Perspective

# COVID-19 disease: a nephrologist's perspective

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Novel Coronavirus disease (COVID-19) is a newly discovered contagious disease caused by severe acute respiratory syndrome (SARS)coronavirus (CoV)-2 virus. The outbreak, which first emerged in Wuhan, Hubei Province, China, in December 2019, has been declared as a global pandemic since March 11, 2020. The disease has affected 18.4 million people globally with 7,01000 deaths till August 6, 2020.

The disease spreads by human-to-human transmission via droplets, or direct contact, and has an incubation period estimated at 1 to 14 days (usually 3 to 7 days). An infection has been reported in all ages, including children**.** It manifests primarily as an acute respiratory illness with interstitial and alveolar pneumonia, but it can affect multiple organs such as the kidney, heart, digestive tract, blood, and nervous system.

Kidney involvement has been recognized as a serious complication of COVID -19 infection. Coronavirus enters into the cells via ACE2 (angiotensin-converting enzyme II) receptors. ACE2 receptors are 100-fold more abundant in kidneys than that in the pulmonary tract. This finding explains that the renal cells are *targeted* and *infected* by the COVID-19. SARS-CoV-2 binds to renal epithelial cells, injure these cells, and subsequently disrupt whole-body fluid, acid-base, and electrolyte homeostasis. By injuring kidney epithelial cells, SARS-CoV-2 also disrupts kidney endocrine production of erythropoietin and vitamin D and impairs blood pressure regulation. Viral entry into renal epithelial cells suggests the possibility that the kidney could also become a viral reservoir once clearance occurs elsewhere and that urine could be an infectious factor. Cheng et al[1] reported that amongst 710 consecutive hospitalized patients with COVID-19, 44% had proteinuria and hematuria and 26.7% had hematuria on admission.

**AKI and COVID-19.**

Early reports from China and Italy found the rate of AKI to range widely from 0.5% to 29%.[2-8]. A recent study by Jamie S. Hirsch et al[9] showed that of 5,449 patients admitted with Covid-19, AKI developed in 1,993 (36.6%). 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 (35%) died, AKI occurs early and in temporal association with respiratory failure. There are numerous potential mechanisms underlying COVID-19 associated AKI. These include the complex interplay of ischemia, hypoxia, sepsis-associated factors, cytokine storm, toxin exposure, hypercoagulability, microangiopathy; with or without overt fibrin thrombus formation, cortical infarction, and virus-induced direct

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cytopathic effects. An autopsy series from China described features of acute tubular injury (ATI) in all 26 (100%) decedents[10]. Other relevant findings included congestion of glomeruli and peritubular capillaries and interstitial inflammation confined to areas of interstitial fibrosis. Glomerular fibrin thrombi, pigmented casts, and ultrastructural evidence of endothelial injury was very rarely seen. Evidence of kidney tropism, including detection of viral RNA and putative virions, has raised concern that direct infection by SAR-CoV-2 could also contribute to kidney injury.[10,11] Reports of COVID-19 associated collapsing FSGS in Blacks (COVAN) suggest that heightened cytokine release associated with COVID-19 infection may place patients with high-risk APOL1 genotypes at increased risk of severe kidney disease[12,13].

**COVID-19 in the dialysis population.**

Strategies to minimize the risk of transmission and acquisition of COVID-19 infection in patients with ESKD receiving in-center hemodialysis has been rapidly implemented across the globe. Despite these measures, acute SARS-CoV-2 infection rates confirmed by RT-PCR testing have been high. Candice Clarke et al [14] conducted a study on 356 in-center hemodialysis patients, 121 had been symptomatic when screened before a dialysis session and received an RT-PCR test; 79 (22.2% of the total study population) tested positive for COVID-19. Serologic testing of all 356 patients found 129 (36.2%) who tested positive for SARS-CoV-2 antibodies. Of the 129 patients with SARS-CoV-2 antibodies, 52 (40.3%) had an asymptomatic disease or undetected disease by PCR testing alone. This highlights the high seroprevalence of SARS-CoV-2 antibodies in patients receiving in-center hemodialysis. Serologic evidence of previous infection in asymptomatic or PCR-negative patients suggests that current diagnostic screening strategies may be limited in their ability to detect acute infection and more strict precautions would need to be taken to decrease transmission. Steps are being taken to encourage home hemodialysis and CAPD.

**COVID-19 and Kidney transplant**

Transplant recipients are expected to be at higher risk for severe bacterial and viral infections. This would suggest that transplant recipients are at higher risk for infection and mortality from COVID-19. There have, however, been very few reports published on COVID-19 in transplant recipients. Vinay Nair et al (15) reported a case series of 10 post kidney transplant patients with rt PCR proven COVID -19 infection. The most common symptom was fever, followed by cough, myalgia, chills, and fatigue. The most common chest X-ray and computed tomography abnormality was multifocal patchy opacities. 9 out of 10 patients required hospitalization. Antimetabolite was stopped in all hospitalized patients. Three patients died (30%), and 5 (50%) developed acute graft dysfunction. Kidney transplant recipients infected with COVID-19 should be monitored closely in the setting of lowered immunosuppression. The clinical manifestations don't seem to be different from the general population however given immunocompromised status worse outcomes in the form of graft loss and death are more likely.

To conclude, renal involvement is common in COVID -19 infection and can manifest in the form of asymptomatic urinary abnormalities to severe dialysis requiring renal failure. The presence of mild acute tubular injury on renal histopathological specimens, out of proportion to the severity of renal failure suggests a role of hemodynamic factors as a putative reason for severe renal failure throwing a ray of hope for possible renal recovery after the resolution of COVID -19 infection. Asymptomatic infection is high in the dialysis population and more strict measures need to be taken to contain the infection.

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