Acute Kidney Injury Associated with Coronavirus Disease 2019 in Urban New Orleans

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Abstract

Background AKI is a manifestation of COVID-19 (CoV-AKI). However, there is paucity of data from the United States, particularly from a predominantly black population. We report the phenotype and outcomes of AKI at an academic hospital in New Orleans.

Methods We conducted an observational study in patients hospitalized at Ochsner Medical Center over a 1-month period with COVID-19 and diagnosis of AKI (KDIGO). We examined the rates of RRT and in-hospital mortality as outcome measures.

Results Among 575 admissions (70% black) with COVID-19 [173 (30%) to an intensive care unit (ICU)], we found 161 (28%) cases of AKI (61% ICU and 14% general ward admissions). Patients were predominantly men (62%) and hypertensive (83%). Median body mass index (BMI) was higher among those with AKI (34 versus 31 kg/m², P<0.0001). AKI over preexisting CKD occurred in 35%. Median follow-up was 25 (1–45) days. The in-hospital mortality rate for the AKI cohort was 50%. Vasopressors and/or mechanical ventilation were required in 105 (65%) of those with AKI. RRT was required in 89 (55%) patients. Those with AKI requiring RRT (AKI-RRT) had higher median BMI (35 versus 33 kg/m², P=0.05) and younger age (61 versus 68, P=0.0003). Initial values of ferritin, C-reactive protein, procalcitonin, and lactate dehydrogenase were higher among those with AKI; and among them, values were higher for those with AKI-RRT. Ischemic acute tubular injury (ATI) and rhabdomyolysis accounted for 66% and 7% of causes, respectively. In 13%, no obvious cause of AKI was identified aside from COVID-19 diagnosis.

Conclusions CoV-AKI is associated with high rates of RRT and death. Higher BMI and inflammatory marker levels are associated with AKI as well as with AKI-RRT. Hemodynamic instability leading to ischemic ATI is the predominant cause of AKI in this setting.

Introduction

Over recent months, the devastating pandemic of coronavirus disease 2019 (COVID-19), which originated in China (1), has dramatically destabilized healthcare systems and societies worldwide. With over 2.5 million infected individuals in <5 months, its effect is unprecedented in modern history. Whereas mortality rates vary among different countries, severe forms of COVID-19 have led to a concerning number of fatalities. In the United States of America (USA), mortality is estimated at approximately 3.8%–67% depending on the population studied (2,3). In vulnerable individuals, the clinical course of COVID-19 can progress from a mild viral illness to one with hypoxia, acute respiratory distress syndrome (ARDS), multiorgan failure, and death (4). Reports list AKI as an uncommon manifestation of COVID-19 in severe cases (5–7). However, there is still paucity of data regarding the incidence and clinical characteristics of AKI associated with COVID-19 (CoV-AKI). The first report in the USA from Washington state described an incidence rate of AKI of 19% among 21 individuals admitted to an intensive care unit (ICU) (3). A larger data set from a hospital network in New York City reported an AKI rate of 22%, but only 3% of patients required dialysis (8). The state of Louisiana rapidly topped the charts with the fastest growth of COVID-19 cases in the USA (9). Because of the growing need in the medical community to better understand the intricacies of treating patients with COVID-19 with renal impairment and more accurately estimate its incidence in various settings, we share here our experience at our quaternary care academic medical center in New Orleans.

Materials and Methods

With approval of the Institutional Review Board and in accordance with the Declaration of Helsinki, we conducted an observational single-center study of patients hospitalized at Ochsner Medical Center in...
the month of March, 2020 with positive PCR for severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) in specimens obtained by nasopharyngeal swab and clinical diagnosis of COVID-19. Data were obtained from electronic medical records. We included cases of AKI diagnosed on admission or during the first 10 days of hospitalization. Exclusion criteria were ESKD and kidney transplantation. AKI was defined according to Kidney Disease Improving Global Outcomes criteria (10). To assess bed location, patients were assigned to the ICU category if they were directly admitted to a full ICU bed or if they were subsequently transferred to an ICU bed. The remainder of the patients were assigned to a general ward location. In order to systematically adjudicate a cause of AKI for each case, manual review of every chart was performed independently by three authors for the purpose of identifying events that preceded the development of AKI and that could be considered causative. Those factors included: (1) those predisposing to ischemic acute tubular injury (ATI): an episode of hemodynamic instability, i.e., hypotension [systolic BP (SBP) <90 mm Hg or mean arterial pressure <60 mm Hg], a large fall in arterial BP from
Table 1. Baseline characteristics of patients admitted with a diagnosis of coronavirus disease 2019

| Characteristic                      | No AKI (n=414) | AKI (n=161) |
|-------------------------------------|----------------|-------------|
| **Race, n (%)**                     |                |             |
| Black                               | 294 (71)       | 120 (75)    |
| White                               | 111 (27)       | 39 (24)     |
| Hispanic                            | 7 (2)          | 2 (1)       |
| Native American                     | 1 (0.2)        | 0 (0)       |
| Asian                               | 1 (0.2)        | 0 (0)       |
| **Body mass index, kg/m²**          |                |             |
|                                     | 31 (14–67)     | 34 (16–67)  |
| **Diabetes mellitus, n (%)**        |                |             |
|                                     | 195 (47)       | 86 (53)     |
| **Hypertension, n (%)**             |                |             |
|                                     | 290 (70)       | 134 (83)    |
| **Prior use of RASi (ACEI/ARB), n (%)** |                |             |
| Yes                                 | 211 (51)       | 72 (45)     |
| No                                  | 162 (39)       | 74 (46)     |
| Undetermined                        | 41 (10)        | 15 (9)      |
| **Heart disease, n (%)**            |                |             |
|                                     | 124 (30)       | 54 (34)     |
| **CKD stages 3–5, n (%)**           |                |             |
| Stage 3                             | 93 (22)        | 38 (24)     |
| Stage 4                             | 21 (5)         | 13 (8)      |
| Stage 5                             | 2 (1)          | 5 (3)       |
| **Admission serum creatinine, mg/dl** | 1.1 (0.4–3.5)  | 1.8 (0.7–22.0)  |
| **Bed location, n (%)**             |                |             |
| ICU                                 | 68 (16)        | 105 (65)    |
| General ward                        | 346 (84)       | 56 (35)     |
| Mechanical ventilation*             | 54 (13)        | 101 (63)    |
| Shock/vasopressors*                 | 50 (12)        | 98 (61)     |

Values not provided as n (%) show median (range). RASi, renin-angiotensin system inhibitors; ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; ICU, intensive care unit.

*P<0.05.
**P<0.0011.
***P<0.0015.
****P<0.0001.
* Included if required either at the time of admission or later within the first 14 days of hospitalization.

A hypertensive level (SBP >180 mm Hg to <110 mm Hg), or rapid atrial fibrillation (with heart rate >140 beats/ min; and prolonged prerenal state or vasomotor insult, i.e., volume depletion unresponsive to intravenous fluids, or exposure to either renin-angiotensin system antagonists [e.g., angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers] or to diuretics accompanied by documented negative fluid balance; (2) those predisposing to toxic ATI: exposure to a nephrotoxic agent, (e.g., vancomycin, intravenous iodinated radiodextrast, aminoglycosides, nonsteroidal anti-inflammatory drugs, trimethoprim-sulfamethoxazole, calcineurin inhibitors, intravenous acyclovir, colistin, or sodium phosphate bowel preparation) or endogenous toxin, i.e., rhabdomyolysis [creatinine phosphokinase (CPK) ≥5000 or coexistence of CPK 2000–4999, ≥2+ heme by dipstick, no red blood cells per high-power field (hpf) in urinalysis, and no alternative explanation for AKI]; and (3) clinical elements suggestive of other cause of AKI [interstitial nephritis (eosinophilia, pyuria, and presence of offending drug), glomerular disease (acanthocyturia or suggestive serology), cardiorenal syndrome, hepatorenal syndrome, obstructive uropathy, etc.]. Review of records included history of present illness, physical examination, fluid balance, flowshwets, medications, procedural reports, radiologic studies, blood and urinary laboratory test results, and urinary sediment microscopy findings. Significant proteinuria was defined as ≥2+ protein by dipstick or a urine protein-to-creatinine ratio ≥0.5 g/g. Nephrotic-range proteinuria was defined as 3+ protein by dipstick and urine protein-to-creatinine ratio ≥3.0 g/g. Significant hematuria was defined as coexistence of ≥2+ heme by dipstick and ≥8 red blood cells per hpf. Significant pyuria was defined as ≥6 white blood cells per hpf. Baseline medical history and laboratory data were extracted, to determine whether the AKI event or the urinary abnormalities were de novo or preexisting. We categorized patients without available baseline kidney function information as de novo. Data entry was terminated after every patient in the cohort had ≥14 days of follow-up.

The primary outcome measure assessed was need for RRT. For the purpose of the analysis, patients who died with rising serum creatinine, oliguria and imminent need of RRT, but did not receive RRT before dying due to comfort care measures or clinical decompensation that impeded initiation of RRT, were also assigned to the outcome of needing RRT. Oliguria was defined as urine output <500 ml/day. In-hospital mortality was a secondary outcome. Need for mechanical ventilation was recorded, as well as occurrence of ARDS, defined as acute onset of hypoxemia (arterial PO2 per fraction of inspired oxygen ≤200 mm Hg with bilateral infiltrates on frontal chest radiograph) with no evidence of left atrial hypertension.

**Statistical Analyses**

Continuous variables were compared using a t test (Mann–Whitney U test was performed for nonparametric
Comparisons of proportions were done by Fisher’s exact test. A \( P \) value <0.05 was considered statistically significant. All calculations were performed with GraphPad Prism 7 (San Diego, CA).

### Results

During the study period, 644 patients were hospitalized at Ochsner Medical Center with COVID-19. After exclusion of 57 patients with ESKD and 12 patients with kidney data). Comparisons of proportions were done by Fisher’s exact test. A \( P \) value <0.05 was considered statistically significant. All calculations were performed with GraphPad Prism 7 (San Diego, CA).

#### Table 2. Laboratory test results of patients with AKI associated with coronavirus disease 2019 (n=161)

| Parameter | Result |
|-----------|--------|
| **Kidney function and blood chemistry values relevant to AKI** | |
| Baseline sCr (mg/dl) | |
| De novo AKI | 1.0 (0.6–1.2) |
| AKI on CKD | 1.6 (1.2–6.5) |
| sCr on admission (mg/dl) | |
| De novo AKI | 1.5 (0.8–11.5) |
| AKI on CKD | 3.1 (1.3–22.0) |
| AKI by KDIGO stage, n (%) | |
| Stage 1 | 30 (19) |
| Stage 2 | 25 (16) |
| Stage 3 | 106 (66) |
| Peak CKP (U/L), n (%) | |
| >1000 | 29 (18) |
| 1000–4999 | 21 (13) |
| >5000 | 8 (5) |
| Peak ferritin (ng/ml) | |
| De novo AKI | 1581 (41–26,000) |
| AKI on CKD | 42.12 (0.36–23.0) |
| Peak CRP (mg/L) | |
| De novo AKI | 262 (30–535) |
| AKI on CKD | 0.78 (0.1–40.2) |
| Peak LDH (U/L) | |
| De novo AKI | 548 (128–8249) |
| AKI on CKD | 37 (23) |
| Metabolic acidosis, n (%) | |
| Carbon dioxide \( \leq 12 \text{ mEq/L} \), n (%) | |
| Hyperkalemia (>5.5 mEq/L), n (%) | |
| Hypernatremia, n (%) | |
| >145 mEq/L | 13 (8) |
| ≥155 | 6 (4) |
| <135 mEq/L | 46 (29) |
| ≤125 mEq/L | 4 (2.5) |
| **Urinary laboratory test results** | |
| Proteinuria, n (%) | |
| Significant (≥2+ dipstick or UPCR ≥0.5 (g/g)) | |
| Preexisting | 112 (69) |
| De novo\(^a\) | 25 (16) |
| Unknown baseline | 63 (39) |
| Nephrotic range (≥3+ dipstick + UPCR ≥3.0 (g/g)) | |
| Preexisting | 14 (9) |
| De novo\(^a\) | 7 (4) |
| Unknown baseline | 6 (4) |
| Hematuria, \(^b\) n (%) | |
| Any level | 111 (69) |
| Significant (≥2+ dipstick + ≥8 rbc/hpf) | 30 (19) |
| Leukocyturia | 17 (11) |
| Coarse granular casts\(^c\) | Present in 17 out of 20 |
| Urinary sodium (mEq/L),\(^d\) n (%) | |
| <20 | 20 (38) |
| ≥20 | 32 (62) |
| Fractional excretion of urinary sodium,\(^n\) n (%) | |
| <1% | 11 (38) |
| 1%–2% | 7 (24) |
| >2% | 11 (38) |

Values are expressed as median (range) unless otherwise indicated. Hyperkalemia, dysnatremia, and metabolic acidosis were counted only if they occurred during the first 5 days of the onset of AKI or before initiation of RRT. sCr, serum creatinine; KDIGO, Kidney Disease Improving Global Outcomes; CPK, creatine phosphokinase; CRP, C-reactive protein; LDH, lactate dehydrogenase; UPCR, urine protein-to-creatinine ratio; rbc/hpf, red blood cells/high-power field.

\(^a\)Value obtained either on admission or before the onset of AKI.

\(^b\)Not tested in 13 patients.

\(^c\)Microscopic examination of the urinary sediment was only performed in 20 patients. Limitations included anuria and contact precautions.

\(^d\)Only obtained in 52 patients.

\(^n\)Only obtained in 29 patients.

\(KIDNEY360\) 1: 614–622, July, 2020 AKI with COVID-19 in NOLA, Mohamed et al. 617
transplantation, 575 patients entered the cohort. Seventy-one percent of the patients were black. The incidence of AKI was 28% (161 patients) (Figure 1). As in the general cohort, patients with AKI were predominantly black (74.5%), with a median age of 65 (36–96) years. More patients in the AKI cohort were men (62%). With regard to comorbidities, 53% had diabetes mellitus and 83% had essential hypertension. The proportion of patients who were men with essential hypertension was higher in the AKI group. The median body mass index (BMI) was higher for the AKI cohort compared with that of the non-AKI group (34 versus 31, \(P=0.0001\)) (Table 1).

De novo AKI accounted for 65% of the patients, whereas AKI superimposed over preexisting CKD accounted for the remaining 35%. A nonoliguric form of AKI occurred in 5% of patients. Ninety-one (57%) patients arrived with AKI on the basis of serum creatinine value on admission, whereas the remaining 43% acquired AKI during the hospitalization [median day of hospitalization when AKI first occurred: hospital day 4 (2–10)]. Two thirds of the patients had stage 3 AKI. Median follow-up was 25 (1–45) days. Hyperkalemia, hyponatremia, and metabolic acidosis were the most common electrolyte and acid-base disorders observed early in the course of AKI. De novo significant proteinuria was seen in 39% of the patients and de novo nephrotic-range proteinuria was seen in 4%, whereas significant hematuria was observed in 19% (Table 2). Baseline proteinuria status before admission could not be determined in 39 (24%) patients.

Sixty-five percent of the patients with AKI were admitted or transferred to an ICU, whereas the remaining 35% were treated on a general ward. ICU stay, mechanical ventilation, and shock were more common for the AKI group compared with those without AKI (Table 1). The incidence of AKI represented 61% of 173 patients admitted to an ICU and 14% of 402 patients admitted to a general ward (Figure 1). The inhospital mortality rates were 50% (80/161), 58% (61/105), and 34% (19/56) for the entire AKI cohort, the ICU AKI cohort, and for those with AKI on a general ward, respectively. Among fatalities, median survival was 10 (1–39) days. All survivors had a median follow-up period of 32 (17–45) days postadmission. Hydroxychloroquine was empirically given to 142 (88%) patients in the cohort. Among baseline laboratory values, AKI was associated with higher baseline values of serum ferritin, C-reactive protein (CRP), procalcitonin, lactate dehydrogenase (LDH), and D-dimer (Table 3).

AKI requiring RRT (AKI-RRT) represented 55% (\(n=89\)) of the AKI cohort, the majority of patients (98%) receiving prolonged intermittent RRT with sustained low-efficiency dialysis, and 2% receiving continuous RRT (CRRT) with

| Marker                | No Acute Kidney Injury (\(n=414\)) | Acute Kidney Injury (\(n=161\)) |
|-----------------------|-----------------------------------|----------------------------------|
| Ferritin, ng/ml       | 680 (315–1416)                    | 1016 (516–2534)\(^a\)           |
| D-dimer, µg/ml        | 1.13 (0.68–2.57)                  | 1.57 (0.96–3.14)\(^b\)          |
| CRP, mg/L             | 93 (46–165)                       | 163 (93–243)\(^b\)             |
| Procalcitonin, ng/ml  | 0.12 (0.06–0.32)                  | 0.37 (0.18–1.58)\(^a\)          |
| LDH, U/L              | 428 (309–548)                     | 532 (365–804)\(^a\)            |

Values are expressed as median (interquartile range). Values obtained from a subset of patients. For non-AKI group: ferritin (\(n=407\)), D-dimer (\(n=381\)), CRP (\(n=411\)), procalcitonin (\(n=404\)), and LDH (\(n=401\)); for AKI group: ferritin (\(n=139\)), D-dimer (\(n=102\)), CRP (\(n=134\)), procalcitonin (\(n=151\)), and LDH (\(n=117\)).

CRP, C-reactive protein; LDH, lactate dehydrogenase.

\(^aP<0.0001\).

\(^bP=0.0004\).
continuous venovenous hemodiafiltration. Because of frequent circuit clotting observed without anticoagulation or with regional citrate anticoagulation, most patients were managed with systemic heparin-based anticoagulation. Only three patients were solely dialyzed by conventional intermittent hemodialysis without requiring prolonged intermittent RRT or continuous RRT at any point. Nineteen (21.6%) patients reached the RRT end point due to death with rising serum creatinine and oliguria. RRT was required in 73% of the patients with AKI in the ICU (Figure 2), and was mainly initiated due to fluid overload and/or electrolyte disturbances (hyperkalemia or severe metabolic acidosis) in the context of oligoanuria. Only 2% were nonoliguric at the time of RRT initiation. Those with AKI-RRT had a greater BMI (35 versus 33, \( p = 0.05 \)) and younger age (61 versus 68, \( p = 0.0003 \)) compared with those with AKI not requiring RRT (Figure 3). No significant difference in the rate of RRT was found on the basis of sex or race. Mechanical ventilation due to presumed ARDS was required in 101 (63%) patients, with a higher frequency among those with AKI-RRT compared with those who did not require RRT [82% (73/89) versus 39% (28/72), \( p<0.0001 \)]. The in-hospital mortality rate for those with AKI-RRT was 72%. For those with AKI-RRT needing mechanical ventilation, the mortality rate was 74%.

Among baseline laboratory values, AKI-RRT was associated with higher baseline values of serum ferritin, CRP, procalcitonin, and LDH (Figure 4). Baseline D-dimer was not different between AKI-RRT and AKI without RRT; however, the median peak D-dimer value was higher for those with AKI-RRT (7.8 versus 3.8 \( \mu \text{g/ml} \), \( p = 0.03 \)). The median time for the D-dimer to reach the peak value after the admission value was 5 (0–25) days.

In 66% of the patients with AKI, a diagnosis of ischemic ATI was assigned on the basis of an episode of hemodynamic instability that preceded the AKI or clear history of prolonged prerenal azotemia (Table 4). In 17 of 20 patients in whom urinary sediment microscopy was performed, the findings were consistent with ATI as revealed by the presence of coarse granular casts (Table 2). Three patients underwent a percutaneous kidney biopsy and the findings revealed lesions of collapsing glomerulopathy in all three. One patient had suspected acute proliferative GN on the basis of acanthocyturia and C4 hypocomplementemia, but expired without kidney biopsy. Prerenal azotemia verified by reversal of AKI upon intravenous fluid expansion was seen in 15 (9%). The remaining 21 (13%) patients were categorized as having unexplained AKI.

**Discussion**

Our study is one of the first reports of CoV-AKI in the USA and the first one in a predominantly black population. The incidence of AKI in our cohort seems higher than reported elsewhere (3.5–8). Comorbidities and social determinants of health may partially account for the observed difference. Because of the observed association of a higher
BMI with the development and severity of AKI in our cohort, we speculate that the high prevalence of morbid obesity in our region may have increased the vulnerability of our patients to acquiring AKI. The association between morbid obesity and risk for AKI in individuals with ARDS in the ICU has been previously recognized (11). The association of higher BMI with a need for RRT was only noted among de novo patients with AKI. The known impaired nutritional status in CKD might have blunted the effect of morbid obesity (12) but that assertion remains speculative at this time. We also observed an increased proportion of men and patients with essential hypertension for the AKI group. Impairment of renal autoregulation associated with chronic hypertension might have increased the vulnerability to hemodynamic derangements in patients with COVID-19.

The observation of greater baseline levels of inflammatory markers ferritin, CRP, procalcitonin, and LDH among those patients who developed CoV-AKI, and even greater levels among those with AKI-RRT, suggests a direct relationship between the magnitude of cytokine release characteristic of COVID-19 and the risk for AKI and the severity of AKI (13). This observation aligns with others that link the severity of systemic inflammatory response syndrome with AKI (14). Peak D-dimer was also higher in the AKI-RRT group, a finding that aligns with the prothrombotic state described in COVID-19 (15). However, it is yet to be established whether renal microthrombi constitute a salient lesion in patients with COVID-19 who develop AKI.

Distinct phenotypes of AKI were observed. A small fraction arrived with prerenal azotemia and recovered after volume expansion. As seen in other infectious diseases that progress to systemic inflammatory response syndrome and shock, the majority of the AKI cases were preceded
by gradual or sudden hemodynamic decompensation, and a clinical course suggestive of ischemic ATI. Viral infection-associated rhabdomyolysis only accounted for 7% of patients. As reported by others (5), significant isomorphic hematuria was present, but bladder trauma from catheterization could not be ruled out as the source. A moderate degree of proteinuria was observed in 54% of the cohort. However, de novo nephrotic-range proteinuria was rare and only present in seven patients (4%), which included three cases of collapsing glomerulopathy. Recent reports suggest a pathogenic link between COVID-19 and the development of collapsing glomerulopathy in black patients with APOL1 polymorphism (16). Thus, it is plausible that some of the evidence of proteinuria seen in our cohort may have arisen from glomerular insult.

On the other hand, we observed that 13% of patients developed an otherwise unexplained progressive and rapid rise in serum creatinine, which began shortly after admission and preceded any subsequent hemodynamic decompensation. Whether COVID-19 directly or indirectly caused AKI in those cases is unknown. It has still not been clearly elucidated if viral entrance into kidney tissue plays a fundamental role in the development of AKI. The original SARS coronavirus has been detected in kidney tissue in autopsy specimens (17). More recently, an autopsy report of 26 patients who died with COVID-19, revealed histopathologic evidence of ATI in all of the cases (18). Interestingly, a SARS-CoV-2 nucleoprotein was identified by immunofluorescence and viral-like particles were visualized by electron microscopy in podocytes and tubular epithelial cells in that report, but not by others (16). Knowing that SARS-CoV-2 enters the cell via ACE2 (19) and that ACE2 is abundantly expressed in tubular epithelia, and to a lesser degree in podocytes (20–22), it could be speculated that disruption of the integrity of either the tubular basement membrane or the glomerular basement membrane could elicit direct viral entry to the tubules or perhaps podocytes, and may contribute to the observed AKI phenotype. However, it has not been proven that the particles visualized by electron microscopy in the report were of viral origin (18). Thus, contention regarding the presence of SARS-CoV-2 in the kidney remains unproven and needs to be replicated before further hypotheses are generated.

As an alternative postulate to direct viral entrance to the kidney, host response and cytokine release may be considered as triggers of a form of subclinical dysregulation in renal microcirculation, and induce an ischemic or toxic “hit” to the tubuli or an IFN-mediated glomerular insult (23,24). Nevertheless, given the high volume of hospitalized patients with COVID-19 during the study period, we cannot discard the possibility that, in some cases, the coexistence of AKI and COVID-19 was of coincidental nature, and that the AKI resulted from an unrelated, undetermined cause.

In summary, we report an incidence rate of CoV-AKI from an urban hospital in New Orleans higher than previously reported elsewhere. The mortality rate of patients with CoV-AKI requiring RRT is very high. High BMI is associated with the development and severity of AKI, the latter being more evident among de novo AKI cases. Higher levels of inflammatory markers are associated with CoV-AKI as well as CoV-AKI requiring RRT. Hemodynamic instability is the dominant driver that likely leads to ischemic ATI as the most common cause of AKI in this setting. Viral-associated rhabdomyolysis only accounts for a fraction of the cases. In a small subset, no explanation was found for the development of AKI beyond the diagnosis of COVID-19 itself. More studies are needed to better characterize this clinical entity.

### Table 4. Causes of CoV-AKI (n=161)

| Cause | n (%) |
|-------|-------|
| **Ischemic ATI** | |
| Hemodynamic instability | 106 (66) |
| Hypotension/shock | 86 (53) |
| Large reduction in SBP | 4 (2.5) |
| Rapid atrial fibrillation | 2 (1.2) |
| Prolonged volume depletion | 14 (9) |
| **Toxic ATI** | |
| Rhabdomyolysis (isolated) | 7 (4) |
| Another toxic agenta | 4 (2.5) |
| Ischemic/toxic (hemodynamic instability and rhabdomyolysis) | 4 (2.5) |
| **AKI otherwise not specified** | |
| Urine sediment microscopy suggestive of ATI | 11 (7) |
| Overt proteinuria suggestive of glomerular lesion | 3 (1.9) |
| Acute interstitial nephritis | 1 (0.6) |
| **De novo glomerular disease** | |
| Collapsing glomerulopathy | 3 (1.9) |
| Proliferative GN | 1 (0.6) |
| Prerenal azotemia | 15 (9) |

Under toxic ATI, five patients were diagnosed with rhabdomyolysis on the basis of CPK >5000 U/L and two on the basis of CPK >2000 U/L + 2+heme dipstick and no urine red blood cells. Under ischemic/toxic ATI, among four patients with ischemic ATI, three patients were diagnosed with concomitant rhabdomyolysis on the basis of CPK >5000 U/L, and one on the basis of CPK >2000 U/L + 2+heme dipstick and no urine red blood cells. ATI, acute tubular injury; SBP, systolic blood pressure .

*aToxic agents that were identified as the only potential culprits for AKI included vancomycin (n=3) and iodinated radiocontrast (n=1)."
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Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions, and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

Author Contributions

I. Lukitsch, M. Mohamed, and J.C. Velez conceptualized the study; M. Alqudsi, C. Hernandez-Arroyo, J. LeDoux, I. Lukitsch, M. Mohamed, A. Torres-Ortiz, J.C. Velez, and J. Walker were responsible for data curation; M. Alqudsi, C. Hernandez-Arroyo, J. LeDoux, M. Mohamed, A. Torres-Ortiz, J.C. Velez, and J. Walker were responsible for investigation; M. Mohamed and J.C. Velez were responsible for methodology and wrote the original draft; A. Torres-Ortiz was responsible for project administration; J.C. Velez was responsible for formal analysis and supervision; J.C. Velez was responsible for resources; and all authors reviewed and edited the manuscript.

Disclosures

J.C. Velez has participated in Advisory Board engagements with Mallinckrodt Pharmaceuticals and Retrophin, and has been a member of a Speaker Bureau for Otsuka Pharmaceuticals. All remaining authors have nothing to disclose.

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