of AKI; onset of AKI [day 1] was defined when serum creatinine increased by at least 1.5 times baseline). Reference ranges: sodium = 135-145 mEq/L, potassium = 3.5-5.2 mEq/L, chloride = 96-108 mEq/L, total carbon dioxide = 22- 30 mEq/L, SUN = 6-23 mg/dL, creatinine = 0.7-1.3 mg/dL, calcium = 8.5-10.5 mg/dL, phosphorus = 2.4-4.7 mg/dL, lactate = 0.5-1.99 mmol/L, albumin = 3.5-4.9 g/dL, IL-6 = 0-15 pg/mL, TNF-α = 0-22 pg/mL, CK = 30-200 U/L, LDH = 100-220 U/L, urate (uric acid) = 4-9 mg/dL, and CRP = 0-5 mg/L. Conversion factors for units: creatinine in mg/dL to μmol/L, ×88.4; calcium in mg/dL to mmol/L, ×0.2495; phosphorus in mg/dL to mmol/L, ×0.3229.
Abbreviations: AKI, acute kidney injury; CK, creatine kinase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ICU, intensive care unit; IL-6, interleukin 6; LDH, lactate dehydrogenase; SUN, serum urea nitrogen; TNF-α, tumor necrosis factor α.
[a]Serum electrolytes: measured the day phosphorus level reached > 10 mg/dL.
[b]Inflammatory markers and other laboratory results: peak values from any time during hospitalization.

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