Kidney360

Effect of COVID-19 on Kidney Disease Incidence and Management

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Abstract

The COVID-19 outbreak has had substantial effects on the incidence and management of kidney diseases, including AKI, ESKD, GN, and kidney transplantation. Initial reports from China suggested a lower AKI incidence in patients with COVID-19, but more recent studies from North America reveal a much higher incidence, likely due to the higher prevalence of comorbid conditions, such as hypertension, diabetes, and CKD. AKI in this setting is associated with worse outcomes, including the requirement for vasopressors or mechanical ventilation and death. Performing RRT in those with AKI poses challenges, such as limiting exposure of staff, preserving PPE, coagulopathy, and hypoxemia due to acute respiratory distress syndrome. Continuous RRT is the preferred modality, with sustained low-efficiency dialysis also an option, both managed without 1:1 hemodialysis nursing support. Regional citrate is the preferred anticoagulation, but systemic unfractionated heparin may be used in patients with coagulopathy. The ultrafiltration rate has to be set carefully, taking into consideration hypotension, hypoxemia, and responsiveness to presser and ventilatory support. The chance of transmission puts in-center chronic hemodialysis and other immunosuppressed patients at particularly increased risk. Limited data show that patients with CKD are also at increased risk for more severe disease, if infected. Little is known about the virus's effects on immunocompromised patients with glomerular diseases and kidney transplants, which introduces challenges for management of immunosuppressant regimens. Although there are no standardized guidelines regarding the management of immunosuppression, several groups recommend stopping the antimetabolite in hospitalized transplant patients and continuing a reduced dose of calcineurin inhibitors. This comprehensive review critically appraises the best available evidence regarding the effect of COVID-19 on the incidence and management of kidney diseases. Where evidence is lacking, current expert opinion and clinical guidelines are reviewed, and knowledge gaps worth investigation are identified.

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Introduction

COVID-19, the disease caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first described in Wuhan, China, but rapidly affected >40 million people worldwide (1). The clinical presentation is highly variable in symptoms, severity, and organ involvement, ranging from asymptomatic to multiorgan failure. One of the major organs involved is the kidney, which manifests as COVID-19–related AKI in hospitalized patients, especially in those requiring intensive care unit (ICU) management. Another important aspect of COVID-19 as relates to kidney disease is, given the highly infectious nature of SAR-CoV-2, patients with ESKD, kidney transplantation recipients, and those with glomerular diseases and other CKD may be at increased risk for infection and associated morbidity, especially in the light of the underlying immunocompromised state. The global COVID-19 pandemic has had a significant influence on clinical aspects and management of these patient populations. In this study, we evaluate the current evidence about the effect of COVID-19 on AKI, CKD, ESKD, renal transplantation, and GN, and address specific management challenges of these vulnerable patient populations.

AKI

Epidemiology and Outcomes

Early reports from Wuhan, China, concluded that COVID-19 does not result in significant AKI (2), with zero cases reported among 119 hospitalized patients, ranging up to 15% in other publications (2–15). Subsequent US studies reported higher incidences of 14%–69% in hospitalized patients, especially if requiring ICU and mechanical ventilation (Figure 1A) (15–23). One study reported a higher incidence of AKI among patients hospitalized for COVID-19 versus for non–COVID-19 indications (17). These differences could be explained by the varying prevalence of comorbidities among Chinese versus US cohorts, with the United States reporting a higher presence of hypertension, diabetes mellitus, and CKD, found to be risk factors for SARS-CoV-2 infection (Figure 1, C and D) (3–14,24–28). Diabetes was present among 16%–49% and hypertension among 31%–74% of patients with COVID-19 (15–17,19–22,29–31) in US cohorts, but in only 7%–24% and 15%–38% in Chinese counterparts. These variations may be, in part, due to differences in racial composition, health care access, and hospitalization thresholds for disease acuity. There was also heterogeneity

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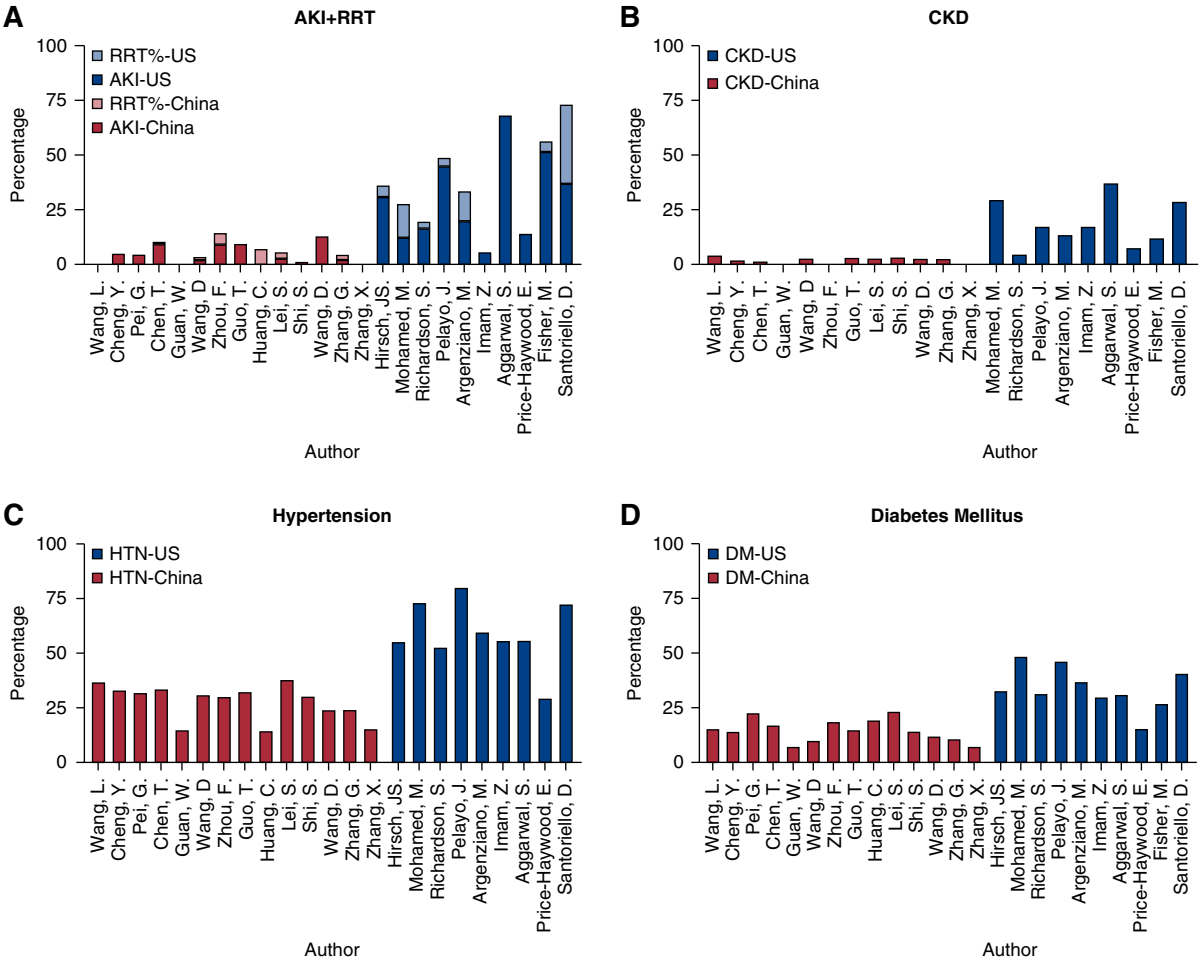

Figure 1. | **Differences in AKI, RRT, and comorbidities in patients with COVID-19 in the United States and in China.** Percentages calculated as proportion of COVID-19–positive individuals in each study, with data from China shown in red and data from the United States in blue. (A) Incidence of AKI in patients with COVID-19 (blue for the United States and red for China), with percentage of AKI patients requiring RRT depicted in light blue for the United States and light red for China. Prevalence of underlying (B) CKD, (C) hypertension, and (D) diabetes mellitus in patients with COVID-19. This figure does not include data from cohorts that only reported patients admitted to intensive care units. HTN, hypertension; DM, diabetes mellitus.

across studies, with some comprised of all hospitalized patients, whereas others only those requiring ICU and, therefore, reporting higher AKI incidence. This is congruent with findings identifying requirement for vasopressors or mechanical ventilation as independent risk factors for COVID-19–related AKI (18). Another factor could be the lack of a standardized method for defining AKI. Most studies used standard Kidney Disease Improving Global Outcomes (32) criteria but varied in how "baseline creatinine" was established.

Reported mortality is also variable, ranging from 1% to 28% in Chinese (2,3,5,6,8–11,14,26), and 15%–24% in US studies (15–18,20–22,31). Factors implicated for heterogeneity may include case mix, socioeconomic status, hospitalization criteria, and availability and delivery of COVID-19–specific treatments. Comorbidities are also considered an important risk factor for COVID-19 disease severity and outcomes, and patients who die have a higher prevalence of hypertension and diabetes versus those who recover (24,25).

Patients with COVID-19–associated AKI have worse outcomes than those without AKI, with higher incidences of ICU admission, acute respiratory distress syndrome (ARDS), mechanical ventilation, and death (27–29). Yang and Xu *et al.* (27,28) reported AKI incidences of 29% and 50% in patients admitted to the ICU. AKI incidence was about 50% in a larger US multicenter cohort of >3000 ICU patients (30). Two studies from China reported AKI occurring more frequently in patients who died than who recovered from COVID-19 (24,25). Association of AKI with poor outcomes in the setting of COVID-19 may be confounded by factors that cause or correlate with AKI and with adverse outcomes among acutely ill patients.

AKI Requiring RRT

In China, the incidence of AKI requiring RRT ranged from 0% to 7% (2,6,7,9–11,13,14,24,27). In one cohort of only ICU patients, the incidence was 17% (28). In the United States, the incidence ranged from 3.1% to 15.5% in all-comers (Figure 1A) (16–20,22) but higher at 20% in ICU patients (30). The higher utilization of RRT in the United States versus China may be due to higher AKI incidence, availability of RRT, or severity of

disease or comorbidities. Specific RRT modalities were not always reported, but acute peritoneal dialysis (PD) is utilized in some centers due to concern for lack of resources (33). Performing PD in patients who are placed in the prone position for ARDS brings up the concern for increased intra-abdominal pressures and subsequent decreased ultrafiltration. PD has been successfully used in prone position, and proning is not an absolute contraindication for PD (34). The risk of intra-abdominal hypertension and decreased ultrafiltration can be mitigated by suspension of the abdominal cavity and using low-volume continuous PD (35).

Delivering RRT in those with COVID-19 poses several challenges (Figure 2) (36–38). In addition to utilization of acute PD, various strategies were implemented to help ease the impending resource shortages. Many centers utilize continuous RRT (CRRT) or prolonged intermittent daily RRT, including sustained low efficiency dialysis, instead of intermittent hemodialysis (HD), which can be managed without 1:1 HD nursing. Other strategies included using a shorter CRRT duration, 10–12 hours, at a higher effluent rate of 40–50 ml/kg per hour, to rotate the same machine for multiple patients. Reducing the effluent dose once the patient becomes stable was recommended to preserve dialysis solutions (37–41).

The virus is easily transmitted, which raises challenges regarding safety, complicated by declining personal protective equipment (PPE). Shortages of health care workers due to illness and need to quarantine poses additional challenges. Solutions include isolation of patients in aggregate in COVID-19–only ICUs or using individual isolation rooms. Training nondialysis staff to assist with dialysis treatments has also been undertaken. Decreasing the intermittent HD length and number of weekly sessions in stable hospitalized patients is another option (38,39). Additional challenges for CRRT include an underlying hypercoagulable state, which can cause increased circuit and filter clotting. Addition of systemic unfractionated heparin to regional citrate may be required, and argatroban has also been successfully used for anticoagulation (36,42,43). To minimize catheter length, vascular access using the right internal jugular vein is preferred, anchored firmly in place, and position checked after pronation. Ultrafiltration rate has to be carefully adjusted, taking into account hypotension, ARDS, and responsiveness to presser and ventilator support.

Renal Outcomes after AKI

Limited long-term data exist regarding AKI recovery versus continued dialysis dependence. One study, median

Figure 2. | **Special challenges and strategies for RRT delivery in patients with COVID-19.** Various challenges noted in the delivery of RRT and solutions that have been implemented and suggested are depicted. CRRT, continuous renal replacement therapy; SLD, sustained low efficiency dialysis; HD, hemodialysis; PPE, personal protective equipment; ICU, intensive care unit.

follow-up 12 days, reported an 18% recovery rate in patients with AKI by Kidney Disease Improving Global Outcomes criteria and 46% by expanded criteria (change in serum creatinine ≥0.3 mg/dl) (8). A multicenter US study of >3000 ICU patients reported that 63% of patients with AKI-RRT died, 34% were discharged, and 3% remained hospitalized at 17 days. Of those discharged, 34% remained RRT dependent at discharge, and 18% remained RRT dependent 60 days after ICU admission (30). More information is needed on long-term renal outcomes of patients with COVID-19.

Potential Mechanisms for AKI

Mechanisms for AKI are likely multifactorial, and usually include prerenal azotemia from intravascular volume depletion; ischemic acute tubular necrosis (ATN) from hypotension and shock; and acute interstitial nephritis from antibiotics, antivirals, and other medications (Figure 3) (19). Other mechanisms include a hypercoagulable state causing kidney ischemia (44). There is increasing evidence that much organ dysfunction is due to complement activation and cytokine release (45). Levels of IL-6 along with other inflammatory biomarkers are elevated, especially in patients with ARDS (46). The presence of SARS-CoV-2 in endomyocardial biopsies in patients with myocarditis or unexplained heart failure suggests SARS-CoV-2 can cause cardiomyopathy (47). Acute heart failure can result in type 1 cardio-renal syndrome (Figure 3).

In an autopsy series of 42 patients, ATN was the most predominant histologic finding (23). Evidence of glomerulosclerosis, myoglobin cast nephropathy, thrombotic microangiopathy, crescentic GN, cortical necrosis, and collapsing glomerulopathy were also reported. The latter was associated with presence of high-risk APOL1 genotype, suggesting that individuals with APOL1 risk alleles are at increased risk (48–52).

There is evidence that SARS-CoV-2 may exert direct cytopathic effects on kidney tissue, although data are not consistent. This is thought to be possible due to the binding of the virus to host angiotensin-converting enzyme 2, which is expressed in the kidney (53). In 26 postmortem patients from China, all revealing ATN, coronavirus-like particles were reported by electron microscopy (EM) in podocyte foot processes and the glomerular basement membrane. There was also immunofluorescent staining for anti–SARS-CoV nucleoprotein antibody in three of seven patients (54). In biopsy findings of six deceased individuals with AKI, SARS-CoV-2 nucleocapsid protein was found in the renal tubules of all. Virus-like particles were seen by EM in two (55). Postmortem findings in another 63 patients revealed detectable SARS-CoV-2 RNA in kidney tissue of 72% of those with AKI and 43% of those without AKI (56). These findings do bring up the possibility that the virus may be causing direct tubular damage (23,57). Another case series of 10 kidney biopsies reported that staining by immunohistochemistry for SARS-CoV-2 was negative in all patients with COVID-19 and tubular injury. These disparate results may be due to viral levels being below the detection threshold in the kidney or that virus-like particles seen on EM may be intracellular components that exhibit viral-like morphology (48).

CKD-Nondialysis

Limited data exist regarding COVID-19 infection and morbidity in patients with CKD-nondialysis (CKD-ND). The prevalence of CKD-ND among patients with COVID-19 varies from 3.5% to 48% in US cohorts (15–17,19–22,29–31). Higher rates were from smaller cohorts, whereas larger samples had a prevalence ranging from 5% to 20% (16,21,30,31). Cohorts

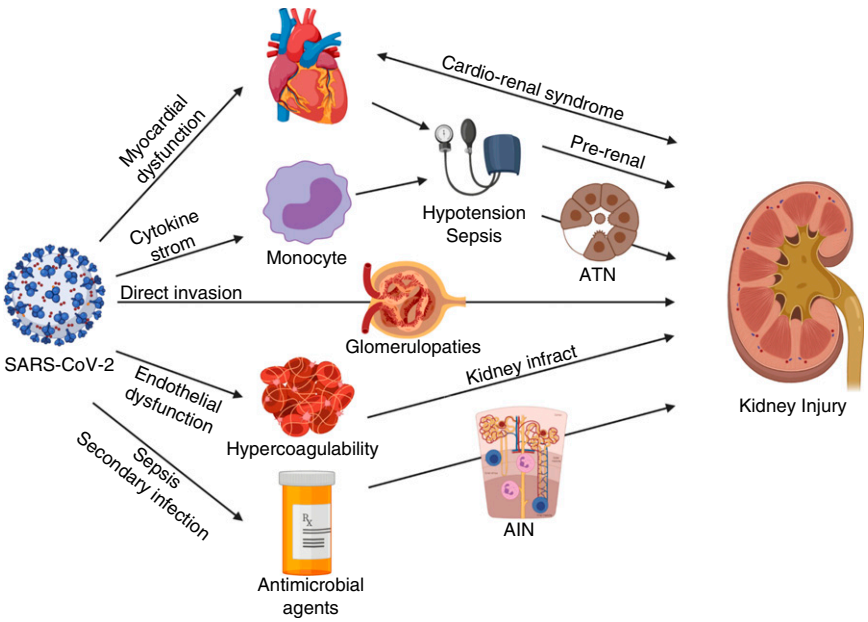

Figure 3. | **Potential mechanisms of COVID-19-related kidney injury.** Diagram showing possible mechanisms of kidney injury in the setting of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). ATN, acute tubular necrosis; AIN, acute interstitial nephritis. Figure developed with BioRender.

Table 1. Summary of studies on patients with ESKD with COVID-19

Study (Reference)	Patients, *n*	Sample	Dialysis Modality, *n* (%)	Black, *n* (%)	Hispanic, *n* (%)	Acute Respiratory Distress Syndrome / Mechanical Ventilation	Continuous Renal Replacement Therapy, *n* (%)	Death, *n* (%)	Geographic Location
Alberici *et al.* (70)	21	Hospitalized, COVID+	21 (100) HD	NA	NA	NA	NA	5 (24)	Italy
Corbett *et al.* (67)	1530	ESKD from one large center, 300 with COVID	290 (97) in-center HD 8 (2.7) PD 2 (0.7) home HD	75/300 (25)	NA	NA	NA	61/300 (20)	London
Fisher *et al.* (71)	114	Hospitalized, COVID+	114 (100) HD	56 (49)	45 (40)	19 (17)	2 (2)	32 (28)	New York
Flythe *et al.* (61)	143 ESKD 4121 non-ESKD	COVID+, in ICU Multicenter	128 (90) in-center HD 9 (6) PD 2 (1) home HD 4 (3) unknown	71 (50)	29 (20)	106 (74)[a]	NA	72 (50)[b]	United States
Goicoechea *et al.* (68)	36	ESKD hospitalized, COVID+	36 (100) HD	NA	NA	NA	0	11 (30.5)	Spain
Ng *et al.* (65)	419 ESKD, 10,063 non-ESKD	Hospitalized, ESKD and non-ESKD, all COVID+	408 (97) HD 11 (2.6) PD	152 (36) ESKD	87 (21)	89 (21)	NA	133 (31.7)	New York
Scarpioni *et al.* (72)	42	ESKD, COVD+	41 (98) HD 1 (2) PD	0	0	NA	NA	18 (41)	Italy
Valeri *et al.* (66)	59	Hospitalized, ESKD, all COVID+	57 (97) HD 2 (3) PD	15 (25)	44 (75)	NA	3 (5)	18 (31)	New York
Wu *et al.* (63)	49 on HD, 52 controls	Hospitalized, ESKD and non-ESKD, all COVID+	49 (100) HD	0	0	10 (20) ESKD 3 (6) controls	17 (35) ESKD	7 (14) ESKD 2 (4) controls	China
Xiong *et al.* (69)	131	ESKD, all COVID+	131 (100) HD	0	0	16/116 (13.8)	36 (28)	41 (31)	China
Yau *et al.* (73)	330	237 HD patients, 93 HD staff 22 COVID+	237 (100) HD	NA	NA	0	NA	0	Toronto

Of studies that reported data on ESKD and non-ESKD, only values for patients with ESKD are included. HD, hemodialysis; PD, peritoneal dialysis.
[a]On d 14.
[b]At d 28.

from China, however, reported lower rates of pre-existing CKD-ND, 0.7% to 4.3% (Figure 1B) (3–5,7,9–14,24,26).

One Chinese meta-analysis of four studies ($N=1389$) found an association between CKD-ND and more severe COVID-19 disease (58). Other meta-analyses showed that CKD was associated with an increased risk of mortality in patients hospitalized with COVID-19, although it is not clear whether models were adjusted for hypertension or diabetes mellitus (59,60). A large, multi-center US study of patients in the ICU with COVID-19 also revealed that patients with pre-existing CKD-ND versus without had a higher risk of in-hospital mortality (61). Although more data are needed to confirm findings, it is important to educate patients with CKD about proper precautions to decrease risk.

ESKD

Epidemiology and Outcomes

The COVID-19 outbreak brings up increased concern for ESKD patients who are intrinsically immunocompromised and have underlying comorbidities (62). Those who receive outpatient in-center HD are in close contact with other patients and staff multiple times a week, putting them at even greater risk. Clinical presentation is atypical when compared with patients not on dialysis, with patients with ESKD presenting without typical symptoms of cough and fever but instead, fatigue and anorexia (63,64). Risk of in-hospital death is significantly higher among patients with ESKD as compared with patients without ESKD, with older age and need for mechanical ventilation increasing risk (63,65,66) (Table 1). Most early reports of mortality came from small cohorts, where mortality ranged from 14% to 30% (66–69). A more recent larger cohort reported mortality of 31.7% in patients with ESKD as compared with 25.4% in patients without ESKD (65).

Management of Outpatient Dialysis

How to best handle outpatient dialysis becomes imperative due to the propensity of COVID-19 to cause cluster outbreaks. A study from London reported cluster outbreaks at specific centers within their network (67). This and other reports illustrated a need for HD center protocols to limit transmission, and subsequently, several opinion-based editorials were published. As Wuhan saw an increase in cases in patients on dialysis and staff, preventative measures, including limiting in-person provider rounds, limiting number of patients on individual shifts, temperature and symptom checks at entry, and increased PPE utilization, were implemented. COVID-19–positive dialysis shifts were set up in designated hospitals where large numbers of patients on dialysis with the infection were treated centrally (74). If this was not feasible, then separate COVID-19–positive dialysis shifts were recommended, preferably utilizing the day's last shift (75–77). Cohort isolation for in-center HD, screening protocols, and adequate PPE are agreed upon by many nephrologists (75,77,78). The US Centers for Disease Control has provided guidance and commented on when to transition patients who are infected to outpatient dialysis units after recovery (79). No clear correlation was found between length of illness and postrecovery shedding of virus in patients on dialysis, but recent data suggest the replication-competent virus likelihood approaches zero by 10 days of symptoms in the general population (80). Currently, the strategy for transitioning patients to outpatient dialysis is either test based, requiring two negative tests >24 hours apart and being symptom free; or, if testing is not available, fever free for ≥72 hours and ≥14 days since symptom onset (81).

Management of Inpatient Dialysis

In anticipation of increased numbers of affected patients on dialysis requiring hospitalization, there was concern for limited resources, for example, dialysis machines, filters, and solutions, and decreased number of available staff due to illness or quarantine. Hospital admissions will include both patients infected with COVID-19 and with AKI and patients on maintenance dialysis requiring RRT. Similar strategies were proposed to what was discussed regarding AKI, including decreasing number of weekly dialysis sessions and shortening treatments. Given mandates to defer elective nonurgent surgeries, some centers were having issues with patients not being scheduled for procedures to place or repair vascular access. This prompted the Centers for Medicare and Medicaid Services to release a statement iterating that procedures to establish dialysis access were essential and should be treated as such (82). Transitioning patients from in-center HD to home dialysis modalities, such as home HD or PD, can also be considered (Figure 3) (64).

Kidney Transplantation

Epidemiology and Outcomes

It would be logical to assume kidney transplantation recipients are at increased risk for contracting COVID-19 and having more severe disease on the basis of their immunocompromised state and common comorbidities of hypertension and diabetes. However, current evidence on the basis of several case series is unclear. Presentation of COVID-19 in transplant recipients appears to be similar to that in patients who are not immunosuppressed, with typical symptoms being cough, fever, and shortness of breath (Table 2) (39,83–85). One study of 36 patients reported a mortality rate of 28%, substantially higher than that in the general population (86). Similarly, Alberici *et al.* (87) described a 25% mortality rate among 20 transplant recipients, and Nair *et al.* a rate of 30% in 10 (39). Both groups also found an increased rate of clinical deterioration. Given small sample sizes, it is difficult to conclude whether kidney transplant recipients are at an increased risk of death from COVID-19.

Immunosuppression Management in Transplant Recipients

Although there are no standardized guidelines regarding the management of immunosuppression in patients with COVID-19, several groups recommended stopping antimetabolites in hospitalized patients, following the thought process that T-cell immunity is likely important for fighting the virus (39,83,86,90). However, there is also concern that the release of cytokines is responsible for many of the severe manifestations of COVID-19, including ARDS (83). Some form of immunosuppression could, therefore, be of benefit. In addition, new data support using corticosteroids in

Table 2. Summary of studies reporting AKI and outcomes in patients with COVID-19

Study (Reference)	Patients, *n*	Sample	Black, *n* (%)	Hispanic, *n* (%)	CKD, *n* (%)	AKI, *n* (%)	AKI-RRT, *n* (%)	Mortality, *n* (%)	Geographic Location
Chen *et al.* (24)	113 deceased and 161 recovered	Hospitalized	0	0	4 (1)	28 (25) versus 1 (1)	3 (1)	113 (41.2)	China
Cheng *et al.* (3)	701	Hospitalized	0	0	14 (2)	36 (5.1)	NA	113 (16.1)	China
Deng *et al.* (25)	109 deceased and 116 recovered	Hospitalized	0	0	NA	20 (18.3) versus 0	NA	109 (49)	China
Guan *et al.* (4)	1099	Hospitalized and outpatients	0	0	8 (0.7)	6 (0.5)	NA	15 (1.4)	China
Guo *et al.* (5)	187	Hospitalized	0	0	6 (3.2)	18 (14.6)	NA	43 (23)	China
Huang *et al.* (6)	41	Hospitalized	0	0	NA	3 (7)	3 (7)	6 (15)	China
Lei *et al.* (7)	34	Underwent elective surgery before diagnosis	0	0	1 (2.9)	2 (5.9)	1 (2.9)	7 (20.6)	China
Pei *et al.* (8)	333	Hospitalized	0	0	0	35 (10.5)	NA	29 (8.7)	China
Shi *et al.* (9)	416	Hospitalized	0	0	14 (3.4)	8 (1.9)	2 (0.5)	57 (13.7)	China
Wang *et al.* (26)	107	Hospitalized	0	0	3 (2.8)	14 (13.1)	NA	19 (17.7)	China
Wang *et al.* (10)	138	Hospitalized	0	0	4 (2.9)	5 (3.6)	2 (1.45%)	6 (4.3)	China
Wang *et al.* (2)	116	Hospitalized	0	0	5 (4.3)	0 (0)	0 (0)	7 (6)	China
Xu *et al.* (27)	239	ICU	0	0	NA	119 (50)	12 (5)	147 (61.5)	China
Yang *et al.* (28)	52	ICU	0	0	NA	15 (29)	9 (17)	32 (51.5)	China
Zhang *et al.* (11)	221	Hospitalized	0	0	6 (2.7)	10 (4.5)	5 (2.3)	12 (5.4)	China
Zhang *et al.* (12)	140	Hospitalized	0	0	2 (1.4)	NA	NA	NA	China
Zhang *et al.* (13)	645	Hospitalized	0	0	6 (0.9)	2 (0.3)	0	NA	China
Zhou *et al.* (14)	191	Hospitalized	0	0	2 (1)	27 (14)	10 (5)	54 (28.3)	China
Aggarwal *et al.* (15)	16	Hospitalized	0	0	6 (38)	11 (69)	NA	3 (19)	Iowa
Arentz *et al.* (29)	21	ICU	NA	NA	10 (47.6)	4 (19.1)	NA	11 (52.4)	Washington State
Argenziano *et al.* (16)	1000 (850 hospitalized)	ED or hospitalized	181 (18.1)	248 (24.8)	137 (13.7)	288/850 (33.9)	117/850 (13.8)	211 (21.1)	New York
Fisher *et al.* (17)	3345	Hospitalized	1201 (35.9)	1247 (37.3)	409 (12.2)	1903 (56.9)	164 (4.9)	775 (23.2)	New York
Gupta *et al.* (30)	3099	ICU	952 (30.7)	1045 (33.7)	897 (28.9)	1685 (54.4%)	637 (20.6)	350/637 (54.9) of AKI-RRT	United States, multicenter
Hirsch *et al.* (18)	5449	Hospitalized	1123 (20.6)	1145 (21)	NA	1993 (36.6)	285 (5.2)	888 (16.3)	New York
Imam *et al.* (31)	1305	Hospitalized	862 (66.1)	NA	228 (17.5)	76 (5.85)[a]	NA	200 (15.3)	Michigan
Mohamed *et al.* (19)	575	Hospitalized	414 (72)	9 (1.57)	172 (29.9)	161 (28)	89 (15.5)	80/161 (50) (AKI cohort)	New Orleans, Louisiana
Pelayo *et al.* (20)	223	Hospitalized	152 (68)	14 (6)	39 (17)	110 (49)	9 (4)	44 (19)	Philadelphia, Pennsylvania
Price-Haywood *et al.* (21)	3481	Hospitalized and outpatient	2451 (70.4)	0	278 (8)	197 (14.25)[b]	NA	326 (23.6)[b]	Louisiana
Richardson *et al.* (22)	5700 total, 2634 discharged or died	Hospitalized	1230 (23)	1230 (23)	186 (3.5)	523/2634 (20)	81/2634 (3.2)	553/2634 (21)	New York
Grasselli *et al.* (88)	1591	ICU	NA	NA	36 (3)	NA	NA	405 (26)	Italy
Lim *et al.* (89)	164	Hospitalized	0	0	Excluded	30 (18.3)	5 (3)	44 (164)	South Korea
Kidney transplant recipients									
Akalin *et al.* (86)	36	Confirmed COVID	14 (39)	15 (42)	NA	NA	6 (21)	10 (28)	New York

Table 2. (Continued)

Study (Reference)	Patients, *n*	Sample	Black, *n* (%)	Hispanic, *n* (%)	CKD, *n* (%)	AKI, *n* (%)	AKI-RRT, *n* (%)	Mortality, *n* (%)	Geographic Location
Alberici *et al.* (87)	20	Hospitalized, confirmed COVID	NA	NA	NA	6 (30)	1 (5)	5 (25)	Italy
Banerjee *et al.* (90)	7	Confirmed COVID	NA	NA	NA	NA	NA	1 (14)	London
Columbia transplant program (85)	15	Confirmed COVID	NA	NA	NA	6 (40)	2 (13)	2 (13)	New York
Husain *et al.* (84)	41	Confirmed or suspected COVID	NA	NA	NA	NA	NA	0	New York
Maritati *et al.* (91)	5	Hospitalized, confirmed COVID	NA	NA	NA	1 (20)	0	2 (60)	Italy
Nair *et al.* (39)	10	Confirmed COVID	3 (30)	NA	NA	5 (50)	NA	3 (30)	New York

Note that references 18,22 come from the same institution and the cohorts overlap. ICU, intensive care unit; ED, emergency department.
[a]Only looked at first 48 h.
[b]Hospitalized only.

patients who are ventilated or have increased oxygen requirements (92). Many transplant centers have practiced continuing corticosteroids and, in some patients, increasing the dose and continuing a reduced dose of calcineurin inhibitors (unless the patient is severely ill) (39,86,90). One study of 40 patients hospitalized with COVID-19 from multiple sites reported the majority were maintained on corticosteroids alone (93). Overall, it is agreed that the specific clinical scenario should guide immunosuppression, including any recent treatments for rejection, which would result in further decline in immunity. Of note, patients in many of these early case series were treated with hydroxychloroquine and azithromycin, which are no longer being recommended. More contemporary data with larger numbers are needed to determine outcomes of patients treated with other agents, including remdesivir, IL-6 inhibitors, and convalescent plasma.

As the pandemic continues, it is important to know how to manage those patients who may not need hospitalization. The transplant nephrology group at Columbia evaluated outpatients with known or suspected COVID-19, and of 41 patients, 32% required hospitalization, the remaining managed as outpatients. After a median follow-up of 12 days, 23 of 41 had resolution of symptoms. However, due to lack of testing availability at the time, not all patients were tested to confirm COVID-19 (84). The ideal outpatient management has not yet been determined, as very limited follow-up data exist on kidney transplant recipients, in particular, and patients recovering from COVID-19 in general. More information is also needed to determine the optimal timing for the reintroduction of immunosuppressants.

Performance of New Transplantations

Most transplant centers limited or temporarily stopped performing kidney transplantations during the pandemic, due risk of transmission to donors with health care contact and recipients who would be immunosuppressed. One report noted that the rate of US deceased-donor kidney transplants decreased by 50% (64). Alternatively, transplantation could mean no further need for in-center dialysis, which would reduce risk. In a recent statement, Centers for Medicare and Medicaid Services reiterated that organ transplantation is an essential procedure (82). The availability of resources is also a consideration (94). There needs to be a balance between the benefit of transplantation for individual patients and risks of nosocomial COVID-19 spread and resource utilization. Massie developed a tool using machine learning to determine the benefit versus harm of kidney transplantation and found that, in 72% of simulated scenarios, immediate transplantation provided a survival benefit to deferring transplantation and remaining on the wait list (95). This tool may be used by transplant centers to individualize transplantation decisions.

GN

Initiating or continuing immunosuppression in patients with glomerular disease is also concerning in this pandemic. There are no evidence-based recommendations, and there is very little information regarding the prevalence of COVID-19 or outcomes of patients who are infected. One group in Italy prospectively evaluated patients with nephrotic syndrome on chronic therapy with anti-CD20 antibodies, the majority of which were pediatric patients. In total, 34% were also being treated with other immunosuppressants (corticosteroids, calcineurin inhibitors, and antimetabolites). All patients had received treatment with B-cell–depleting therapy, with a median time since last treatment of 18 months. At follow-up, none developed signs of COVID-19. Six were living with an individual who was found to be COVID-19 positive. On the basis of these observations, the authors recommended not to pre-emptively alter the immunosuppression regimen in children with nephrotic syndrome, regardless of possible COVID-19 exposure (96).

To strike a balance between COVID-19 complications and kidney outcomes, the glomerular disease group at Columbia proposed recommendations on the basis of their experience in a COVID-19 hotspot (97). Initiate standard-of-care for patients with rapidly progressing glomerular disease and severe nephrotic syndrome who have decreased kidney function and/or complications of nephrotic syndrome. Defer treatment for patients who do not meet these criteria but would typically be started on immunosuppression. For those who had begun treatment before the pandemic onset, the decision to continue treatment would be made on a case-by-case basis, weighing risks and benefits. For patients started on intravenous protocols, switch to oral regimens to decrease health care visits. Consider home infusions when no equivalent oral regimen exists. For patients in remission on maintenance regimen, stop antimetabolites and avoid maintenance B-cell–depleting infusions. Tapering and discontinuing corticosteroids has also been suggested for stable patients, whereas calcineurin inhibitors are continued on the basis of experience in the transplant community. Immunosuppression adjustments for patients with confirmed COVID-19 should be on the basis of specific clinical scenarios. Other strategies to decrease exposure include limiting kidney biopsies to only those necessary for critical decision making, using home urine dipsticks versus those done at a laboratory, and utilizing telemedicine (97).

Discussion

The effect of the COVID-19 pandemic has been felt in all facets of kidney disease management. There is still much to be learned, including the long-term kidney outcomes in patients with COVID-19–related AKI. The best strategies for managing immunosuppression in kidney transplant recipients and patients with GN are unknown. Similarly, strategies on how to best manage patients with ESKD receiving outpatient in-center dialysis or patients hospitalized with COVID-19 and ESKD or AKI requiring RRT are anecdotal. As new experiences and data become available, it becomes paramount to continue sharing and publication of evidence, and to be hypervigilant in adjusting our practice to provide the best clinical care.

Disclosures

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Author Contributions

M. McAdams was responsible for the investigation, wrote the original draft, and reviewed and edited the manuscript; M. Ostrosky-Frid was responsible for the investigation, and wrote the original draft; N. Rajora wrote the original draft, and reviewed and edited the manuscript; and S. Hedayati was responsible for the conceptualization, investigation, methodology, resources, supervision, and validation, wrote the original draft, and reviewed and edited the manuscript.

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