

COVID-19 in Patients with Kidney Disease

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CJASN 15: 1087–1089, 2020. doi: <https://doi.org/10.2215/CJN.09730620>

SARS-CoV-2, the virus that causes coronavirus disease 19 (COVID-19), has caused a major global pandemic with over 8 million infections worldwide and over 430,000 deaths as of mid-June 2020. Kidney disease is a common chronic disease. The patients with kidney disease who appear most at risk for COVID-19 are those with a kidney transplant, due to immunosuppression, and those who undergo in-center hemodialysis treatments thrice weekly, due to inability to self-isolate. Patients with kidney disease also have other comorbidities, including hypertension, diabetes mellitus, and cardiovascular disease, that are risk factors for poor outcomes in COVID-19. Two reports in *CJASN* examine these high-risk populations, patients requiring dialysis and kidney transplant recipients, in the setting of COVID-19 (1,2). Although these reports are small, they should help to guide clinical nephrologists to several concrete steps to prepare for our collective “new normal” in caring for our high-risk patients in the setting of a global pandemic.

Wu *et al.* (2) described the clinical presentation of 49 hospitalized patients on dialysis in Wuhan, China, and they had less fever (47% versus 90%) and dry cough (49% versus 71%) and more lymphopenia compared with the general population control group. In patients with kidney failure, the disease course was generally more severe than in the general population. The percentage of abnormalities in bilateral lung fields was higher on computed tomography scan (82% versus 69%; $P=0.15$) and unilateral lung was lower (10% versus 27%; $P=0.03$) when compared with the control group (2). Compared with controls, more patients on hemodialysis received noninvasive ventilation (25% versus 6%; $P=0.008$) and had a higher rate of common complications, including shock, acute respiratory distress syndrome, arrhythmia, and acute cardiac injury. The authors concluded that patients on hemodialysis with COVID-19 were at a higher risk of death (14% versus 4%) (2).

These findings highlight the importance of atypical clinical presentations in patients on dialysis, such as the lack of fever and cough, also found in previous studies (3). The main presenting symptoms were fatigue (in 59%) and anorexia (in 57%) (2), which are also uremic symptoms, making the diagnosis difficult and suggesting the need for a more systematic screening approach and the need for universal respiratory precautions. This was a single-center study, and the sample size was relatively small, limiting the ability to perform

multivariable adjustment in statistical modeling. Notwithstanding the limitations, the work by Wu *et al.* (2) has important implications for clinical nephrologists, revealing different presenting symptoms and a higher mortality compared with the general population.

Husain *et al.* (1) described the outcomes of 41 outpatient kidney transplant recipients with known (54%) or suspected (46%) COVID-19. In this cohort, patients most commonly reported fever (80%), cough (56%), and dyspnea (39%). At the end of follow-up, 13 patients (32%) required hospitalization. Patients who required hospitalization were more likely to have reported dyspnea (77% versus 21%; $P=0.003$) and had higher baseline creatinine (median of 2.0 versus 1.3 mg/dl; $P=0.02$). A total of 23 patients (56%) had a reduction in their immunosuppression regimen (including 42% of suspected and 82% of patients with confirmed cases; $P=0.008$), whereas the remaining 18 (44%) had no change. The authors highlight the importance of dyspnea and hypoxia as the main reason for hospital admission. These results should be interpreted with caution given the lack of testing in 46% of patients, short follow-up, 12% of patients with ongoing illness, lack of inflammatory biomarkers, and no mortality data. Nevertheless, it outlines a practical approach on how to manage kidney transplant recipients with COVID-19 as outpatients.

In a separate study, Akalin *et al.* (4) identified 36 consecutive adult kidney transplant recipients who tested positive for COVID-19. The most common initial symptom was fever (58%); 22% who were in stable condition without major respiratory symptoms were monitored at home, and 78% were admitted to the hospital. The vast majority (96%) of hospitalized patients had radiographic findings that were consistent with viral pneumonia, and 39% received mechanical ventilation. Six patients (21%) required KRT with dialysis; ten of the 36 kidney transplant recipients (28%) and seven of the 11 patients who were intubated (64%) died. Two of the eight patients who were monitored as outpatients died at home. Antimetabolite was withheld in 86% of patients, and tacrolimus was stopped in 21% of severely ill patients (4). However, the approach of immunosuppression withdrawal and anti-inflammatory combination of drugs was still associated with significant mortality. By contrast, the series from Husain *et al.* (1), with gentle immunosuppression reduction and no anti-inflammatory drugs, did not report mortality in patients managed outside the hospital.

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Lessons for the practicing nephrologists include the need to implement and strictly follow new infection control measures, including screening of body temperature and symptoms before entering dialysis or transplant clinics, universal masking, physical distancing and frequent hand hygiene within clinics, and, if possible, universal rapid testing for SARS-CoV-2 infection upon entry to clinics. Because the presentation of COVID-19 in patients on dialysis and kidney transplant recipients is often atypical (with fewer presenting with fever or respiratory symptoms), it is even more important in this population to rapidly screen for SARS-CoV-2 infection and practice universal respiratory precautions. Nephrologists, especially medical directors in dialysis units and in hospitals, should prepare for the logistical challenges that may be presented by another surge of infections (*e.g.*, identifying a room dedicated for isolated patients awaiting the SARS-CoV-2 nucleic acid test results, having locations for donning and doffing personal protective equipment, ensuring that adequate dialysis supplies are available, and planning for onsite and offsite locations where patients can be safely dialyzed and where patients with COVID-19 can be dialyzed separately to prevent further transmission).

Transplant nephrologists are faced with the challenge of resuming transplantation because the rate of deceased transplant decreased by 50% across the United States during this pandemic. Balancing the unforeseeable consequences of common immunosuppressive induction regimens and the benefit of kidney transplant, most centers are limiting kidney transplants (live and deceased donor) to patients with low immunologic risk who do not require antithymoglobulin or alemtuzumab induction regimens and have low cardiovascular risk. There is an absence of consensus about how immunosuppression should be adjusted in COVID-19 kidney transplant recipients. In the current situation, the practice is that patients on the transplant waiting list need to sign a form stating that they are aware of the potential risks associated with transplantation during the COVID-19 pandemic.

Other important actions that can be taken now are shared decision-making discussions with patients about choices of modality selection and end-of-life care. Because thrice weekly in-center hemodialysis, the predominant treatment modality in the United States, places patients at risk of contracting COVID-19 by not allowing self-isolation, it is worth discussing home dialysis modalities with patients. Because SARS-CoV-2 and the global pandemic will likely be our “new normal” until an effective vaccine is created, switching to home dialysis modalities may help save lives. This, of course, needs to be a shared decision between the patient and the physician. In addition to discussing possible modality changes, it is a good time to discuss goals of care and code status with patients. Reports of 28% mortality in kidney transplant recipients (4) and 14% mortality in patients receiving dialysis in Wuhan (2) should spur patients, physicians, and families to have these important discussions before patients get sick.

Most patients with COVID-19 become sicker during the second week of symptoms, underscoring the need for increased vigilance of continued close outpatient follow-up

for the early detection of clinical deterioration. In the report by Husain *et al.* (1), patients were followed up by phone or televisit “every 6, 24, or 48 hours depending on the severity of symptoms.” Home monitoring may play a crucial role in dealing with COVID-19 disease because it can keep patients out of overwhelmed hospitals and facilitates decreasing contact and, therefore, transmission of the virus. Patients at home need appropriate monitoring equipment, potentially including a thermometer, a pulse oximeter, a home BP machine, and a glucometer for patients with diabetes. This is a new level of outpatient care. The health care system needs to ascertain a source of funding for monitoring equipment and appropriate reimbursement for providers monitoring patients with COVID-19 at home. Research is urgently needed to identify patients who can safely be monitored at home. In the study by Husain *et al.* (1), only 32% of the outpatients required admission to the hospital. Thus, appropriate and safe outpatient monitoring of these high-risk patients will be needed and should be planned for by nephrologists and the health care system.

As a nephrology community, we know that optimal COVID-19 disease management is still being debated, and the therapeutic approach still lacks significant evidence. No clear guidelines exist for the management of patients with COVID-19 in general and for patients on hemodialysis and kidney transplant recipients in particular. As time passes, a treatment protocol on the basis of patient characteristics, phase of illness, and disease severity using antivirals, anticoagulation, immunomodulators, and immunosuppressive agents will be formulated. However, there are concrete steps that the nephrology community can take immediately to optimize the safety of our patients and ourselves.

Acknowledgments

We would like to dedicate this work to Dr. Priya Khanna and other nephrologists and dialysis staff members who have lost their lives to COVID-19.

The content of this article reflects the personal experience and views of the authors and should not be considered medical advice or recommendation. The content does not reflect the views or opinions of the American Society of Nephrology (ASN) or *CJASN*. Responsibility for the information and views expressed herein lies entirely with the authors.

Disclosures

M.L. Melamed reports receiving personal fees from the American Board of Internal Medicine and Icon Medical Consulting outside the submitted work. All remaining authors have nothing to disclose.

Funding

None.

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- Published online ahead of print. Publication date available at www.cjasn.org.
- See related articles, “Clinical Features of Maintenance Hemodialysis Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China,” and “Early Outcomes of Outpatient Management of Kidney Transplant Recipients with Coronavirus Disease 2019,” on pages 1139–1145 and 1174–1178, respectively.